The effect of micronutrient supplementation on growth and hepatic metabolism in diploid and triploid Atlantic salmon (*Salmo salar*) parr fed a low marine ingredient diet

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Abstract

The effects of low marine ingredient diets supplemented with graded levels (L1, L2, L3) of a micronutrient package (NP) on growth and metabolic responses were studied in diploid and triploid salmon parr. Diploids fed L2 showed significantly improved growth and reduced liver, hepatic steatosis, and viscerosomatic indices, while fish fed L3 showed suppressed growth rate 14 weeks post feeding. In contrast, dietary NP level had no effect on triploid performance. Whole body mineral composition, with exception of copper, did not differ between diet or ploidy. Whole fish total AAs and N-metabolites showed no variation by diet or ploidy. Free circulating AAs and white muscle N-metabolites were higher in triploids than diploids, while branch-chained amino acids were higher in diploids than triploids. Diploids had higher whole body α-tocopherol and hepatic vitamins K_1 and K_2 than triploids. Increased tissue B-vitamins for niacin and whole-body folate with dietary NP supplementation were observed in diploids but not triploids, while whole body riboflavin was higher in diploids than triploids. Hepatic transcriptome profiles showed that diploids fed diet L2 was more similar to that observed in triploids fed diet L3. In particular, sterol biosynthesis pathways were down-regulated, whereas cytochrome P450 metabolism was up-regulated. One-carbon metabolism was also affected by increasing levels of supplementation in both ploidies. Collectively, results suggested that, for optimised growth and liver function, micronutrient levels be supplemented above current National Research Council (2011) recommendations for Atlantic salmon when fed low marine ingredient diets. The study also suggested differences in nutritional requirements between ploidy.

Keywords: Atlantic salmon; micronutrient; vegetable; ingredients; nutrition

1. Introduction

All animals, including fish, have specific macro- and micronutrient requirements for optimal growth, development and health (Halver and Hardy, 2002). Whereas macro-nutrient requirements (e.g. protein and lipid) have been extensively studied in Atlantic salmon (*Salmo salar* L.) (e.g. Hillestad and Johnsen, 1994; Einen and Roem, 1997; Grisdale-Helland et al., 2013), micronutrients (e.g. vitamins and minerals) have been less well researched and only a few have been the subject of empirical studies (see Waagbø, 2010; NRC, 2011; Hansen et al., 2015; Hamre, et al., 2016; Hemre, et al., 2016). This lack of empirically derived data in salmon for many micronutrients has not prevented the development of a large and highly successful salmon farming industry worldwide (Kontali, 2015). Traditionally, many of the micronutrients were provided by raw materials, such as fishmeal (FM) and fish oil (FO) (NRC, 2011). However, FM and FO are finite, on an annual basis, and limited resources (Shepherd and Jackson, 2013; IFFO, 2014) and, with steadily increasing price, their use in fish feed has become commercially less viable (Tacon and Metian, 2008; Jackson and Shepherd, 2012).

Plant products have increasingly replaced FM and FO in salmon feeds (Gatlin et al., 2007; Hardy et al., 2010; Turchini et al., 2011). For example, in Norwegian salmon feeds from 1990 to 2013, the proportions of marine ingredients decreased from almost 90 % to under 30 %, with plant ingredients increasing from very low levels to around 67 % of feeds (Ytrestøyl et al., 2015). This has been a progressive change as shown by the levels in 2000 (65 % marine and 33 % plant) and 2010 (42 % marine and 56 % plant). Therefore today, commercially available feeds for salmon are predominantly formulated with plant ingredients, with consequent changes to the nutritional profile (Sissener et al., 2013). While it seems that salmon can tolerate and grow well on diets with very low levels of marine ingredients, such that they can be considered as net producers of marine protein and oil (Bendiksen et al., 2011; Crampton et al., 2010; Sanden et al., 2011), in some cases high dietary levels of plant proteins and vegetable oils (VO) can result in lower weight gain, increased adiposity and lower feed efficiency in salmon, even when requirements for all essential nutrients are met (Torstensen et al., 2008, 2011; Collins et al., 2013). Furthermore, replacement of FM and FO with plant-based alternatives has been shown to have a wide range of metabolic effects that can also impact on fish development and health, as well as nutritional quality of the final product (Montero and Izquierdo, 2011; Rosenlund et al., 2011; Oliva-Teles, 2012; Pohlenz and Gatlin, 2014). There are now concerns that, with these major changes in raw materials, low marine / high plant feeds will affect not only the composition and contents of nutrients, but also the bioavailability and, combined with the limited knowledge of micronutrient requirements for Atlantic salmon, this might impact growth performance and health of the fish (Bell and Waagbø, 2008; Hemre et al., 2009; Torstensen and Tocher, 2011; Tocher and Glencross, 2015; Shepherd et al., 2017). Therefore, knowledge of practical nutrient requirements of Atlantic salmon when fed plant-based diets is pivotal (Hansen et al., 2015).

In this respect, there is growing interest within the Scottish and Norwegian farming sector to consider commercial implementation of triploid Atlantic salmon within certain farming localities. Triploid salmons are fish carrying a chromosomal abnormality (i.e. an extra set of chromosomes) that can be artificially induced by hydrostatic pressure, thermal or chemical shock (Benfey, 2016). As a result of their chromosomal state, triploids are sterile, hence offering potential advantages for farming such as reproductive containment of escapees and potential for faster growth with subsequent reduction of production cycle length (Benfey, 2016). However, specific dietary requirement trials in triploids are limited to date, although it was previously suggested that differences between ploidy might exist (Fjelldal & Hansen, 2010). Apparent digestibility coefficients for dry matter, protein, or lipid do not appear to differ between ploidy (Burke et al., 2010; Tibbetts et al., 2013), whereas energy and nitrogen retention efficiencies may be higher in triploids than diploids (Burke et al., 2010). Evidence exists to hypothesise that triploids may have higher dietary requirement for certain macro-minerals such as phosphorous, which must be met to prevent the onset of skeletal deformities (Fjelldal et al., 2015). In addition, a higher requirement for the essential amino acid histidine was also reported to prevent cataract formation in post-smolts and, possibly, to improve feed conversion efficiency (Taylor et al., 2015). It stands to reason that, similar to phosphorus and histidine, other dietary requirements may vary between ploidy, especially in respect to nutrient profile alterations in low marine ingredients diets. However, few studies have examined triploid performance in response to a diet with low levels of FM or FO (Ganga et al., 2015), or how dietary micronutrient supplementation would affect growth and metabolism. It is therefore essential to establish the dietary requirements of triploid Atlantic salmon, and ensure their performance is at least equal or better than their diploid counterparts under a dietary regime with low marine ingredients in order to establish their viability for integration in commercial operations.

The present study investigated the effects of feeding graded levels of a nutrient package (NP) containing 24 nutrients in total (NRC, 2011 minimum nutrient recommendations for Atlantic salmon modified based on the studies by Hamre et al., 2016; Hemre et al. 2016) supplemented to feeds formulated with low levels of marine ingredients in diploid and triploid Atlantic salmon from parr until smolt. Specifically, fish were fed a diet supplemented with one of three inclusion levels of the NP (L1, 100 %; L2, 200 % and L3, 400% NP) and the effects on growth performance, biochemical composition, liver histology, hepatic gene expression (transcriptome) and smoltification efficiency determined.

2. Methods and Materials

2.1 Fish Stock

All experimental procedures and husbandry practices were conducted in compliance with the Animals Scientific Procedures Act 1986 (Home Office Code of Practice) in accordance with EU regulation (EC Directive 2010/63/EU) and approved by the Animal Ethics and Welfare Committee of the University of Stirling. All fish were monitored daily by the Named Animal Care and Welfare Officer (NACWO).

The feeding trial was carried out at the Niall Bromage Freshwater Research Facility, University of Stirling (Buckieburn, Scotland) for just over a year from March one year to April the following year using a mixed population of fish obtained from a commercial Atlantic salmon stock (Landcatch Natural Selection, Ormsary, UK). Briefly, ova and milt were collected from a total of 20 unrelated dams and 5 sires. Per dam, ova were fertilised as one batch and a 1 L sub-sample was removed to induce triploidy using hydrostatic pressure shock (9500 PSI applied 300 degree minutes post-fertilisation at 8 ˚C for a duration of 6.25 min). This procedure was repeated for each dam x sire cross creating 20 diploid incubators and 20 triploid incubators, reared in constant darkness at 8.0 ± 0.5 ˚C. Eyed ova (380 °days post fertilisation) were shipped to University of Stirling facilities and ova were pooled per ploidy and reared in 6 x 250 L tanks in complete darkness until first feeding (~ 850 °dpf). At first feeding, diploids were fed a standard commercial salmon fry feed (Inicio Plus, BioMar, UK; 13.0g kg^{-1} total phosphorus) whereas triploids were fed the same standard commercial formulation but with a boosted phosphorous level (16.7g kg^{-1} total phosphorus) based on data obtained in previous studies on triploid salmon (Smedley et al., 2018). All other dietary components were comparable between starter feeds. Fry were reared under constant light, and feed was supplied throughout the 24 h by belt feeders according to manufacturer's tables (specific feeding rate [SFR], 2-3 % body weight day^{-1}).

To verify ploidy status, smears were prepared according to Woznicki & Kuzminski, (2002) from blood collected following the caudal peduncle from euthanised fish at 5 g (100 / ploidy). After air drying, slides were fixed in 100 % methanol and then placed into Giemsa stain for 10 min. Erythrocyte length and diameter were measured at 100× magnification using image capture software (Image-Pro Premier, MediaCybernetics, Rockville, USA). A total of 20 randomly chosen nuclei per slide were measured to the nearest 0.01 μm. Diploid control groups had significantly smaller erythrocyte nuclear lengths with no overlaps with the pressure shock triploid groups (2N 6.8–7.7 μm; 3N 9.0–10.2 μm) confirming that the majority of fish subjected to hydrostatic pressure shock were likely to be triploids. Cumulative mortality from first-feeding to start of the feeding trial was 2.8 ± 0.02 % for diploids and 3.5 ± 0.01 % for triploids.

2.2 Feeding Trial

Two groups of Atlantic salmon parr of mean weight 37.5 ± 2.2 g (diploid) and 27.4 ± 0.7 g (triploid) were stocked into 12 x 1.8 m^3 circular fibreglass tanks (6 tanks / ploidy, n = 1000 / tank). Fish were acclimated to the experimental conditions for 2 weeks before being fed the experimental diets. Duplicate groups were fed low FM / FO diets (≡ 15% FM / 8% FO) formulated to have identical protein / oil content (480 / 215 g kg^{-1} respectively of which 72 / 17 g kg^{-1} were of marine origin) and supplemented with a nutrient package (NP) at graded inclusion levels. The NP contained 24 nutrients in total these being; vitamins (A, D_3, E, K_3, C, thiamin, riboflavin, B6, B12, niacin, pantothenic acid, folic acid and biotin), minerals (Ca, Co, I, Se, Fe, Mn, Cu and Zn), crystalline amino acids (L-histidine and taurine) and cholesterol. Specifically, the NP was added at three inclusion levels to produce 3 dietary treatments: L1, 100 % NP; L2, 200 % NP; L3, 400 % NP, the assumption being that the 100% NP package should contain 100 % of assumed requirement based on the given requirement levels reported for Atlantic salmon at the time (NRC, 2011) and modified according to an earlier trial as part of the EU-funded ARRAINA project (Hamre et al., 2016). Total and available phosphorus were fixed in all diets at 13.0 and 9.0 g kg^{-1} respectively, and magnesium at 1.5 g kg^{-1}, and were not part of the NP. Pellet size was adjusted according to fish weight, with a 2 mm pellet fed for 23 weeks and a 3 mm pellet fed for the final 8 weeks. All non-oil ingredients were mixed and pellets produced by extrusion to produce three base pellets that had oil added by vacuum coating. All feeds were produced at the BioMar Tech-Centre (Brande, Denmark). Feed formulations, added micronutrient concentrations within the nutrient package and analysed micronutrient concentration are provided in Tables 1, 2 and 3 respectively, while fatty acid profiles are provided in **Supplementary file 1**. With the exception of histidine, there were generally positive relationships between added and analysed nutrients in the 2 mm pellet (Table 3). In the 3 mm pellet, vitamin A, vitamin K3, pantothenic and folic acid, vitamin C, iron and manganese deviated from the positive relationship.

Fish were fed continuously during the light period of the light-dark cycle by automatic feeders (Arvotec T2000, Arvotec, Finland) controlled by a PC system. Although feed collection was not possible due to system constraints, presence of waste feed was ensured each day prior to tank flushing. Specific feeding rates (SFR; % tank biomass per day) were adjusted automatically according to predicted growth and daily temperature. A simulated natural photoperiod (SNP) was applied to produce S1+ smolts, with lighting provided by two 28 W fluorescent daylight bulbs (4000 °K, RS Components, UK) mounted centrally within the tank lid. Water was supplied by an upstream reservoir under flow through conditions (10 L min^{-1}), with ambient temperatures decreasing from 15.5 ˚C (September) to 2.0 ˚C (February), and increasing to 9 ˚C by April. Oxygen levels were consistently >8 mg L^{-1}.

2.3 Sampling Procedures

Fish were sampled for growth at 3, 7, 14 and 31 weeks post application of the experimental feeds. At each time point, 50 fish / tank were anaesthetised (MS222, PHARMAQ, UK), individual weights (± 0.1 g) and fork lengths (± 1.0 mm) measured, and fish allowed to recover in aerated water before returning to experimental tanks. Sex was not assessed. Fulton's condition factor (K) was calculated using: $K = (WL^{-3})100$; where W is body weight (g) and L is fork length (cm). Weight data were used to calculate specific growth rate (SGR_{wt}), and feed conversion rate (FCR) for each sampling period where SGR_{wt} was calculated as: $(e^{g-1})\times100$, where $g = (\ln(W_f) - \ln(W_i)) \times (t_2 - t_1)^{-1}$. Relative Weight gain (RWG) was calculated as $(Wf-Wi)/Wi \times 100$. FCR was calculated as: $F / (B_f - B_i + B_m)^{-1}$ where F is the feed fed (kg), B_f is the final biomass (kg), B_i is the initial biomass (kg), and B_m is the mortality biomass for the period (kg). Uneaten feed recovery was not feasible for this study and, therefore, FCR provided only a crude estimate of feed conversion.

At the end of the feeding trial (31 weeks), a total of 7 fish / tank were euthanised by an overdose of MS222 and 3 carcasses frozen at -20 ˚C for whole fish proximate composition analyses. Livers were dissected from the remaining 4 fish / tank (n = 8 / diet) and a small sample (~ 100 mg) collected into RNALater® (Sigma, Poole, UK) for transcriptomic analyses, before the liver was divided into two portions. One portion was stored in 10 % neutral buffered formalin prior to histological analyses with the remaining portion snap frozen in liquid nitrogen, then stored at -20 ˚C prior to fatty acid composition analysis. Finally, further 10 fish / tank were euthanised and viscera (intestines and associated fat deposits without liver or gonad) and livers dissected, individually weighed to calculate viscerosomatic (VSI, %) and hepatosomatic (HSI, %) indices: where VSI was calculated as viscera weight / (body weight – viscera weight) x 100; and HSI as liver weight / (body weight – liver weight) x 100.

Liver and white muscle were dissected after fish were anaesthetised from five fish per tank, divided into two, and used for analysis of vitamins, S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH) and free amino acids at week 31. Samples were frozen at -30 °C until analysed. In addition, samples of whole fish were collected, minced and analysed for total amino acids and vitamins. Whole fish were pooled into 3 samples of 2 fish (1 per tank/replicate) and homogenised in a blender (Waring Laboratory Science, Winsted, CT, USA) to produce pates, and feeds were ground prior to analyses.

2.4 Histological analysis

Formalin-fixed livers from 4 fish per tank (n = 8 / diet) were assessed for micro- and macro-vesicular steatosis by light microscopy of haematoxylin and eosin-stained sections (Gu et al., 2013). Sections were viewed at 20 × original magnification and scored for presence of vesicles in individual hepatocytes. The term steatosis was applied when clear vacuoles with a diameter greater than 5 μm were observed in the hepatocytes, and measurement was achieved using a four-point scoring system (Fig.1; 0 - no vacuolation; 1 - mild vacuolation, < 25 % of hepatocyte area (one small vacuole not displacing the nucleus); 2 - moderate vacuolation, 25-75 % of hepatocyte area (one or more small vacuoles mildly displacing the nucleus); and 3 - severe vacuolation, > 75 % of hepatocyte area (one large vacuole filling the cytoplasm, and displacing the nucleus).

2.5 Biochemical analysis of diets, whole fish and liver

Proximate compositions of feeds and whole fish were determined according to standard procedures (AOAC, 2000). Moisture contents were obtained after drying in an oven at 110 °C for 24 h and ash content determined after incineration at 600 °C for 16 h. Crude protein content was measured by determining nitrogen content (N × 6.25) using automated Kjeldahl analysis (Tecator Kjeltec Auto 1030 analyser, Foss, Warrington, U.K), and crude lipid content determined after acid hydrolysis followed by Soxhlet lipid extraction (Tecator Soxtec system 2050 Auto Extraction apparatus, Foss, Warrington, U.K). Total lipid was extracted from liver by homogenisation in chloroform/methanol (2:1, v/v) and content determined gravimetrically (Folch et al., 1957). Fatty acid methyl esters (FAME) were prepared from total lipid by acid-catalysed transesterification at 50 ˚C for 16 h (Christie, 2003), and FAME extracted and purified as described previously (Tocher and Harvie, 1988). FAME were separated and quantified by gas-liquid chromatography using a Fisons GC-8160 (Thermo Scientific, Milan, Italy) equipped with a 30 m × 0.32 mm i.d. × 0.25 μm ZB-wax column (Phenomenex, Cheshire, UK), on-column injector and a flame ionisation detector. Data were collected and processed using Chromcard for Windows (version 2.01; Thermoquest Italia S.p.A., Milan, Italy). Individual FAME were identified by comparison to known standards and published data (Tocher and Harvie, 1988). Whole fish samples were hydrolysed in 6M HCL for 22 h before being analysed for total amino acid content and composition by UPLC as described (Espe et al., 2014), while free amino acids and N-metabolites in muscle and liver were analysed after deproteinisation using sulfosalicylic acid, and separated on Biochrome and detected by post-column derivatisation with ninhydrin, as described elsewhere (Espe et al., 2006). Liver, plasma and muscle samples were analysed for SAM and SAH after extraction using 4 % per chloric acid and separated on HPLC as described in detail previously (Espe et al., 2008). The B-vitamins, biotin, niacin, folate, pantothenic acid and cobalamin were all determined by microbiological methods (Feldsine et al., 2002; Mæland et al., 2000). Other B-vitamins were determined by HPLC; thiamine (CEN, 2003), vitamin B6 (CEN, 2006) and riboflavin (Brønstad et al., 2002). Ascorbic acid was determined by HPLC (Mæland and Waagbø, 1998), as were tocopherols and vitamin K (CEN, 1999). Total TBARS was determined according to Hamre et al. (2001). Multi-element determination of macro- and microminerals in the feed and tissue samples was performed by ICP-MS (inductively coupled plasma mass spectrometry) (Julshamn et al., 1999).

2.6 Smoltification assessment

Smoltification was confirmed through a combination of smolt index scoring (Sigholt et al, 1995), gill Na^+K^+-ATPase activity, and 24 h saltwater challenge and plasma chloride analysis were conducted during the feeding trial on 28-Jan, 27-Feb, 21-Mar, and at final smolt, 21-Apr 2014 (equivalent to 122, 199, 324 and 430 ˚days post-winter solstice rise in daylength respectively). Thirty individuals per tank were scored for smolt index. Na^+K^+-ATPase activity was determined from 5 individual gill biopsy / tank (3-6 gill filaments in 100 µl SEI buffer, snap frozen in liquid nitrogen), with a kinetic assay run in 96-well microplates at 26 °C and read at a wavelength of 340 nm for 10 min according to the method of McCormick (1993). Protein concentrations were determined thereafter using a BCA (Bicinchoninic acid) protein assay kit (SIGMA, Aldrich, UK). Saltwater challenge was conducted for 24 h in 100 L tanks of 10 °C aerated seawater (35 ppt) (Instant Ocean; Animal House, Batley, UK). Ten individual fish per diet (5 / tank) were placed into separate 100 L saltwater challenge tanks at respective time points, and following challenge, all fish were removed, numbers of surviving fish counted to determine seawater survival, and were then culled and blood removed from the caudal vein before centrifugation at 500 g for 15 min at 4 °C. Plasma was collected and stored at −20 °C until analysis using a chloride analyser (Sherwood Instruments Inc., UK). Plasma samples were analysed in triplicate per individual and the average taken of the three technical replicates.

2.7 Hepatic transcriptome analysis

Transcriptomic analysis was conducted using a custom-made 4 x 44K Atlantic salmon oligo microarray (Agilent Technologies, Wokingham, UK; ArrayExpress accession no. **A-MEXP-2065**) as described in detail previously (Tacchi et al., 2011). Furthermore, this salmon custom array and the laboratory protocols used in the present study have been used widely and validated by previous studies (Morais et al., 2012; Betancor et al., 2016; Vera et al., 2017). Briefly, RNA was extracted from 50 mg of liver tissue, originating from six individual fish from each feed group, using TRI Reagent (Sigma-Aldrich, Dorset, UK). The resulting RNA samples were amplified using TargetAmp™ 1-Round Aminoallyl-aRNA Amplification Kit, (Epicentre Technologies Corporation, Madison, Wisconsin, USA) following recommended procedures. Aminoallyl-amplified RNA (aRNA) samples were labelled with Cy3 dye (GE HealthCare Life Sciences, Buckinghamshire, UK) while a pool of all aRNA samples was labelled with Cy5 dye (GE HealthCare Life Sciences) and used as a common reference in a dual-label common reference design, and finally hybridised to one array. Scanning was performed using a GenePix 4200 AL Scanner (Molecular Devices (UK) Ltd., Wokingham, UK), and the resulting images analysed with Agilent Feature Extraction Software v.9.5 (Agilent Technologies) to extract intensity values and identify the features. Features considered outliers (i.e., defined as those probes whose background intensity was between the 0.05th and 99.95th percentile of the distribution) in two or more replicates within at least one treatment were excluded from further analyses. Additionally, features consistently expressed just above background noise (defined as those features whose intensity was lower than 5th percentile of the distribution in 75 % or more of the analysed samples) were also removed. The full protocol for microarray laboratory and data analysis has been reported previously (De Santis et al., 2015). The output of the microarray experiment was submitted to ArrayExpress under accession number **E-MTAB-6302**. In order to avoid confounding effects associated with differential expression associated with the increased genetic material possessed by triploid fish, the two ploidy were analysed separately and independently and are herein presented relative to diet L1.

2.8 Statistical and data analysis

Differences between weight, condition factor (K), plasma chloride and gill Na^+K^+-ATPase activity were assessed using a general linear model (GLM) and two-way ANOVA (diet x ploidy) with replicate tank nested within treatment. Percentage data (Mortality, SGRwt, HSI and VSI) were subjected to arcsine square-root transformation prior to statistical analyses. Data were tested for normality and homogeneity of variances with Levene's test prior to two-way ANOVA (diet x ploidy) followed by a Tukey–Kramer HSD multiple comparisons of means. Contingency Chi-square tests were used to compare significant differences between survival under saltwater challenge. Vitamins, minerals, amino acids, SAM and SAH were analysed by two-way ANOVA (ploidy x diet) using the tank means as the statistical unit. ANOVA was used to test the hypothesis that diet was more influential than ploidy. Tank means were accepted as statistical different at $p < 0.05$. Results are reported as mean ± standard deviation (SD).

Transcriptomic data analysis was performed using Bioconductor v.2.13 (Gentleman et al., 2004). Quality control, data pre-processing and analysis of differential expression were conducted using the software package limma (Smyth, 2004). To avoid redundancy, features representing the same target gene as implied from KEGG annotation were reduced into a unique value obtained by selecting the feature with the highest F-value calculated on all contrasts. For analysis of gene expression, gene-set testing was adopted using the function *roast* of the limma package (Wu et al., 2010). Gene set testing is a differential expression analysis in which a set of *a priori* defined (putatively co-regulated) genes is treated as a unit. All *p*-values reported in this work were corrected for false discovery rate (FDR) unless otherwise specified (Benjamini and Hochberg, 1995).

3. Results

3.1 Mortality, Maturation, Growth and Deformity

There were no significant differences in cumulative mortality between dietary treatments or between ploidy (Table 4). However, in diploids, for diet L1 there was a tank effect, in which one tank showed higher mortality due to fungus in the final 3 weeks of the trial (7.5 % out of 9.1 % total mortality).

Precocious parr-maturation (n = 50 /tank) was not observed in any of the populations assessed any time point.

Diploids had a significantly higher initial weight than triploids that was maintained for the 31 weeks of experimental feeding until smolt (Table 4). However, diet significantly affected weight in diploids, with fish fed diet L2 having a significantly higher final smolt weight than fish fed diets L1 and L3. In contrast, diet did not affect final smolt weight in triploids (Table 4). Although weight differed between ploidy, overall growth rate (SGRwt) and subsequent weight gain did not differ between ploidy and diet, with the exception of diploids fed diet L2, which showed a significantly higher SGRwt than all other treatments. However, examining growth profiles over time showed that diploids fed diets L2 and L3 exhibited the fastest weight gain, with significant differences evident as early as 3 weeks of feeding on the experimental diets. By 14 weeks post-feeding, diet L3 weight gain slowed, such that weight of fish fed diets L3 and L1 were no longer significantly different (Fig. 2). As such, ploidy did not affect relative % weight gain (RWG, $p = 0.215$), while a significant effect of diet and an interaction with ploidy was evident (Table 4). RWG was not statistically different between ploidy in fish fed diet L1, significantly higher in triploids fed diet L3 relative to diploids, but significantly lower in triploids fed diet L2 relative to diploids. Within triploids, RWG did not differ between diets, while in diploids RWG was significantly higher in fish fed diet L2 than diets L1 and L3. The crude FCR data suggested an interaction between diet and ploidy, whereby diploids fed diet L2 had lower FCR than triploids fed L2, while there were no other significant effects on FCR between ploidy or diet (Table 4).

Both VSI and HSI were affected by diet, ploidy and their interaction (Table 4). Within diploids, fish fed diet L2 had a significantly lower VSI and HSI than fish fed diets L1 and L3, while in triploids VSI and HSI were not affected by diet. Within diets, VSI and HSI differed only in diet L1 between ploidy.

Externally visible deformity was < 1 % in fish fed all diets and ploidy at the end of the freshwater phase.

3.2 Proximate composition of fish and fatty acid composition of liver

Whole fish % oil and ash composition did not differ significantly between dietary micronutrient inclusion level or ploidy (Table 5). Triploids had significantly lower whole body % protein and a higher % moisture at smolt than diploids, but was not affected by diet. Although not always statistically different, the fatty acid compositions of liver showed some trends that might be informative. Specifically, in diploids the proportion of total saturated fatty acids, particularly 16:0, significantly increased, and total monoenes, especially 18:1n-9 and 20:1n-9, significantly decreased with increasing micronutrient supplementation (Table 5). Furthermore, there was an increasing trend, albeit non-significant, in the proportions of total polyunsaturated fatty acids (PUFA) and total n-3 PUFA, due mainly to increasing trends in eicosapentaenoic (EPA, 20:5n-3) and docosahexaenoic (DHA, 22:6n-3) acids, whereas the proportions of n-6 PUFA showed a decreasing trend with increasing dietary micronutrient concentrations.

The effect of dietary micronutrient supplementation on liver fatty acid composition in triploid salmon was less pronounced than in diploids and the trends appeared to be in the opposite direction compared with diploid fish (Table 5). Thus, in triploids lower proportions of saturated fatty acids and n-3 PUFA, and higher proportions of monoenes and n-6 PUFA were found in fish fed diet L3 compared to those fed diet L1.

3.3 Total amino acid concentration in whole body and free amino acids and N-metabolites in white muscle tissue

Whole fish total amino acids and N-metabolites, at the end of the experiment, showed no variation by treatment (Table 6). There was a tendency that whole fish taurine was slightly higher in triploids than in diploids ($p = 0.048$). Muscle free amino acids and N-metabolites including taurine, asparagine, hydroxyproline, glutamine, glutamate, and β-alanine were all higher in triploids than in diploids, while branched chain amino acids, lysine and anserine were higher in diploids than in triploids (Table 7). All the other metabolites analysed in muscle were not affected by treatments (data not shown). The varying dietary nutrient package had little influence on muscle free amino acids or N-metabolites as only a significant increase in threonine and a decrease in cystathionine was observed.

3.4 Vitamin concentrations in whole fish and tissues

For the B-vitamins, increasing dietary levels led to increasing tissue levels for niacin ($p = 0.006$), while whole body pantothene showed a trend of dietary effect ($p = 0.051$) (Table 8). Whole body folate increased in diploids, but not in triploids, giving a significant interaction between diet and ploidy ($p = 0.035$). Riboflavin was higher in whole body of diploids compared to triploids ($p = 0.016$). The tissue concentrations of the lipid soluble vitamins and vitamin C increased with increasing concentration in the diet ($p < 0.015$), except for muscle α-TOH where the apparent increase was non-significant. Alpha-tocopherol (TOH) and vitamin K showed higher retention in diploids compared to triploids ($p < 0.001$). Gamma-TOH, which was present in the feed ingredients but not supplemented in the diets, decreased in response to increasing nutrient supplementation in both muscle and whole body ($p < 0.001$).

3.5 Mineral concentrations in whole fish

Whole body mineral concentrations were not affected by diet (Table 9). Diploid fish had a slightly higher whole body concentration of Cu than triploid fish ($p = 0.01$) but the other minerals were not affected by ploidy.

3.6 Liver histology and steatosis

A significant interaction between diet and ploidy was evident (*p* = 0.003). In diploids, steatosis was significantly greater in fish fed diet L2 than fish fed diet L1, but not diet L3, while fish fed diets L1 and L3 were comparable (Table 4). Steatosis did not differ significantly between diets in triploids. However, steatosis was affected by ploidy (p = 0.004), and was generally higher in triploids than diploids. Surprisingly, steatosis scores appeared to be inversely related to HSI (Table 4).

3.7 Smoltification efficiency

Diploid salmon fed dietary treatment L2 showed 100 % survival during seawater challenge from 28-Jan final smolt (21-Apr) (Fig. 3). Diploids fed diet L1 had 100 % mortality on 28-Jan 2014. A slight dip in survival was observed in diploids fed diets L1 and L3 at 300 °days post-winter solstice (21-Mar), but survival at smolt (21-Apr) was 100 % irrespective of diet. In triploid salmon, seawater challenge mortalities were only observed on 28-Jan, thereafter and irrespective of diet, survival was 100 % during seawater challenge until smolt (21-Apr).

In both ploidy, plasma chloride levels decreased with time post-winter solstice (Fig. 3). Significant differences were apparent between diploids fed diets L2 and L3 on 28-Jan, and between fish fed diet L1 and diets L2 and L3 on 21-Mar (~300 °days), however, no differences were apparent between dietary treatments at final smolt (21-Apr 2014). In triploids, fish fed diet L1 had significantly higher plasma chloride levels on 28-Jan 2014 (~100 °days) than fish fed diet L2, with fish fed diet L3 intermediary to both. Thereafter, plasma chloride level steadily declined to smolt, at which point triploids fed diet L3 had a significantly higher plasma chloride level than fish fed either diets L1 or L2.

In both ploidy, gill Na^+,K^+-ATPase activity increased post-winter solstice until final smolt 21-Apr 2014 (Fig. 3). In diploids, fish fed diet L1 showed lower activity than fish fed diets L2 and L3 on 21-Mar (~300 °days), which correlated with differences evident in seawater challenge survival at this time point. At no other time point were significant differences observed between diets in diploids. In triploids, no significant differences were observed between fish fed the different diets at any time point.

3.8 Liver gene expression

At individual gene level and using cut-off measures generally applied to microarray studies (i.e. FDR $p < 0.1$, Fold Change, FC > 1.3) no significant differences were found in any of the contrasts except for diet L3 versus L1 in triploids, where 7 differentially expressed genes (DEGs) were identified. However, to identify interesting trends similarly affected in both ploidies a less stringent cut-off was used ($p < 0.05$, FC > 1.3). Under these conditions a larger number of affected genes were identified ($L2_{dip}$ vs. $L1_{dip} = 300$, $L3_{dip}$ vs. $L1_{dip} = 192$, $L2_{trip}$ vs. $L1_{trip} = 134$, $L2_{trip}$ vs. $L3_{trip} = 398$). To restrict the range of potentially interesting pools of candidate markers affected by micronutrient supplementation, genes affected in diploids (either diets L2 or L3 versus L1) were intersected with those affected in triploids (either L2 or L3 versus L1) (Fig. 4). A total of 63 DEGs were obtained explaining common mechanisms affected in diploids and triploids. Noteworthy, this pool of markers suggested that diet L2 in diploids triggered a hepatic profile that highly resembled that triggered by diet L3 in triploids, sharing approximately 80 % of the similarities. This list of genes contained several genes regulating the terpenoid backbone biosynthesis and sterol biosynthetic processes, such as sterol 14-demethylase, 7-dehydrocholesterol reductase, squalene monooxygenase genes, and farnesyl diphosphate synthase. KEGG pathway analysis suggested that the DEGs were enriched for biological processes involved in cholesterol and lipid biosynthetic process, whereas for the cellular components indicated that endoplasmic reticulum and membranes structures were differentially regulated between diet groups. In addition, microarray analysis revealed that lipid digestion and absorption, steroid biosynthesis and PPAR signalling pathways were significantly altered due to diet nutrient package.

Gene-set testing enables focus on biologically meaningful processes and provides a more powerful and robust approach than traditional gene-wise tests as evidence is accumulated from many genes. Using this approach, a significantly higher number of processes potentially affected by dietary micronutrient supplementation was identified (**Supplementary file 2**). In diploids, diets L2 and L3 differed from L1 for only one gene-set, respectively circadian rhythm (increased expression in fish fed diet L2 vs. L1) and insulin signalling pathway (lower expression in fish fed diet L3 vs. L1). In contrast, triploid livers appeared to be more affected by dietary treatments compared with diploids. In fact, diet L2 resulted in at least six gene-sets significantly affected whereas diet L3 triggered the response of 43 gene-sets. Within these 43 sets, up-regulation of key pathways involved in carbohydrate metabolism, digestion and absorption of carbohydrate, protein and lipid as well as bile acid biosynthesis was observed. Immune functions were also up-regulated in triploid salmon fed diet L3 (complement and coagulation cascades, leukocyte transendothelial migration and intestinal immune network for IgA production), as well as metabolism of xenobiotics by cytochrome P450. However, diet L3 in triploids resulted in down-regulation of steroid biosynthesis, terpenoid backbone biosynthesis and energy metabolism (oxidative phosphorylation). In addition, several functional categories within genetic information processing were also down-regulated (RNA degradation, proteasome, RNA polymerase, spliceosome and ribosome).

Different supplementation levels of micronutrients affected the expression of key enzymes involved in one-carbon metabolism in both ploidies. In particular, increasing levels of supplementation resulted in up-regulation of genes involved in cysteine biosynthesis and catabolism (*cysteine beta-synthase, cysteine dioxygenase*), methionine synthesis (*betaine-homocysteine S-methyltransferase*), folate homeostasis (*folylpolyglutamate synthase*), histidine catabolism and glutamate synthesis (*glutamate formiminotransferase*) and serine conversion to glycine and tetrahydrofolate (*glycine hydroxymethyltransferase*). In diploids, several genes involved in carbohydrate and lipid metabolism, and using B-vitamins as cofactors and coenzymes, were also affected. Thus, *acetyl-CoA carboxylase* (fatty acid biosynthesis), *6-phosphogluconate dehydrogenase* and *transketolase* (pentose phosphate pathway) were up-regulated in diploid fish fed diet L2 (compared to fish fed diet L1). In addition, the expression of specific *cytochrome P450* genes were also up-regulated in fish fed diets L2 and L3 in both diploids and triploids (**Supplementary file 3**).

4. Discussion

In the present study, diploids were significantly larger at the start of the trial, and maintained a significantly greater weight than their triploid siblings irrespective of dietary micronutrient supplementation. However, growth rates (SGRwt) were comparable between ploidy and relative weight gain did not differ between ploidy, with the exception of diet L2. Recent studies have shown triploids to have greater growth potential than diploids in freshwater phases of development (Fjelldal & Hansen, 2010; Taylor et al., 2012; Fraser et al., 2013; Taylor et al., 2013; Fjelldal et al., 2016), so the apparent lack of better growth was unexpected. This may in part be due to higher water temperatures (15-16 °C) experienced for 7 weeks prior to, and the initial first two weeks of feeding at start of the trial, under which conditions triploids have been reported to show sub-optimal growth (Sambraus et al., 2017). However, specific dietary requirement trials in triploids are also limited to date, although it has been suggested that differences between ploidy might exist (Fjelldal & Hansen, 2010) particularly with regards to energy and nitrogen retention efficiencies (Burke et al., 2010), dietary phosphorous (Fjelldal et al., 2015; Smedley et al., 2018) and histidine requirements (Taylor et al., 2015; Sambraus et al., 2017). To date, no study has examined the interaction of ploidy and micronutrients when fed low marine ingredient diets. However, the results of the current study may indicate that specific dietary micronutrients could be different between diploid and triploid siblings when they are fed low marine feeds. More specifically, the present data may suggest that dietary micronutrient levels could be rate-limiting for triploid growth potential when fed low marine ingredient diets. However, the specific nutrients that may be rate-limiting could not be determined within the present study. As such, it was evident that diploids supplemented with double the nutrient package levels significantly outperformed their diploid siblings and all triploid groups when fed a low marine ingredient diet. They also had lower HSI and VSI than the diploids fed the L1 diet, which was consistent with results from Hemre et al., (2016). Given the approximate halving of the FM/FO content compared to a traditional marine ingredient based salmon diet, it appeared that a doubling of the specific nutrients is required to satisfy all dietary requirements for growth in diploid Atlantic salmon at least. However, care must be taken with respect to regulation for feed additive inclusion that they do not exceed current EU limits (**Supplementary File 4**). Should recommendations for any nutrient exceed current limits, then successful implementation within industrial aquafeeds may require revision of current legislation. Of further interest was the apparent loss in growth performance of diploids fed diet L3 (400 % premix) after 14 weeks of feeding. Collectively, the results suggest that, for minerals at least, dietary levels provided by diet L1 were probably sufficient, as there was no significant effect on whole body mineral composition of diet or ploidy with the exception of copper. It is plausible that the addition of extra minerals and vitamins, especially with respect to diet L3 in the case of diploids, may require that the fish expend additional energy in detoxification and excretion, which may subsequently be the cause of reduced growth in these fish towards the latter part of the experiment. In fact, high levels of some minerals in fish diets has been previously associated with reduced growth and feed efficiency (Al-Ghanem, 2011; Berntssen et al., 2017), indicating that mineral levels in fish diets need to be optimised and that their inclusion in excess might be counterproductive.

Regarding amino acid and N-metabolite concentrations, higher levels of free amino acids and N-metabolites including taurine, asparagine, hydroxyproline, glutamine, glutamate and β-alanine were observed in muscle of triploids. Methionine was not included in the nutrient package thus the higher taurine present in muscle in triploids might indicate that more methionine has been trans-sulfurated to taurine in triploids as compared to diploids (Espe et al 2008). Free amino acids are precursors for protein synthesis and so these data are consistent with other studies that have provided evidence of higher nitrogen retention and growth potential in triploid salmon as compared to diploids (Burke et al., 2010; Smedley et al., 2016). In particular, elevated levels of free hydroxyproline have been associated to high connective tissue degradation and protein turnover for remodelling of protein in white muscle during growth

(Rungruangsak-Torrissen and Fosseidengen, 2007). In addition, glutamine has been shown to inhibit muscle proteolysis and correlates with muscle protein synthesis (Millward, 1989), whereas high levels of free alanine and taurine may be related to higher intracellular buffering capacity in white muscle (Rungruangsak Torrissen and Male, 2000).

Although some variation in plasma chloride and gill Na^+,K^+-ATPase activity was observed during the spring increase in daylength, diet or ploidy appeared to have little effect on achieving successful parr-smolt transformation and osmotic competence. However, in diploids, it was apparent that the rate of increase in gill Na^+,K^+-ATPase activity was slower in fish fed diet L1 than in fish fed diets L2 and L3. This may reflect a stimulatory effect on increased gill ion excretion following increased dietary mineral supplementation as in diets L2 and L3, which has been previously reported to stimulate osmoregulatory adaptation in salmonids (Zaugg, 1992). Conversely, it may also represent a deficiency in certain minerals such as magnesium, which have been reported to impair osmoregulation when in deficit (El-Mowafi et al., 1997). This effect was, however, not evident in triploids, but may reflect differential patterns of smoltification between ploidy (Taylor et al., 2012) or differences in gill architecture between ploidy (Leclercq et al., 2011) and cellular physiology and function (Maxime, 2008).

Microarray analysis revealed that the hepatic transcriptome profile of diploid fish fed diet L2 was more similar to that observed in triploids fed diet L3 than to those fed L2, suggesting that micronutrient requirements of triploid salmon may differ from levels accepted in diploid salmon, as reported previously (Taylor et al., 2015; Fjelldall et al., 2016; Smedley et al., 2016). Different levels of micronutrient supplementation affected the expression of key genes involved in lipid metabolism. In particular sterol biosynthesis pathways (steroid and terpenoid backbone synthesis) were down-regulated in both L2-fed diploids and L3-fed triploids, when compared with diet L1-fed diploids and triploids, respectively. This effect on gene expression may be in response to the increased supplementation of cholesterol in the L2 and L3 diets, as part of the micronutrient premix, and therefore probably reflects increased requirement and synthesis of this lipid in fish fed diet L1. However, bile acid biosynthesis was up-regulated in these groups. These results are consistent with a previous study by Kortner et al. (2014) showing that supplementation of plant-based diets with cholesterol suppressed cholesterol synthesis and induced bile acid production in Atlantic salmon. In fact, the conversion of cholesterol into bile acids represents the main route for cholesterol elimination in fish and, consequently, the transcriptomic response observed in the present study would be a mechanism of cholesterol homeostasis in fish being fed diets containing higher levels of cholesterol.

Gene sets analysis showed an up-regulation of genes involved in immune processes in triploid salmon fed diet L3. This fact might be related to higher levels of vitamin C in whole body and liver as well as higher vitamin E levels in whole body of fish from this experimental group, when compared to triploid salmon fed diet L1. In particular, there was an up-regulation of complement and coagulation cascades, which agreed with previous research showing an effect of vitamin C supplementation on complement activity in Atlantic salmon (Hardie et al., 1991). Vitamin E content in salmon diets has also been correlated to variations in the response of fish to infectious diseases and immune response (Hardie et al., 1990). Both vitamin C and E can improve the immune status of fish due to their antioxidant activity and previous studies have indicated interaction between these vitamins (Hamre et al., 1997, 2011). In diploid salmon, there was also a positive correlation between increasing levels of micronutrient supplementation and body content of vitamins C and E, however no sets of genes involved in immune functions were differentially expressed. This fact further supports the hypothesis that triploid salmon may have different micronutrient requirements and responses to feed supplementation with vitamins. The expression of cytochrome P450 enzymes was also up-regulated in response to higher levels of micronutrient supplementation in both ploidies. These enzymes are involved in the activation of vitamin D to its hormonal form, which then regulates the expression of a broad range of genes, including osteocalcin, osteopontin, calbindin and calcium channels that play key roles in the control of calcium homeostasis and skeletal integrity (Suzuki et al., 2008). In addition, different P450 enzymes control vitamin D metabolism and inactivation, which can also be induced by vitamin D itself via CYP24A1 activation (Schuster, 2011). In the present study, up-regulation of *cyp24a1* (*vitamin D3 24-hydroxylase*) was observed in diploid salmon fed diet L3. However, in triploid fish the expression of this gene was not affected by diet. In the present study, vitamin D was included in the micronutrient mix and therefore vitamin D concentration in diet L3 was four times higher than in diet L1, which might have induced the expression of its metabolising enzyme, suggesting that levels in diet L3 may be excessive for diploid Atlantic salmon. However, the microarray results also suggested that this may not be the case for triploids. In fact, triploid salmon have a higher predisposition to develop skeletal deformities, when compared to diploid fish, which seems to be reduced when feeds are supplemented with phosphorus (Fjelldal et al., 2016; Smedley et al., 2016, 2018). It is also known that vitamin D is an important regulator of phosphorus metabolism (DeLuca, 1980) and, consequently, results suggest that vitamin D requirements in triploid salmon may also be different, although further research is required to define its optimal concentration in feeds for triploids.

Another biological category affected by diet in triploid salmon was genetic information processing. In fish fed diet L3, down-regulation of RNA degradation, proteasome, RNA polymerase, spliceosome and ribosome was observed, suggesting a decrease in protein turnover in this group, which may indicate a decrease in energy expenditure (Houlihan et al., 1995) that was consistent with down-regulation of oxidative phosphorylation in this group. However, this was in contrast to the growth and feed conversion rates observed in triploid fish, since no differences were found in these parameters between dietary treatments. In contrast, growth was affected by micronutrient supplementation in diploid salmon that showed better performance when fed diet L2. In addition, microarray data also revealed higher expression of *igf1* in this group. Regarding carbohydrate metabolism, there was up-regulation of key pathways in triploids fed diet L3, which could be related to higher availability of B-vitamins, when compared to L1-fed fish. Vitamins B1 (thiamine), B7 (biotine) and B12 (cobalamine) are involved in several reactions of carbohydrate metabolism, acting as coenzymes, and vitamin B12 deficiency has been linked to gluconeogenesis impairment in mammals (Mahmood, 2014). In diploids, microarray analysis also found a number of vitamin B-dependent genes that were up-regulated in the fish fed diet L2. In particular, these genes were involved in lipid and carbohydrate metabolism, in accordance with the functions previously reported for these vitamins (Waagbø, 2010).

One-carbon metabolism comprises a number of biochemical reactions that provide methyl groups for biological methylation of proteins, phospholipids and nucleic acids (Friso et al., 2017). B-vitamins act as coenzymes and methyl acceptors and donors in one-carbon metabolism and, consequently, deficiency of some of these vitamins can have an impact on these biochemical processes. In the present study, one-carbon metabolism was affected by diet in diploid and triploid salmon. In diploids, homocysteine re-methylation to form methionine by *betaine-homocysteine S-methyltransferase* (*bhmt*) was up-regulated in fish fed L2 compared to L1. Previous studies have shown an inverse correlation between B-vitamins status and homocysteine concentrations (Wallace et al., 2008) and therefore higher dietary levels of these vitamins may increase methionine synthesis from homocysteine. In addition, homocysteine can also enter the transulfuration pathway and be degraded to cystathionine by *cysteine beta-synthase* (*cbs*) and then to cysteine, which can be metabolised ultimately into glutathione and taurine (Friso et al., 2017). In diploids fed diet L2, there was up-regulation of *cbs* and cysteine catabolism by *cysteine dioxygenase* that, in turn, could be related to up-regulation of glutathione metabolism in this group, since cysteine is one of the major determinants of glutathione synthesis (Stipanuk et al., 2006). Regarding triploid salmon, microarray data revealed up-regulation of *glycine hydroxymethyltransferase*, a vitamin B6-containing enzyme that converts glycine to serine, and tetrahydrofolate (THF) to 5,10-methylenetetrahydrofolate (5,10-MTHF) in the folate cycle (Friso et al., 2017), suggesting than higher dietary levels of B-vitamins may have induced up-regulation of this key pathway within one-carbon metabolism. In addition, *glutamate formiminotrasferase* was also up-regulated in this group. This enzyme is involved in glutamate synthesis and depends on histidine and folate (Mahmood, 2014).

Conclusions

As the industry moves towards achieving increased sustainability and greater utilisation of plant-based ingredients there is a clear need adjust micronutrient supplementation accordingly to ensure optimal growth and metabolic function. Results, certainly in the case of diploids, suggest that under low marine ingredient diets, while micromineral requirements appear to be met within the refined NP levels as suggested by the short-term studies of Hamre et al., (2016) and Hemre et al., (2016), that for other micronutrients (specific amino acids, water- and fat-soluble vitamins) it is recommended that levels be supplemented above current NRC (2011) recommendations for optimised growth and liver function of Atlantic salmon in long-term freshwater grow out. The differential effect between ploidy for certain micronutrients also supports the hypothesis that there are yet further differences in nutritional requirements beyond the previously established increased histidine and phosphorous requirements of triploid salmon.

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Figure Legends

Figure 1. Scoring system for hepatocyte steatosis. Representative examples of the histopathological scoring of steatosis in hepatic sections. Bars represent 100 μm.

Figure 2. Weight gain profiles (mean ± SD) of diploid and triploid Atlantic salmon parr fed a low FM/FO formulation (15/8 %) supplemented with a micronutrient premix (modified NRC 2011 recommendation) at three inclusion levels: Diet L1 100 % premix, Diet L2 200 % premix, and Diet L3 400 % premix. Superscripts denote significant differences (Two-Way ANOVA, $p < 0.05$) between dietary treatments.

Figure 3. Changes in survival, plasma chloride concentration of seawater (SWC) challenged (24h, 35ppt at 10˚C) and gill Na^+,K^+-ATPase of diploid and triploid Atlantic salmon parr fed a low FM/FO formulation (15/8 %) supplemented with a micronutrient premix (modified NRC 2011 recommendation) at three inclusion levels: Diet L1 100 % premix, Diet L2 200 % premix, and Diet L3 400 % premix. Superscripts denote significant differences (Two-Way ANOVA, $p < 0.05$) between diets. SWC or gill Na^+,K^+-ATPase were conducted were conducted on 28-Jan, 27-Feb, 21-Mar, and 21-Apr 2014 (equivalent to 122, 199, 324 and 430 ˚days post-winter solstice rise in daylength respectively).

Figure 4. Heatmap of differentially expressed genes ($p < 0.05$, $FC > 1.3$) in both diploids (either diets L2 or L3 compared with diet L1) and triploids (either diets L2 or L3 compared with diet L1). Red denotes upregulation whereas green denotes downregulation. Expression data is log2 transformed. P-values were corrected for false discovery rate. The heatmap was generated using the package gplots (Warnes et al., 2013).

Supplementary File Captions

Supplementary File 1. Fatty acid compositions (percentage of total fatty acids) of the experimental base feed.

Supplementary File 2. Gene sets significantly affected by different micronutrient supplementation in diploid and triploid salmon. Red denotes upregulation and green downregulation.

Supplementary File 3. - List of genes differentially expressed and affected by different micronutrient levels in diploid and triploid salmon. Red denotes upregulation and green downregulation.

Supplementary File 4. Current EU limits for additive inclusion within fish feeds

Table 1. Formulation (g.100g diet^{-1}) and proximate composition (analysed) of experimental diets

	Diet		
Ingredients	**L1**	**L2**	**L3**
Fish Meal[1]	13.00	13.00	13.00
Krill Meal[2]	2.00	2.00	2.00
Soy Protein Concentrate[3]	17.94	18.00	17.65
Corn Gluten[4]	4.49	3.00	3.00
Pea Protein Concentrate[5]	17.94	18.49	18.15
Wheat Gluten[4]	14.36	14.79	14.52
Wheat[6]	8.63	8.26	7.46
Fish Oil[7]	8.00	8.00	8.00
Rapeseed oil[4]	5.25	5.32	5.47
Linseed oil	1.27	1.28	1.32
Palm kernel oil	3.17	3.21	3.30
ARRAINA Nutrient Package[8]†‡	0.75	1.50	3.00
Monosodium phosphate	2.52	2.53	2.54
Amino acid Premix[9,*]	0.68	0.62	0.59
Proximate Composition (Analysed)			
Moisture (%)	6.3	6.8	6.1
Crude lipid (%)	20.8	21.1	22.7
Crude protein (%)	48.9	47.0	48.1
Ash (%)	6.5	6.8	7.4
Energy (MJ / kg)	23.4	23.4	23.4

[1]Feed Services, Bremen, Germany; [2]Aker Biomarine, Norway; [3]Caramuru, Brazil; [4]Cargill, Germany; [5]Agrident, Germany; [6]WN Lindsey, UK; [7]ED & F Man, Germany; [8]DSM, Netherlands; [9]Evonik, Germany; †Added as components of the nutrient package (NP), and times requirement based on NRC (2011) minimum requirement for Atlantic salmon and modified according to Hamre et al., (2016), diet L1 achieving assumed 100 % minimum requirement; *Balanced for lysine, methionine, threonine and valine. Contains antioxidant.

Table 2. Added micronutrient concentrations (mg.kg^{-1}) within the nutrient package (NP): selected amino acids (histidine and taurine), minerals, vitamins and cholesterol.

	Diet		
Premix Formulations	**L1**	**L2**	**L3**
Vitamin A	3.79	7.58	15.16
Vitamin D3	0.05	0.10	0.20
Vitamin E	102.44	204.88	409.76
Vitamin K3	9.82	19.64	39.28
Thiamin	2.67	5.34	10.68
Riboflavin	8.30	16.60	33.20
B6	4.77	9.54	19.08
B12	0.25	0.50	1.00
Niacin	24.80	49.60	99.20
Pantothenic Acid	17.15	34.30	68.60
Folic Acid	2.82	5.64	11.28
Biotin	0.14	0.28	0.56
Vitamin C	80	160	320
Calcium	0.4	0.8	1.6
Cobalt	0.94	1.88	3.76
Iodine	0.67	1.34	2.68
Selenium	0.23	0.46	0.92
Iron	32.64	65.28	130.56
Manganese	12.03	24.06	48.12
Copper	3.24	6.48	12.96
Zinc	66.92	133.84	267.68
Taurine	2450	4900	9800
Histidine	1400	2800	5600
Cholesterol	1100	2200	4400

Table 3. Analysed concentrations of selected amino acids (taurine, histidine and methionine $g.kg^{-1}$) macro-minerals (calcium, magnesium and phosphorous, $g.kg^{-1}$) micro-minerals and vitamins ($mg.kg^{-1}$) of the experimental diets for the 2 mm and 3 mm pellets. Nutrients added at graded levels to the feeds are shown with an asterisk. "-" denotes not analysed.

Pellet Size	**2mm**			**3mm**			
	L1	**L2**	**L3**	**L1**	**L2**	**L3**	**NRC 2011‡**
Vitamin A*	5.2	7.2	14.2	6.2	5.1	7.2	0.75[a]
Vitamin D3*	0.17	0.19	0.29	0.17	0.18	0.26	0.04[a]
Vitamin E*	85	146	203	75	151	273	60[b]
Vitamin K3*	0.43	0.78	1.60	0.70	1.12	1.12	<10[b]
Thiamin*	3.3	5.8	9.3	3.7	20.2	29.9	1[a],
Riboflavin*	12.1	20.6	35.8	11.7	34.4	57.6	4[a],
Vitamin B6*	11.5	14.3	22.2	11.0	18.1	30.5	5[b]
Vitamin B12*	0.17	0.30	0.49	0.14	0.34	0.66	NT
Niacin*	75	107	163	80	221	434	10[a],
Pantothenic acid*	18.6	33.2	50.2	20.2	74.3	66.0	20[a,]
Folic acid*	2.82	-	7.53	2.82	19.95	12.54	1[a]
Biotin*	0.44	0.71	1.03	0.47	1.10	1.91	0.15[a]
Vitamin C*	83	180	312	77	238	244	20[b]
Cobalt*	1.0	1.6	3.5	0.95	2.3	3.4	NT
Iodine*	-	-	-	1.1	3.4	6.1	1.1[a]
Selenium*	1.2	1.5	2.2	1.3	1.6	2.5	0.15[a]
Iron*	300	330	510	330	310	410	30-60[b]
Manganese*	43	57	110	47	49	75	10[b]
Copper*	10	12	19	10	13	19	5[b]
Zinc*	160	190	300	100	200	350	37[b]
Taurine*	2.8	4.6	8.1	2.7	5.0	9.5	NR[b]
Methionine	8.7	8.8	8.6	9.0	8.8	9.1	7.0[b]
Histidine*	11.6	11.7	14.0	11.9	13.1	14.5	8.0[b]
Calcium*	6.6	6.9	8.6	6.3	6.7	7.5	NR[b]*
Magnesium	1.5	1.5	1.5	1.3	1.3	1.3	0.4[b]
Phosphorus	12.0	12.0	12.0	11.0	11.0	11.0	8.0[b]
Cholesterol*	n.a.	n.a.	n.a	n.a	n.a.	n.a.	NR

‡Current NRC, 2011 minimum requirement recommendations determined in [a] rainbow trout, [b] Atlantic salmon are shown for comparison. n.a. not analysed; NR* no requirement freshwater; NT, not tested.

Table 4. Mortality, initial and final weight and somatic indices recorded at the end (week 31) of freshwater rearing of juvenile diploid and triploid Atlantic salmon fed low marine diets (FM 15 % / FO 8 %) diets with differing micronutrient supplementation level (diets L1, L2 and L3). Superscripts denote significant differences between diets and ploidy.

	Diploid			**Triploid**			**P values**		
Diet	**L1**	**L2**	**L3**	**L1**	**L2**	**L3**	**P**	**D**	**P * D**
Mortality (%)† (n=2)	4.8 ± 4.3	1.4 ± 0.6	0.6 ± 0.1	1.6 ± 0.5	1.1 ± 0.2	1.1 ± 0.3	n/a	n/a	n/a
Initial Parr Wt (g) (n=50)	37.2 ± 1.8 ^{a}	37.2 ± 1.8 ^{a}	37.2 ± 1.8 ^{a}	27.6 ± 0.8 ^{b}	27.6 ± 0.8 ^{b}	27.6 ± 0.8 ^{b}	0.005	0.378	0.299
Final Smolt Wt (g) (n=50)	94.4 ± 14.2 ^{b}	113.8 ± 9.4 ^{a}	94.1 ± 15.7 ^{b}	75.4 ± 6.8 ^{c}	75.2 ± 2.6 ^{c}	77.5 ± 0.9 ^{c}	0.001	0.065	0.036
SGRwt (n=2)	0.62 ± 0.02 ^{b}	0.70 ± 0.04 ^{a}	0.61 ± 0.04 ^{b}	0.63 ± 0.02 ^{b}	0.61 ± 0.03 ^{b}	0.63 ± 0.02 ^{b}	0.056	0.063	0.001
RWG (%) (n=2)	150.8 ± 12.2 ^{bc}	206.5 ± 4.8 ^{a}	138.9 ± 17.2 ^{c}	175.3 ± 13.0 ^{ab}	163.3 ± 13.6 ^{bc}	180.2 ± 8.8 ^{ab}	0.215	0.008	0.001
FCR (n=2)	0.90 ± 0.24 ^{ab}	0.71 ± 0.10 ^{b}	0.87 ± 0.03 ^{ab}	0.93 ± 0.12 ^{ab}	1.02 ± 0.18 ^{a}	0.92 ± 0.00 ^{ab}	0.015	0.716	0.050
VSI (%) (n=10)	8.61 ± 0.55 ^{a}	7.24 ± 0.23 ^{b}	8.48 ± 0.65 ^{a}	6.99 ± 0.32 ^{b}	7.11 ± 0.09 ^{b}	7.42 ± 0.21 ^{ab}	0.001	0.009	0.031
HSI (%) (n=10)	1.36 ± 0.19 ^{a}	1.19 ± 0.03 ^{b}	1.35 ± 0.25 ^{a}	1.05 ± 0.06 ^{b}	1.12 ± 0.07 ^{ab}	1.15 ± 0.01 ^{ab}	0.057	0.018	0.006
Hepatic Steatosis (%) (n=4)	1.6 ± 0.8 ^{c}	2.5 ± 0.5 ^{ab}	1.7 ± 0.2 ^{bc}	2.3 ± 0.5 ^{abc}	2.2 ± 0.2 ^{abc}	2.8 ± 0.1 ^{a}	0.004	0.183	0.003

Data are presented as means ± SD. † Mortality data analysed by Contingency Chi-square tests

FCR, feed conversion ratio; HSI, hepatosomatic index; RWG, relative weight gain (%); SGRwt, specific growth rate weight (% day^{-1}); VSI, viscerosomatic index

Table 5. Whole fish proximate composition (%) and fatty acid compositions (% of total fatty acids) of liver of diploid and triploid salmon fed low marine diets with differing micronutrient supplementation level. Significant effect is highlighted in bold and superscripts denote significant differences between diets and ploidy (two-way ANOVA).

Ploidy (P)	**Diploid**			**Triploid**			***p* values**		
Diet (D)	**L1**	**L2**	**L3**	**L1**	**L2**	**L3**	**P**	**D**	**P * D**
Moisture (%)	68.9 ± 0.1	68.2 ± 0.1	69.0 ± 0.2	69.7 ±0.3	69.2 ± 0.1	69.2 ± 0.7	0.011	0.087	0.316
Oil (%)	10.4 ± 1.0	10.5 ± 0.4	10.4 ± 0.1	9.9 ± 0.0	10.6 ± 0.0	10.5 ± 0.3	0.719	0.429	0.493
Protein (%)	17.5 ± 0.6	18.1 ± 0.6	17.7 ± 0.6	17.2 ± 0.4	16.8 ± 0.1	16.9 ± 0.6	0.035	0.885	0.443
Ash (%)	2.3 ± 0.1	2.3 ± 0.1	2.2 ± 0.1	2.3 ± 0.0	2.3 ± 0.0	2.3 ± 0.0	0.191	0.546	0.955
14:0	2.3 ± 0.3^{ab}	2.3 ± 0.3^{a}	1.9 ± 0.1^{ab}	1.7 ± 0.1^{b}	1.7 ± 0.3^{b}	2.1 ± 0.3^{ab}	0.006	0.888	0.015
16:0	16.1 ± 0.6^{b}	17.5 ± 0.5^{ab}	18.7 ± 0.8^{a}	18.4 ± 1.8^{a}	18.8 ± 0.5^{a}	16.9 ± 0.9^{b}	0.250	0.354	0.015
18:0	4.7 ± 0.2^{a}	4.3 ± 0.5^{ab}	4.2 ± 0.4^{ab}	4.6 ± 0.3^{a}	4.2 ± 0.5^{ab}	3.6 ± 0.2^{b}	0.126	0.009	0.508
Total Saturated[1]	**23.4 ± 0.3^{b}**	**24.4 ± 0.5^{ab}**	**25.1 ± 0.5^{a}**	**25.0 ± 1.7^{a}**	**25.0 ± 0.7^{a}**	**22.9 ± 0.9^{b}**	**0.968**	**0.457**	**0.017**
16:1n-7	2.4 ± 0.3^{a}	2.2 ± 0.3^{ab}	1.9 ± 0.1^{ab}	1.8 ± 0.0^{b}	1.8 ± 0.1^{b}	2.1 ± 0.2^{ab}	0.009	0.777	0.009
18:1n-9	21.6 ± 2.9^{a}	17.3 ± 1.9^{ab}	16.5 ± 0.8^{b}	15.3 ± 1.6^{b}	14.7 ± 1.1^{b}	18.0 ± 2.5^{ab}	0.019	0.130	0.015
18:1n-7	2.8 ± 0.3^{a}	2.4 ± 0.2^{ab}	2.3 ± 0.1^{ab}	2.2 ± 0.2^{b}	2.0 ± 0.0^{b}	2.1 ± 0. ^{b}	0.001	0.056	0.177
20:1n-9	2.5 ± 0.4^{a}	2.4 ± 0.2^{ab}	1.8 ± 0.0^{b}	1.7 ± 0.3^{b}	1.7 ± 0.6^{b}	2.6 ± 0.4^{a}	0.213	0.756	0.002
22:1n-11	0.6 ± 0.1	0.6 ± 0.1	0.4 ± 0.1	0.5 ± 0.1	0.5 ± 0.2	0.7 ± 0.1	0.307	0.865	0.150
Total Monoenes[2]	**31.3 ± 3.7^{a}**	**26.3 ± 2.6^{ab}**	**24.2 ± 0.7^{b}**	**23.3 ± 1.6 ^{b}**	**22.4 ± 2.2^{b}**	**27.4 ± 3.2^{ab}**	**0.031**	**0.168**	**0.007**
18:2n-6	6.8 ± 0.7^{ab}	6.6 ± 0.2 ^{ab}	5.9 ± 0.1 ^{ab}	5.5 ± 0.7^{b}	6.1 ± 1.1^{ab}	7.4 ± 0.1^{a}	0.710	0.412	0.004
20:4n-6	2.3 ± 0.1^{a}	1.6 ± 0.1^{bc}	2.1 ± 0.3^{ab}	1.9 ± 0.2 ^{abc}	1.8 ± 0.3 ^{abc}	1.4 ± 0.2^{c}	0.017	0.008	0.10
Total n-6 PUFA[3]	**12.0 ± 0.6**	**10.8 ± 0.3**	**10.5 ± 1.0**	**9.7 ± 1.3**	**9.9 ± 1.0**	**11.6 ± 0.6**	**0.103**	**0.447**	**0.022**
18:3n-3	1.7 ± 0.3	1.9 ± 0.1	1.6 ± 0.1	1.5 ± 0.1	1.8 ± 0.3	2.0 ± 0.3	0.460	0.226	0.066
18:4n-3	0.4 ± 0.2	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.1	0.4 ± 0.0	0.824	0.329	0.156
20:4n-3	0.7 ± 0.2 ^{b}	0.9 ± 0.1 ^{ab}	0.7 ± 0.1 ^{b}	0.8 ± 0.1 ^{ab}	0.9 ± 0.2 ^{ab}	1.1 ± 0.1^{a}	0.023	0.80	0.058
20:5n-3	4.4 ± 0.5	5.0 ± 0.3	5.3 ± 0.4	4.7 ± 0.3	4.9 ± 0.2	5.2 ± 0.2	0.744	0.017	0.600
22:5n-3	0.9 ± 0.2	1.1 ± 0.1	1.2 ± 0.2	1.1 ± 0.0	1.1 ± 0.1	1.2 ± 0.1	0.288	0.049	0.833
22:6n-3	25.0 ± 3.5 ^{b}	29.0 ± 2.5 ^{ab}	30.9 ± 1.5 ^{ab}	33.3 ± 0.7^{a}	33.3 ± 3.4 ^{a}	27.8 ± 2.9 ^{ab}	0.020	0.337	0.006
Total n-3 PUFA[4]	**33.2 ± 4.1 ^{b}**	**38.3 ± 2.7 ^{ab}**	**40.1 ± 1.0 ^{ab}**	**41.9 ± 0.6 ^{a}**	**42.6 ± 2.5 ^{a}**	**38.0 ± 3.0 ^{ab}**	**0.011**	**0.186**	**0.010**
Total PUFA[5]	**45.3 ± 3.5 ^{b}**	**49.2 ±3.0 ^{ab}**	**50.7 ± 0.3 ^{ab}**	**51.6 ± 1.2 ^{a}**	**52.6 ± 1.5^{a}**	**49.6 ± 2.6 ^{ab}**	**0.019**	**0.201**	**0.45**

Data are mean ± SD (n = 2). [1]Totals include 15:0, 20:0, 22:0 and 24:0 at up to 0.3%; [2]Totals include 16:1n-9, 20:1n-11, 20:1n-7, 22:1n-9 and 24:1n-9 at up to 1.9%; [3]Totals include 18:3n-6, 20:2n-6, 20:3n-6 and 22:5n-6 at up to 2.9%; [4]Totals include20:3n-3 at up to 0.2%; [5]Includes C16 PUFA at up to 0.1%

Table 6. Whole fish total amino acids (g.kg wet wt^{-1}) in diploid and triploid salmon fed low marine diets with differing micronutrient supplementation level. The supplemented amino acids (histidine, taurine and methionine) are marked with an asterisk (*). Superscripts denote significant differences between diets within ploidy (two-way ANOVA).

Ploidy (P)	**Diploids**			**Triploids**			***p*-values**		
Diet (D)	**L1**	**L2**	**L3**	**L1**	**L2**	**L3**	**Ploidy**	**Diet**	**P * D**
OH-pro	0.7±0.0	0.7±0.0	0.7±0.2	0.6±0.0	0.8±0.0	0.6±0.0	0.59	0.32	0.35
His*	3.9±0.0	4.1±0.1	4.1±0.2	4.0±0.1	4.1±0.0	3.9±0.1	0.64	0.42	0.61
Taurine*	1.2±0.0	1.1±0.0	1.2±0.1	1.4±0.1	1.3±0.0	1.2±0.0	**0.048**	0.29	0.65
Ser	6.7±0.0	7.0±0.2	6.9±0.1	6.9±0.0	7.0±0.0	6.6±0.0	0.72	0.07	0.06
Arg	9.0±0.0	9.2±0.1	9.0±0.2	9.0±0.3	9.2±0.0	8.7±0.1	0.59	0.16	0.73
Gly	9.1±0.1	9.2±0.1	8.9±0.3	9.5±0.9	9.2±0.0	8.8±0.2	0.74	0.52	0.77
Asp	17.0±1	18±1	17±1	17.3±0.6	17.9±0.2	17.6±0.3	0.67	0.31	0.93
Glu	23±0	24±0	22±1	22.7±0.6	23.1±0.1	22.4±0.1	0.64	0.19	0.91
Thr	7.6±0.1	7.9±0.1	7.9±0.1	7.7±0.1	7.9±0.0	7.6±0.1	0.76	0.09	0.24
Ala	9.9±0.1	10±0.2	9.9±0.3	9.8±0.0	10.1±0.1	9.9±0.0	0.67	0.22	0.82
Pro	5.9±0.0	6.2±0.1	6.0±0.2	6.1±0.2	6.1±0.0	5.9±0.1	0.79	0.30	0.58
Lys	15±1	16±0	16±1	15.3±0.8	16.1±0.3	16.0±0.3	0.95	0.35	0.84
Tyr	5.3±0.0	5.4±0.0	5.5±0.1	5.3±0.2	5.5±0.0	5.2±0.1	0.60	0.23	0.17
Met*	5.0±0.0	5.2±0.1	5.1±0.1	5.1±0.0	5.2±0.0	4.9±0.1	0.67	0.08	0.09
Val	8.8±0.1	9.2±0.1	8.7±0.5	8.4±0.0	8.6±0.2	8.7±0.2	0.16	0.44	0.63
Ile	7.0±0.1	5.5±1.9	7.0±0.4	6.7±0.0	7.0±0.2	7.0±0.2	0.61	0.63	0.55
Leu	13±0.0	13±0.2	13±0.4	12.6±0.2	13.0±0.1	12.6±0.3	0.63	0.11	0.69
Phe	6.8±0.0	6.9±0.1	7.0±0.1	6.9±0.2	7.1±0.0	6.6±0.1	0.87	0.39	0.21

Data are presented as mean ± SD (n=2).

Table 7. Free amino acids and N-metabolites within white muscle tissues (μmol / 100g wet wt) of diploid and triploid salmon fed low marine diets with differing micronutrient supplementation level. Only the N-metabolites being significantly affected are shown (two-way ANOVA, Tukey $p < 0.05$, Kruskall Wallis when not fulfilling ANOVA assumptions). Histidine and taurine were supplemented in graded levels. Significant effect is highlighted in bold and superscripts denote significant differences between diets within ploidy (two-way ANOVA).

Ploidy (P)	**Diploids**			**Triploids**			***p*-values**		
Diet (D)	**L1**	**L2**	**L3**	**L1**	**L2**	**L3**	**Ploidy**	**Diet**	**P * D**
Taurine*	195±21	124±7	195±46	266±19	222±47	260±22	**0.020**	0.192	0.85
Asp	9±0.3	10±2.	9±0.4	12±1	13±0.6	15±0.7	**0.008**	0.41	0.40
OH-pro	19±11	40±12	25±15	53±5	45±7	48±7	**0.021**	0.81	0.44
Thr	55±2^{b}	65±1^{a}	68±5^{a}	45±1^{b}	55±4^{a}	53±4^{a}	0.24	**0.019**	0.69
Glu	60±5	55±4	57±3	66±3	67±5	71±1	**0.021**	0.78	0.58
Gln	22±3	26±8	23±5	35±0.5	30±2	34±1	**0.035**	0.99	0.62
Val	39±4	27±3	37±5	23±1	27±0.1	28±0.1	**0.024**	0.26	0.11
Cystath	4±0.3^{a}	1±0.3^{b}	3±1^{b}	5±0.4^{a}	2±0.1^{b}	1±0.1^{b}	0.85	**0.004**	0.13
Ile	23±1	13±2	20±4	11±0.1	14±0.6	14±0.1	**0.025**	0.32	0.12
Leu	36±2	25±1	34±6	22±2	26±1	26±1	**0.025**	0.26	0.06
β-Ala	69±14	63±12	41±5	104±3	105±25	93±11	**0.006**	0.315	0.80
Lys	23±3	15±2	24±2	10±1	14±3	15±1	**0.007**	0.17	0.09
Anserine	1810±71	1972±184	21441	1560±7	1756±15	1710±9	**0.014**	0.057	0.41

Data are presented as mean ± SD (n=2). Muscle N-metabolites (μmol/100g wet wt, n=2), Cystath, cystathionine.

Table 8. Concentrations of vitamins (mg kg^{-1} wet wt) in whole body, muscle, liver and gill in diploid and triploid salmon fed low marine diets with differing micronutrient supplementation level (Diets L1, L2 and L3). The supplemented vitamins are marked with an asterisk. Significant effect is highlighted in bold and superscripts denote significant differences between diets within ploidy (two-way ANOVA).

Ploidy (P)	**Diploid**			**Triploid**			***p*-values**		
Diet (D)	**L1**	**L2**	**L3**	**L1**	**L2**	**L3**	**Ploidy**	**Diet**	**P * D**
Whole body									
Biotin*	63±4	67±10	60±4	80±4	74±9	74±4	0.129	0.925	0.546
Folate*	0.21±0.04	0.27±0.05	0.30±0.01	0.27±0.01	0.26±0.01	0.27±0.01	0.084	0.149	**0.035**
Niacin*	43±3^{a}	48±4^{ab}	54±4^{b}	41±1^{a}	45±1^{ab}	49±2^{b}	0.273	**0.006**	0.083
Pantothene*	5.3±2.1	7.3±0.4	8.0±1.9	5.5±0.6	7.4±0.8	6.9±0.3	0.372	**0.051**	0.184
Riboflavine*	1.60±0.14^{b}	1.75±0.07^{b}	1.90±0.14^{b}	1.50±0.00^{a}	1.55±0.21^{a}	1.50±0.00^{a}	**0.016**	0.286	0.286
Thiamin*	0.70±0.14	0.80±0.14	0.90±0.14	0.75±0.07	0.80±0.00	0.80±0.00	0.791	0.304	0.609
Vit-C*	11.1±1.3^{a}	18.5±0.1^{ab}	26±10^{b}	12.6±0.5^{a}	19.7±1.5^{ab}	23.1±0.6^{b}	0.994	**0.015**	0.746
α-TOH*	28±0^{a}	41±0^{c}	48±2^{c}	28±1^{a}	30±3^{bc}	40±4^{c}	**<0.001**	**<0.001**	**0.037**
γ-TOH	2.8±0.4^{b}	2.6±0.1^{b}	1.7±0.0^{a}	3.1±0.4^{b}	2.6±0.3^{b}	1.6±0.1^{a}	0.922	**<0.001**	0.559
Muscle									
Vit-B6*	5.6±0.1	6.3±1.1	5.0±2.4	4.8±0.4	5.3±0.4	5.8±0.4	0.331	0.416	0.593
Riboflavin*	1.10±0.00	0.95±0.07	1.15±0.21	1.10±0.00	1.05±0.07	1.05±0.07	0.631	0.475	0.475
Thiamin*	0.55±0.21	0.80±0.28	0.55±0.21	0.85±0.07	0.70±0.14	0.90±0.42	0.128	0.962	0.594
α-TOH*	12.0±0.0	14.5±0.7	17.0±5.7	12.0±4.2	13.0±0.0	16.0±2.8	0.521	0.063	0.981
γ-TOH	1.60±0.14^{b}	1.25±0.07^{a}	0.90±0.28^{a}	1.85±0.35^{b}	1.25±0.07^{a}	0.80±0.14^{a}	0.527	**<0.001**	0.594
Liver									
Folate*	7.4±1.6	8.5±0.8	7.9±0.9	7.3±0.8	8.9±0.7	9.4±0.7	0.689	0.132	0.281
A1*	9.5±2.1^{a}	12.0±2.8^{a}	21.5±6.4^{b}	7.5±2.1^{a}	14.0±5.7^{a}	19.0±2.8^{b}	0.446	**0.012**	0.746
A2	70±12^{a}	83±21^{a}	135±21^{b}	51±5^{a}	79±30^{a}	115±7^{b}	0.089	**0.004**	0.849
C*	82±5^{a}	108±18^{b}	114±2^{c}	78±7^{a}	102±5^{b}	140±10^{c}	0.914	**<0.001**	0.052
K1^{1}	40±9	37±12	31±4	20±8	12±3	17±0	**0.001**	**0.004**	0.238
MK4^{1}	31±4	34±10	40±5	14±0	14±3	17±1	**<0.001**	0.051	0.292
Gill									
Pantothene*	5.3±1.8	8.9±1.1	9.1±0.1	7.2	7.3±0.0	6.1±3.0	0.423	0.416	0.248

Data are presented as mean ± SD (n=2). ^{1}Menadione sodium bisulfate (vitamin K_3) was added.

Table 9. Concentrations of minerals (mg kg^{-1} wet wt) in whole body of diploid and triploid salmon fed low marine diets with differing micronutrient supplementation level. The supplemented elements are marked with an asterisk. Significant effect is highlighted in bold (two-way ANOVA)

Ploidy (P)	**Dip**			**Trip**			***p*-values**		
Diet (D)	**L1**	**L2**	**L3**	**L1**	**L2**	**L3**	**Ploidy**	**Diet**	**P *D**
Ca*	3782±1018	4788±1182	4634±565	4094±684	3536±378	3850±981	0.28	0.87	0.45
Cu*	0.98±0	0.96±0	1±0	0.9±0	0.9±0	0.85±0	**0.01**	0.96	0.36
Fe*	9.03±0.7	8.8±0	10±1	10±0.8	10±0.7	10±0.3	0.24	0.27	0.7
I*	0.08±0	n.d.	0.12±0	0.30±0.3	0.14±0	0.25±0.1	0.11	0.66	0.61
K	3528±40	3663±18	3469±118	3523±2	3570±56	3609±262	0.84	0.54	0.43
Mn*	1.6±0.4	1.8±0.2	2±0	1.7±0.2	1.3±0	1±0.3	0.19	0.83	0.43
Mg	274±3	292±7	283±16	291±6	277±7	287±33	0.85	0.96	0.39
Na	551±24	605±88	588±9	669±56	600±5	589±63	0.24	0.83	0.23
P	3925±369	4616±748	4423±352	4135±324	3918±220	4064±560	0.33	0.73	0.42
Se*	0.22±0	0.25±0	0.26±0	0.25±0	0.2±0	0.3±0	0.46	0.09	0.60
Zn*	32±1.8	42±11	34±6	39±6	28±0.8	32±1	0.19	0.83	0.43

Data are presented as mean ± SD (n=2).

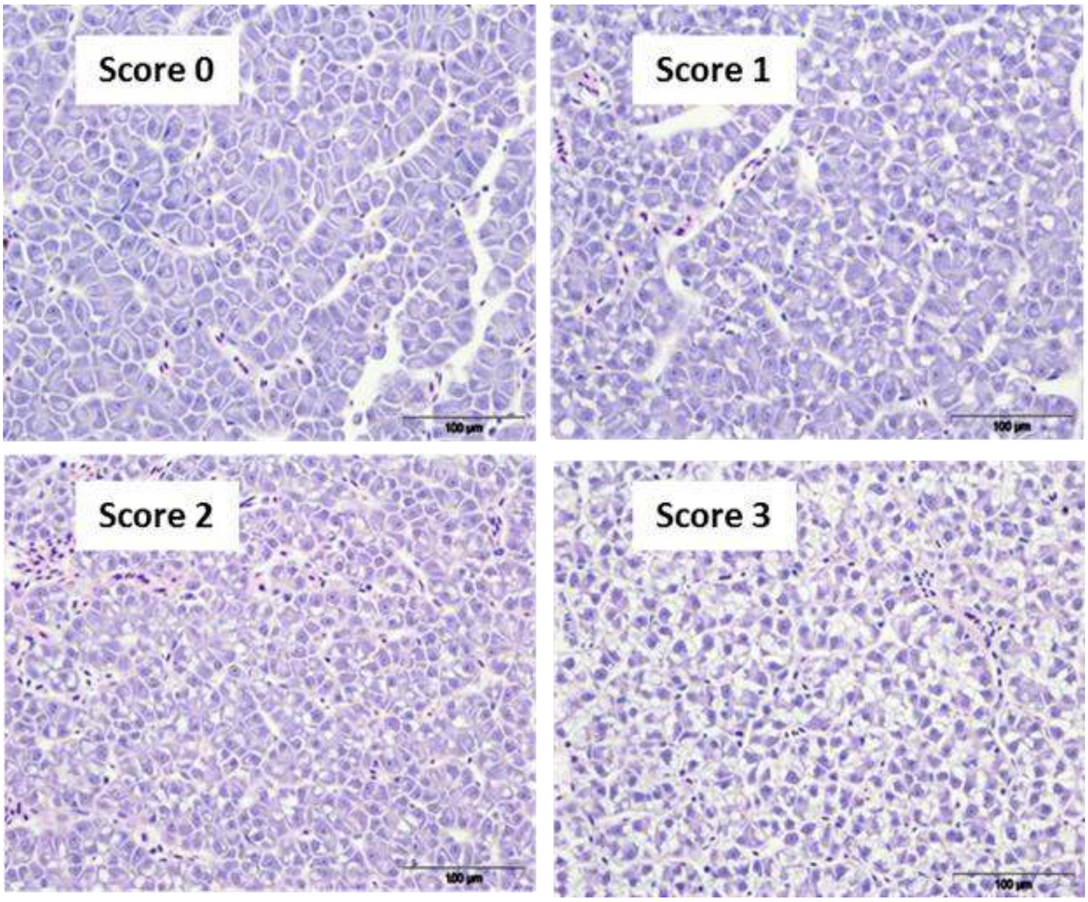


Figure 1.

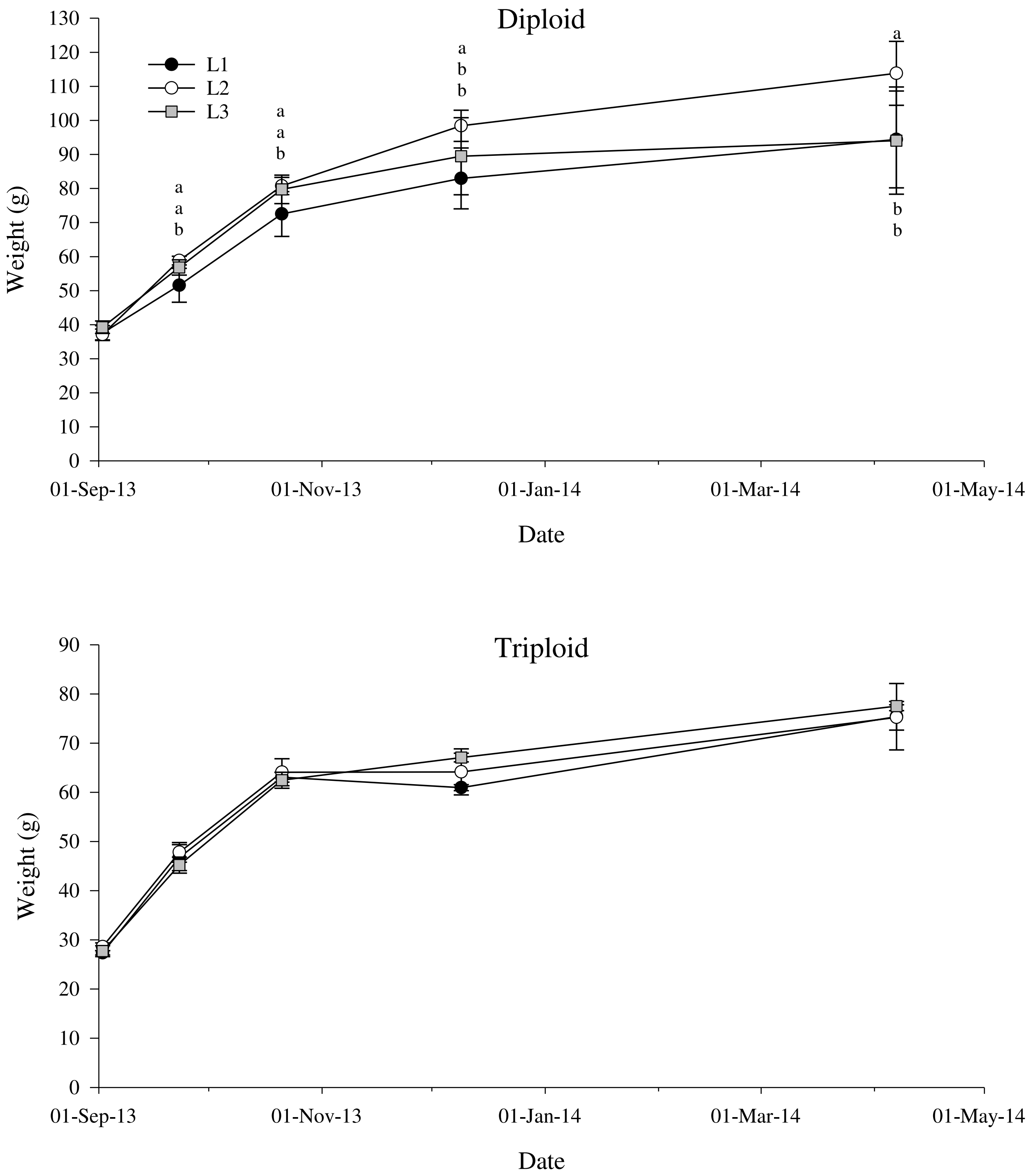
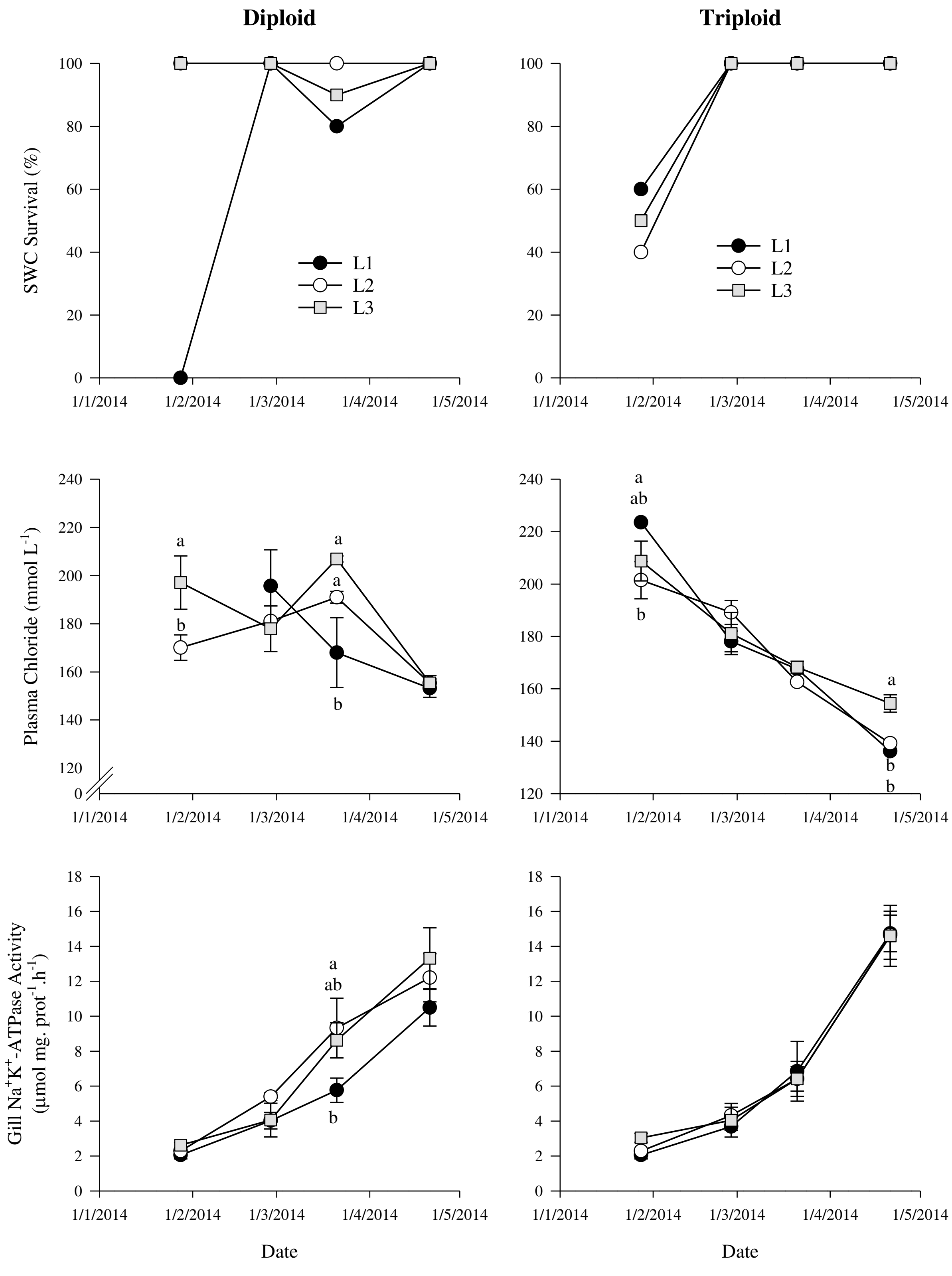

Diploid
L1
L2
L3
Weight (g)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
a
a
b
a
a
b
a
b
b
a
b
b
01-Sep-13
01-Nov-13
01-Jan-14
01-Mar-14
01-May-14
Date
Triploid
Weight (g)
90
80
70
60
50
40
30
20
10
0
01-Sep-13
01-Nov-13
01-Jan-14
01-Mar-14
01-May-14
Date

Figure 2.


Diploid
Triploid
SWC Survival (%)
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20
40
60
80
100
L1
L2
L3
Plasma Chloride (mmol L^{-1})
0
120
140
160
180
200
220
240
a
b
a
a
b
ab
Gill Na^{+}K^{+}-ATPase Activity (µmol mg. prot^{-1}.h^{-1})
0
2
4
6
8
10
12
14
16
18
1/1/2014
1/2/2014
1/3/2014
1/4/2014
1/5/2014
Date

Figure 3.

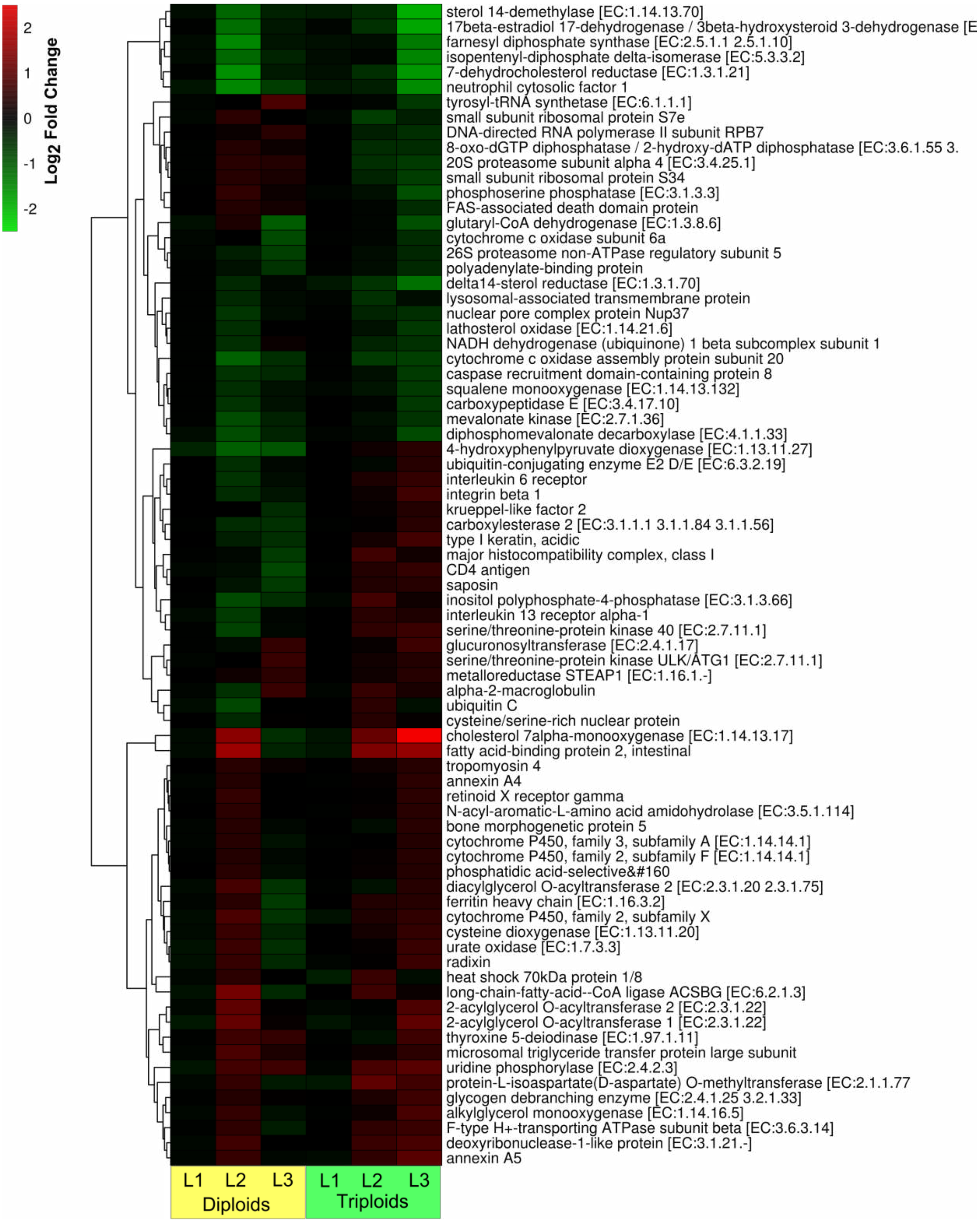

2
1
0
-1
-2
Log2 Fold Change
sterol 14-demethylase [EC:1.14.13.70]
17beta-estradiol 17-dehydrogenase / 3beta-hydroxysteroid 3-dehydrogenase [E
farnesyl diphosphate synthase [EC:2.5.1.1 2.5.1.10]
isopentenyl-diphosphate delta-isomerase [EC:5.3.3.2]
7-dehydrocholesterol reductase [EC:1.3.1.21]
neutrophil cytosolic factor 1
tyrosyl-tRNA synthetase [EC:6.1.1.1]
small subunit ribosomal protein S7e
DNA-directed RNA polymerase II subunit RPB7
8-oxo-dGTP diphosphatase / 2-hydroxy-dATP diphosphatase [EC:3.6.1.55 3.
20S proteasome subunit alpha 4 [EC:3.4.25.1]
small subunit ribosomal protein S34
phosphoserine phosphatase [EC:3.1.3.3]
FAS-associated death domain protein
glutaryl-CoA dehydrogenase [EC:1.3.8.6]
cytochrome c oxidase subunit 6a
26S proteasome non-ATPase regulatory subunit 5
polyadenylate-binding protein
delta14-sterol reductase [EC:1.3.1.70]
lysosomal-associated transmembrane protein
nuclear pore complex protein Nup37
lathosterol oxidase [EC:1.14.21.6]
NADH dehydrogenase (ubiquinone) 1 beta subcomplex subunit 1
cytochrome c oxidase assembly protein subunit 20
caspase recruitment domain-containing protein 8
squalene monooxygenase [EC:1.14.13.132]
carboxypeptidase E [EC:3.4.17.10]
mevalonate kinase [EC:2.7.1.36]
diphosphomevalonate decarboxylase [EC:4.1.1.33]
4-hydroxyphenylpyruvate dioxygenase [EC:1.13.11.27]
ubiquitin-conjugating enzyme E2 D/E [EC:6.3.2.19]
interleukin 6 receptor
integrin beta 1
krueppel-like factor 2
carboxylesterase 2 [EC:3.1.1.1 3.1.1.84 3.1.1.56]
type I keratin, acidic
major histocompatibility complex, class I
CD4 antigen
saposin
inositol polyphosphate-4-phosphatase [EC:3.1.3.66]
interleukin 13 receptor alpha-1
serine/threonine-protein kinase 40 [EC:2.7.11.1]
glucuronosyltransferase [EC:2.4.1.17]
serine/threonine-protein kinase ULK/ATG1 [EC:2.7.11.1]
metalloreductase STEAP1 [EC:1.16.1.-]
alpha-2-macroglobulin
ubiquitin C
cysteine/serine-rich nuclear protein
cholesterol 7alpha-monooxygenase [EC:1.14.13.17]
fatty acid-binding protein 2, intestinal
tropomyosin 4
annexin A4
retinoid X receptor gamma
N-acyl-aromatic-L-amino acid amidohydrolase [EC:3.5.1.114]
bone morphogenetic protein 5
cytochrome P450, family 3, subfamily A [EC:1.14.14.1]
cytochrome P450, family 2, subfamily F [EC:1.14.14.1]
phosphatidic acid-selective&#160
diacylglycerol O-acyltransferase 2 [EC:2.3.1.20 2.3.1.75]
ferritin heavy chain [EC:1.16.3.2]
cytochrome P450, family 2, subfamily X
cysteine dioxygenase [EC:1.13.11.20]
urate oxidase [EC:1.7.3.3]
radixin
heat shock 70kDa protein 1/8
long-chain-fatty-acid--CoA ligase ACSBG [EC:6.2.1.3]
2-acylglycerol O-acyltransferase 2 [EC:2.3.1.22]
2-acylglycerol O-acyltransferase 1 [EC:2.3.1.22]
thyroxine 5-deiodinase [EC:1.97.1.11]
microsomal triglyceride transfer protein large subunit
uridine phosphorylase [EC:2.4.2.3]
protein-L-isoaspartate(D-aspartate) O-methyltransferase [EC:2.1.1.77
glycogen debranching enzyme [EC:2.4.1.25 3.2.1.33]
alkylglycerol monooxygenase [EC:1.14.16.5]
F-type H+-transporting ATPase subunit beta [EC:3.6.3.14]
deoxyribonuclease-1-like protein [EC:3.1.21.-]
annexin A5
L1
L2
L3
Diploids
L1
L2
L3
Triploids

Figure 4

Supplementary File 1.

	L1-L3
14:0	5.3 ± 0.2
16:0	11.8 ± 0.3
18:0	2.5 ± 0.0
Total Saturates[1]	**25.7 ± 0.3**
16:1n-7	3.6 ± 0.1
18:1n-9	26.3 ± 0.2
18:1n-7	2.7 ± 0.1
20:1n-9	3.9 ± 0.2
22:1n-11	4.7 ± 0.2
Total Monoenes[2]	**42.8 ± 0.6**
18:2n-6	12.9 ± 0.1
20:4n-6	0.3 ± 0.0
Total n-6 PUFA[3]	**13.5 ± 0.1**
18:3n-3	6.9 ± 1.1
18:4n-3	1.1 ± 0.0
20:4n-3	0.3 ± 0.0
20:5n-3	4.5 ± 0.1
22:5n-3	0.5 ± 0.0
22:6n-3	3.6 ± 0.1
Total n-3 PUFA[4]	**16.8 ± 0.9**
Total PUFA[5]	**31.5 ± 0.8**

Values are the averaged data for the L1, L2, and L3 in both 2 and 3 mm feeds (± SD provided to illustrate variance between feeds).

PUFA, polyunsaturated fatty acids.

[1] Totals include 14:0, 15:0, 20:0 and 22:0;

[2] Totals include 16:1n-9, 20:1n-11, 20:1n-722:1n-9 and 24:1n-9;

[3] Totals include 18:3n-6, 20:2n-6, and 22:5n-6;

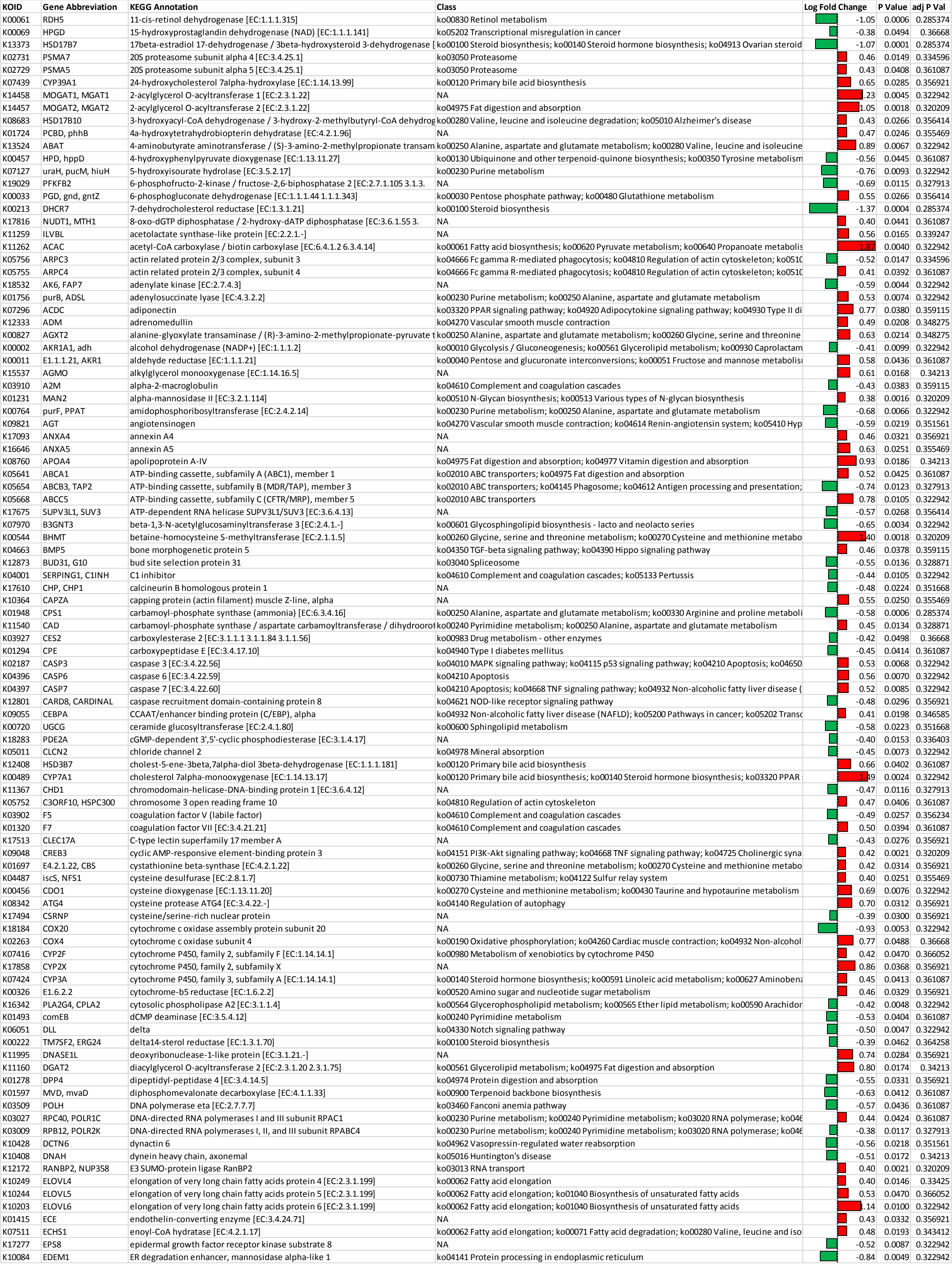
[4] Totals include 20:3n-3; [5] Totals include C16 PUFA.

Supplementary File 2.

Diet	Ploidy	Pathway	NGenes	Prop Down	Prop Up	FDR	Class
L2	DIPLOIDS	ko04710 Circadian rhythm	19	5.3%	52.6%	0.0124	Environmental adaptation
L3	DIPLOIDS	ko04910 Insulin signaling pathway	67	28.4%	13.4%	0.0185	Endocrine system
L2	TRIPLOIDS	ko00562 Inositol phosphate metabolism	34	8.8%	17.6%	0.0648	Carbohydrate metabolism
L2	TRIPLOIDS	ko04973 Carbohydrate digestion and absorption	16	6.3%	31.3%	0.0648	Digestive system
L2	TRIPLOIDS	ko03018 RNA degradation	53	34.0%	7.5%	0.0648	Folding, sorting and degradation
L2	TRIPLOIDS	ko04740 Olfactory transduction	11	0.0%	27.3%	0.0679	Sensory system
L2	TRIPLOIDS	ko04512 ECM-receptor interaction	45	6.7%	35.6%	0.0371	Signaling molecules and interaction
L2	TRIPLOIDS	ko04514 Cell adhesion molecules (CAMs)	71	9.9%	25.4%	0.0667	Signaling molecules and interaction
L3	TRIPLOIDS	ko00360 Phenylalanine metabolism	12	8.3%	33.3%	0.0854	Amino acid metabolism
L3	TRIPLOIDS	ko00010 Glycolysis / Gluconeogenesis	32	15.6%	40.6%	0.0854	Carbohydrate metabolism
L3	TRIPLOIDS	ko00040 Pentose and glucuronate interconversions	13	0.0%	53.8%	0.0967	Carbohydrate metabolism
L3	TRIPLOIDS	ko00052 Galactose metabolism	17	5.9%	41.2%	0.0807	Carbohydrate metabolism
L3	TRIPLOIDS	ko00500 Starch and sucrose metabolism	21	0.0%	52.4%	0.0025	Carbohydrate metabolism
L3	TRIPLOIDS	ko04510 Focal adhesion	120	17.5%	25.8%	0.0278	Cell communication
L3	TRIPLOIDS	ko04520 Adherens junction	56	12.5%	25.0%	0.0278	Cell communication
L3	TRIPLOIDS	ko04810 Regulation of actin cytoskeleton	116	15.5%	23.3%	0.0497	Cell motility
L3	TRIPLOIDS	ko04973 Carbohydrate digestion and absorption	16	6.3%	56.3%	0.0025	Digestive system
L3	TRIPLOIDS	ko04974 Protein digestion and absorption	41	12.2%	26.8%	0.0497	Digestive system
L3	TRIPLOIDS	ko04975 Fat digestion and absorption	19	15.8%	47.4%	0.0278	Digestive system
L3	TRIPLOIDS	ko04976 Bile secretion	43	11.6%	25.6%	0.0270	Digestive system
L3	TRIPLOIDS	ko03320 PPAR signaling pathway	43	11.6%	44.2%	0.0434	Endocrine system
L3	TRIPLOIDS	ko04910 Insulin signaling pathway	68	14.7%	25.0%	0.0497	Endocrine system
L3	TRIPLOIDS	ko04916 Melanogenesis	46	13.0%	23.9%	0.0436	Endocrine system
L3	TRIPLOIDS	ko00190 Oxidative phosphorylation	107	45.8%	15.9%	0.0872	Energy metabolism
L3	TRIPLOIDS	ko03018 RNA degradation	53	45.3%	5.7%	0.0053	Folding, sorting and degradation
L3	TRIPLOIDS	ko03050 Proteasome	40	72.5%	2.5%	0.0025	Folding, sorting and degradation
L3	TRIPLOIDS	ko04610 Complement and coagulation cascades	57	5.3%	54.4%	0.0587	Immune system
L3	TRIPLOIDS	ko04623 Cytosolic DNA-sensing pathway	36	36.1%	8.3%	0.0484	Immune system
L3	TRIPLOIDS	ko04662 B cell receptor signaling pathway	43	23.3%	30.2%	0.0967	Immune system
L3	TRIPLOIDS	ko04670 Leukocyte transendothelial migration	64	20.3%	32.8%	0.0293	Immune system
L3	TRIPLOIDS	ko04672 Intestinal immune network for IgA production	26	7.7%	26.9%	0.0232	Immune system
L3	TRIPLOIDS	ko00100 Steroid biosynthesis	14	57.1%	0.0%	0.0233	Lipid metabolism
L3	TRIPLOIDS	ko00140 Steroid hormone biosynthesis	23	4.3%	34.8%	0.0612	Lipid metabolism
L3	TRIPLOIDS	ko00564 Glycerophospholipid metabolism	48	14.6%	37.5%	0.0025	Lipid metabolism
L3	TRIPLOIDS	ko00830 Retinol metabolism	22	9.1%	45.5%	0.0340	Metabolism of cofactors and vitamins
L3	TRIPLOIDS	ko00900 Terpenoid backbone biosynthesis	16	50.0%	0.0%	0.0270	Metabolism of terpenoids and polyketides
L3	TRIPLOIDS	ko00230 Purine metabolism	111	27.9%	17.1%	0.0755	Nucleotide metabolism
L3	TRIPLOIDS	ko00240 Pyrimidine metabolism	73	35.6%	8.2%	0.0270	Nucleotide metabolism
L3	TRIPLOIDS	ko03420 Nucleotide excision repair	36	44.4%	11.1%	0.0325	Replication and repair
L3	TRIPLOIDS	ko04740 Olfactory transduction	11	0.0%	27.3%	0.0293	Sensory system
L3	TRIPLOIDS	ko04742 Taste transduction	12	0.0%	16.7%	0.0484	Sensory system
L3	TRIPLOIDS	ko04012 ErbB signaling pathway	50	14.0%	34.0%	0.0807	Signal transduction
L3	TRIPLOIDS	ko04020 Calcium signaling pathway	89	13.5%	20.2%	0.0445	Signal transduction
L3	TRIPLOIDS	ko04310 Wnt signaling pathway	73	15.1%	26.0%	0.0379	Signal transduction
L3	TRIPLOIDS	ko04340 Hedgehog signaling pathway	23	13.0%	26.1%	0.0325	Signal transduction
L3	TRIPLOIDS	ko04512 ECM-receptor interaction	45	20.0%	24.4%	0.0484	Signaling molecules and interaction
L3	TRIPLOIDS	ko04514 Cell adhesion molecules (CAMs)	71	11.3%	25.4%	0.0025	Signaling molecules and interaction
L3	TRIPLOIDS	ko03020 RNA polymerase	27	44.4%	0.0%	0.0053	Transcription
L3	TRIPLOIDS	ko03040 Spliceosome	111	43.2%	11.7%	0.0235	Transcription
L3	TRIPLOIDS	ko03010 Ribosome	120	61.7%	5.8%	0.0270	Translation
L3	TRIPLOIDS	ko00980 Metabolism of xenobiotics by cytochrome P450	15	0.0%	46.7%	0.0278	Xenobiotics biodegradation and metabolism

Supplementary File 3.

Diploid L2 vs L1



KOID	Gene Abbreviation	KEGG Annotation	Class	Log Fold Change	P Value	adj P Val
K00061	RDH5	11-cis-retinol dehydrogenase [EC:1.1.1.315]	ko00830 Retinol metabolism	-1.05	0.0006	0.285374
K00069	HPGD	15-hydroxyprostaglandin dehydrogenase (NAD) [EC:1.1.1.141]	ko05202 Transcriptional misregulation in cancer	-0.38	0.0494	0.36668
K13373	HSD17B7	17beta-estradiol 17-dehydrogenase / 3beta-hydroxysteroid 3-dehydrogenase [	ko00100 Steroid biosynthesis; ko00140 Steroid hormone biosynthesis; ko04913 Ovarian steroid	-1.07	0.0001	0.285374
K02731	PSMA7	20S proteasome subunit alpha 4 [EC:3.4.25.1]	ko03050 Proteasome	0.46	0.0149	0.334596
K02729	PSMA5	20S proteasome subunit alpha 5 [EC:3.4.25.1]	ko03050 Proteasome	0.43	0.0408	0.361087
K07439	CYP39A1	24-hydroxycholesterol 7alpha-hydroxylase [EC:1.14.13.99]	ko00120 Primary bile acid biosynthesis	0.65	0.0285	0.356921
K14458	MOGAT1, MGAT1	2-acylglycerol O-acyltransferase 1 [EC:2.3.1.22]	NA	1.23	0.0045	0.322942
K14457	MOGAT2, MGAT2	2-acylglycerol O-acyltransferase 2 [EC:2.3.1.22]	ko04975 Fat digestion and absorption	1.05	0.0018	0.320209
K08683	HSD17B10	3-hydroxyacyl-CoA dehydrogenase / 3-hydroxy-2-methylbutyryl-CoA dehydrog	ko00280 Valine, leucine and isoleucine degradation; ko05010 Alzheimer's disease	0.43	0.0266	0.356414
K01724	PCBD, phhB	4a-hydroxytetrahydrobiopterin dehydratase [EC:4.2.1.96]	NA	0.47	0.0246	0.355469
K13524	ABAT	4-aminobutyrate aminotransferase / (S)-3-amino-2-methylpropionate transam	ko00250 Alanine, aspartate and glutamate metabolism; ko00280 Valine, leucine and isoleucine	0.89	0.0067	0.322942
K00457	HPD, hppD	4-hydroxyphenylpyruvate dioxygenase [EC:1.13.11.27]	ko00130 Ubiquinone and other terpenoid-quinone biosynthesis; ko00350 Tyrosine metabolism	-0.56	0.0445	0.361087
K07127	uraH, pucM, hiuH	5-hydroxyisourate hydrolase [EC:3.5.2.17]	ko00230 Purine metabolism	-0.76	0.0093	0.322942
K19029	PFKFB2	6-phosphofructo-2-kinase / fructose-2,6-biphosphatase 2 [EC:2.7.1.105 3.1.3.	NA	-0.69	0.0115	0.327913
K00033	PGD, gnd, gntZ	6-phosphogluconate dehydrogenase [EC:1.1.1.44 1.1.1.343]	ko00030 Pentose phosphate pathway; ko00480 Glutathione metabolism	0.55	0.0266	0.356414
K00213	DHCR7	7-dehydrocholesterol reductase [EC:1.3.1.21]	ko00100 Steroid biosynthesis	-1.37	0.0004	0.285374
K17816	NUDT1, MTH1	8-oxo-dGTP diphosphatase / 2-hydroxy-dATP diphosphatase [EC:3.6.1.55 3.	NA	0.40	0.0441	0.361087
K11259	ILVBL	acetolactate synthase-like protein [EC:2.2.1.-]	NA	0.56	0.0165	0.339247
K11262	ACAC	acetyl-CoA carboxylase / biotin carboxylase [EC:6.4.1.2 6.3.4.14]	ko00061 Fatty acid biosynthesis; ko00620 Pyruvate metabolism; ko00640 Propanoate metabolis	1.87	0.0040	0.322942
K05756	ARPC3	actin related protein 2/3 complex, subunit 3	ko04666 Fc gamma R-mediated phagocytosis; ko04810 Regulation of actin cytoskeleton; ko0510	-0.52	0.0147	0.334596
K05755	ARPC4	actin related protein 2/3 complex, subunit 4	ko04666 Fc gamma R-mediated phagocytosis; ko04810 Regulation of actin cytoskeleton; ko0510	0.41	0.0392	0.361087
K18532	AK6, FAP7	adenylate kinase [EC:2.7.4.3]	NA	-0.59	0.0044	0.322942
K01756	purB, ADSL	adenylosuccinate lyase [EC:4.3.2.2]	ko00230 Purine metabolism; ko00250 Alanine, aspartate and glutamate metabolism	0.53	0.0074	0.322942
K07296	ACDC	adiponectin	ko03320 PPAR signaling pathway; ko04920 Adipocytokine signaling pathway; ko04930 Type II di	0.77	0.0380	0.359115
K12333	ADM	adrenomedullin	ko04270 Vascular smooth muscle contraction	0.49	0.0208	0.348275
K00827	AGXT2	alanine-glyoxylate transaminase / (R)-3-amino-2-methylpropionate-pyruvate t	ko00250 Alanine, aspartate and glutamate metabolism; ko00260 Glycine, serine and threonine	0.63	0.0214	0.348275
K00002	AKR1A1, adh	alcohol dehydrogenase (NADP+) [EC:1.1.1.2]	ko00010 Glycolysis / Gluconeogenesis; ko00561 Glycerolipid metabolism; ko00930 Caprolactam	-0.41	0.0099	0.322942
K00011	E1.1.1.21, AKR1	aldehyde reductase [EC:1.1.1.21]	ko00040 Pentose and glucuronate interconversions; ko00051 Fructose and mannose metabolisı	0.58	0.0436	0.361087
K15537	AGMO	alkylglycerol monooxygenase [EC:1.14.16.5]	NA	0.61	0.0168	0.34213
K03910	A2M	alpha-2-macroglobulin	ko04610 Complement and coagulation cascades	-0.43	0.0383	0.359115
K01231	MAN2	alpha-mannosidase II [EC:3.2.1.114]	ko00510 N-Glycan biosynthesis; ko00513 Various types of N-glycan biosynthesis	0.38	0.0016	0.320209
K00764	purF, PPAT	amidophosphoribosyltransferase [EC:2.4.2.14]	ko00230 Purine metabolism; ko00250 Alanine, aspartate and glutamate metabolism	-0.68	0.0066	0.322942
K09821	AGT	angiotensinogen	ko04270 Vascular smooth muscle contraction; ko04614 Renin-angiotensin system; ko05410 Hyp	-0.59	0.0219	0.351561
K17093	ANXA4	annexin A4	NA	0.46	0.0321	0.356921
K16646	ANXA5	annexin A5	NA	0.63	0.0251	0.355469
K08760	APOA4	apolipoprotein A-IV	ko04975 Fat digestion and absorption; ko04977 Vitamin digestion and absorption	0.93	0.0186	0.34213
K05641	ABCA1	ATP-binding cassette, subfamily A (ABC1), member 1	ko02010 ABC transporters; ko04975 Fat digestion and absorption	0.52	0.0425	0.361087
K05654	ABCB3, TAP2	ATP-binding cassette, subfamily B (MDR/TAP), member 3	ko02010 ABC transporters; ko04145 Phagosome; ko04612 Antigen processing and presentation;	-0.74	0.0123	0.327913
K05668	ABCC5	ATP-binding cassette, subfamily C (CFTR/MRP), member 5	ko02010 ABC transporters	0.78	0.0105	0.322942
K17675	SUPV3L1, SUV3	ATP-dependent RNA helicase SUPV3L1/SUV3 [EC:3.6.4.13]	NA	-0.57	0.0268	0.356414
K07970	B3GNT3	beta-1,3-N-acetylglucosaminyltransferase 3 [EC:2.4.1.-]	ko00601 Glycosphingolipid biosynthesis - lacto and neolacto series	-0.65	0.0034	0.322942
K00544	BHMT	betaine-homocysteine S-methyltransferase [EC:2.1.1.5]	ko00260 Glycine, serine and threonine metabolism; ko00270 Cysteine and methionine metabo	1.40	0.0018	0.320209
K04663	BMP5	bone morphogenetic protein 5	ko04350 TGF-beta signaling pathway; ko04390 Hippo signaling pathway	0.46	0.0378	0.359115
K12873	BUD31, G10	bud site selection protein 31	ko03040 Spliceosome	-0.55	0.0136	0.328871
K04001	SERPING1, C1INH	C1 inhibitor	ko04610 Complement and coagulation cascades; ko05133 Pertussis	-0.44	0.0105	0.322942
K17610	CHP, CHP1	calcineurin B homologous protein 1	NA	-0.48	0.0224	0.351668
K10364	CAPZA	capping protein (actin filament) muscle Z-line, alpha	NA	0.55	0.0250	0.355469
K01948	CPS1	carbamoyl-phosphate synthase (ammonia) [EC:6.3.4.16]	ko00250 Alanine, aspartate and glutamate metabolism; ko00330 Arginine and proline metaboli	-0.58	0.0006	0.285374
K11540	CAD	carbamoyl-phosphate synthase / aspartate carbamoyltransferase / dihydroorot	ko00240 Pyrimidine metabolism; ko00250 Alanine, aspartate and glutamate metabolism	0.45	0.0134	0.328871
K03927	CES2	carboxylesterase 2 [EC:3.1.1.1 3.1.1.84 3.1.1.56]	ko00983 Drug metabolism - other enzymes	-0.42	0.0498	0.36668
K01294	CPE	carboxypeptidase E [EC:3.4.17.10]	ko04940 Type I diabetes mellitus	-0.45	0.0414	0.361087
K02187	CASP3	caspase 3 [EC:3.4.22.56]	ko04010 MAPK signaling pathway; ko04115 p53 signaling pathway; ko04210 Apoptosis; ko04650	0.53	0.0068	0.322942
K04396	CASP6	caspase 6 [EC:3.4.22.59]	ko04210 Apoptosis	0.56	0.0070	0.322942
K04397	CASP7	caspase 7 [EC:3.4.22.60]	ko04210 Apoptosis; ko04668 TNF signaling pathway; ko04932 Non-alcoholic fatty liver disease (	0.52	0.0085	0.322942
K12801	CARD8, CARDINAL	caspase recruitment domain-containing protein 8	ko04621 NOD-like receptor signaling pathway	-0.48	0.0296	0.356921
K09055	CEBPA	CCAAT/enhancer binding protein (C/EBP), alpha	ko04932 Non-alcoholic fatty liver disease (NAFLD); ko05200 Pathways in cancer; ko05202 Transc	0.41	0.0198	0.346585
K00720	UGCG	ceramide glucosyltransferase [EC:2.4.1.80]	ko00600 Sphingolipid metabolism	-0.58	0.0223	0.351668
K18283	PDE2A	cGMP-dependent 3',5'-cyclic phosphodiesterase [EC:3.1.4.17]	NA	-0.40	0.0153	0.336403
K05011	CLCN2	chloride channel 2	ko04978 Mineral absorption	-0.45	0.0073	0.322942
K12408	HSD3B7	cholest-5-ene-3beta,7alpha-diol 3beta-dehydrogenase [EC:1.1.1.181]	ko00120 Primary bile acid biosynthesis	0.66	0.0402	0.361087
K00489	CYP7A1	cholesterol 7alpha-monooxygenase [EC:1.14.13.17]	ko00120 Primary bile acid biosynthesis; ko00140 Steroid hormone biosynthesis; ko03320 PPAR	1.49	0.0024	0.322942
K11367	CHD1	chromodomain-helicase-DNA-binding protein 1 [EC:3.6.4.12]	NA	-0.47	0.0116	0.327913
K05752	C3ORF10, HSPC300	chromosome 3 open reading frame 10	ko04810 Regulation of actin cytoskeleton	0.47	0.0406	0.361087
K03902	F5	coagulation factor V (labile factor)	ko04610 Complement and coagulation cascades	-0.49	0.0257	0.356234
K01320	F7	coagulation factor VII [EC:3.4.21.21]	ko04610 Complement and coagulation cascades	0.50	0.0394	0.361087
K17513	CLEC17A	C-type lectin superfamily 17 member A	NA	-0.43	0.0276	0.356921
K09048	CREB3	cyclic AMP-responsive element-binding protein 3	ko04151 PI3K-Akt signaling pathway; ko04668 TNF signaling pathway; ko04725 Cholinergic syna	0.42	0.0021	0.320209
K01697	E4.2.1.22, CBS	cystathionine beta-synthase [EC:4.2.1.22]	ko00260 Glycine, serine and threonine metabolism; ko00270 Cysteine and methionine metabo	0.42	0.0314	0.356921
K04487	iscS, NFS1	cysteine desulfurase [EC:2.8.1.7]	ko00730 Thiamine metabolism; ko04122 Sulfur relay system	0.40	0.0251	0.355469
K00456	CDO1	cysteine dioxygenase [EC:1.13.11.20]	ko00270 Cysteine and methionine metabolism; ko00430 Taurine and hypotaurine metabolism	0.69	0.0076	0.322942
K08342	ATG4	cysteine protease ATG4 [EC:3.4.22.-]	ko04140 Regulation of autophagy	0.70	0.0312	0.356921
K17494	CSRNP	cysteine/serine-rich nuclear protein	NA	-0.39	0.0300	0.356921
K18184	COX20	cytochrome c oxidase assembly protein subunit 20	NA	-0.93	0.0053	0.322942
K02263	COX4	cytochrome c oxidase subunit 4	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932 Non-alcoholi	0.77	0.0488	0.36668
K07416	CYP2F	cytochrome P450, family 2, subfamily F [EC:1.14.14.1]	ko00980 Metabolism of xenobiotics by cytochrome P450	0.42	0.0470	0.366052
K17858	CYP2X	cytochrome P450, family 2, subfamily X	NA	0.86	0.0368	0.356921
K07424	CYP3A	cytochrome P450, family 3, subfamily A [EC:1.14.14.1]	ko00140 Steroid hormone biosynthesis; ko00591 Linoleic acid metabolism; ko00627 Aminobenz	0.45	0.0413	0.361087
K00326	E1.6.2.2	cytochrome-b5 reductase [EC:1.6.2.2]	ko00520 Amino sugar and nucleotide sugar metabolism	0.46	0.0329	0.356921
K16342	PLA2G4, CPLA2	cytosolic phospholipase A2 [EC:3.1.1.4]	ko00564 Glycerophospholipid metabolism; ko00565 Ether lipid metabolism; ko00590 Arachidor	-0.42	0.0048	0.322942
K01493	comEB	dCMP deaminase [EC:3.5.4.12]	ko00240 Pyrimidine metabolism	-0.53	0.0404	0.361087
K06051	DLL	delta	ko04330 Notch signaling pathway	-0.50	0.0047	0.322942
K00222	TM7SF2, ERG24	delta14-sterol reductase [EC:1.3.1.70]	ko00100 Steroid biosynthesis	-0.39	0.0462	0.364258
K11995	DNASE1L	deoxyribonuclease-1-like protein [EC:3.1.21.-]	NA	0.74	0.0284	0.356921
K11160	DGAT2	diacylglycerol O-acyltransferase 2 [EC:2.3.1.20 2.3.1.75]	ko00561 Glycerolipid metabolism; ko04975 Fat digestion and absorption	0.80	0.0174	0.34213
K01278	DPP4	dipeptidyl-peptidase 4 [EC:3.4.14.5]	ko04974 Protein digestion and absorption	-0.55	0.0331	0.356921
K01597	MVD, mvaD	diphosphomevalonate decarboxylase [EC:4.1.1.33]	ko00900 Terpenoid backbone biosynthesis	-0.63	0.0412	0.361087
K03509	POLH	DNA polymerase eta [EC:2.7.7.7]	ko03460 Fanconi anemia pathway	-0.57	0.0436	0.361087
K03027	RPC40, POLR1C	DNA-directed RNA polymerases I and III subunit RPAC1	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polymerase; ko046	0.44	0.0424	0.361087
K03009	RPB12, POLR2K	DNA-directed RNA polymerases I, II, and III subunit RPABC4	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polymerase; ko046	-0.38	0.0117	0.327913
K10428	DCTN6	dynactin 6	ko04962 Vasopressin-regulated water reabsorption	-0.56	0.0218	0.351561
K10408	DNAH	dynein heavy chain, axonemal	ko05016 Huntington's disease	-0.51	0.0172	0.34213
K12172	RANBP2, NUP358	E3 SUMO-protein ligase RanBP2	ko03013 RNA transport	0.40	0.0021	0.320209
K10249	ELOVL4	elongation of very long chain fatty acids protein 4 [EC:2.3.1.199]	ko00062 Fatty acid elongation	0.40	0.0146	0.33425
K10244	ELOVL5	elongation of very long chain fatty acids protein 5 [EC:2.3.1.199]	ko00062 Fatty acid elongation; ko01040 Biosynthesis of unsaturated fatty acids	0.53	0.0470	0.366052
K10203	ELOVL6	elongation of very long chain fatty acids protein 6 [EC:2.3.1.199]	ko00062 Fatty acid elongation; ko01040 Biosynthesis of unsaturated fatty acids	1.14	0.0100	0.322942
K01415	ECE	endothelin-converting enzyme [EC:3.4.24.71]	NA	0.43	0.0332	0.356921
K07511	ECHS1	enoyl-CoA hydratase [EC:4.2.1.17]	ko00062 Fatty acid elongation; ko00071 Fatty acid degradation; ko00280 Valine, leucine and iso	0.48	0.0193	0.343412
K17277	EPS8	epidermal growth factor receptor kinase substrate 8	NA	-0.52	0.0087	0.322942
K10084	EDEM1	ER degradation enhancer, mannosidase alpha-like 1	ko04141 Protein processing in endoplasmic reticulum	-0.84	0.0049	0.322942

K00894	ETNK, EKI	ethanolamine kinase [EC:2.7.1.82]	ko00564 Glycerophospholipid metabolism	0.85	0.0125	0.327913
K15593	ETV5	ets translocation variant 5	ko05202 Transcriptional misregulation in cancer	-0.38	0.0443	0.361087
K18645	EIF4EBP3	eukaryotic translation initiation factor 4E binding protein 3	NA	0.81	0.0263	0.356414
K00787	FDPS	farnesyl diphosphate synthase [EC:2.5.1.1 2.5.1.10]	ko00900 Terpenoid backbone biosynthesis; ko05164 Influenza A; ko05166 HTLV-I infection	-1.23	0.0036	0.322942
K02373	FADD	FAS-associated death domain protein	ko04210 Apoptosis; ko04620 Toll-like receptor signaling pathway; ko04622 RIG-I-like receptor s	0.41	0.0193	0.343412
K10226	FADS2	fatty acid desaturase 2 (delta-6 desaturase) [EC:1.14.19.-]	ko00592 alpha-Linolenic acid metabolism; ko01040 Biosynthesis of unsaturated fatty acids; ko0	-0.44	0.0424	0.361087
K00665	FASN	fatty acid synthase, animal type [EC:2.3.1.85]	ko00061 Fatty acid biosynthesis; ko04910 Insulin signaling pathway	1.15	0.0329	0.356921
K08751	FABP2	fatty acid-binding protein 2, intestinal	ko03320 PPAR signaling pathway; ko04975 Fat digestion and absorption	1.68	0.0141	0.330936
K05717	FN1	fibronectin 1	ko04151 PI3K-Akt signaling pathway; ko04510 Focal adhesion; ko04512 ECM-receptor interactio	-0.42	0.0187	0.34213
K01930	FPGS	folylpolyglutamate synthase [EC:6.3.2.17]	ko00790 Folate biosynthesis	0.59	0.0111	0.327913
K03096	FRAT2	frequently rearranged in advanced T-cell lymphomas 2	ko04310 Wnt signaling pathway	0.68	0.0272	0.356732
K02133	ATPeF1B, ATP5B, ATP2	F-type H+-transporting ATPase subunit beta [EC:3.6.3.14]	ko00190 Oxidative phosphorylation; ko05010 Alzheimer's disease; ko05012 Parkinson's disease	0.50	0.0354	0.356921
K02135	ATPeF1E, ATP5E, ATP1	F-type H+-transporting ATPase subunit epsilon	ko00190 Oxidative phosphorylation; ko05010 Alzheimer's disease; ko05012 Parkinson's disease	0.47	0.0106	0.324819
K02140	ATPeFG, ATP5L, ATP20	F-type H+-transporting ATPase subunit g	ko00190 Oxidative phosphorylation	0.39	0.0468	0.366052
K02136	ATPeF1G, ATP5C1, ATP	F-type H+-transporting ATPase subunit gamma	ko00190 Oxidative phosphorylation; ko05010 Alzheimer's disease; ko05012 Parkinson's disease	0.42	0.0188	0.34213
K01555	FAH, fahA	fumarylacetoacetase [EC:3.7.1.2]	ko00350 Tyrosine metabolism; ko00643 Styrene degradation	0.95	0.0401	0.361087
K08892	FRK, PTK5	fyn-related kinase [EC:2.7.10.2]	NA	0.54	0.0056	0.322942
K13134	GEMIN6, SIP2	gem associated protein 6	ko03013 RNA transport	-0.39	0.0237	0.354448
K01084	G6PC	glucose-6-phosphatase [EC:3.1.3.9]	ko00010 Glycolysis / Gluconeogenesis; ko00052 Galactose metabolism; ko00500 Starch and sucr	-0.40	0.0132	0.328024
K02366	EXT1	glucuronyl/N-acetylglucosaminyl transferase EXT1 [EC:2.4.1.224 2.4.1.225]	ko00534 Glycosaminoglycan biosynthesis - heparan sulfate / heparin	-1.15	0.0044	0.322942
K11205	GCLM	glutamate--cysteine ligase regulatory subunit	ko00480 Glutathione metabolism	0.60	0.0042	0.322942
K01196	AGL	glycogen debranching enzyme [EC:2.4.1.25 3.2.1.33]	ko00500 Starch and sucrose metabolism	0.42	0.0307	0.356921
K18443	GBF1	golgi-specific brefeldin A-resistance guanine nucleotide exchange factor 1	NA	-0.60	0.0259	0.356414
K01495	GCH1, folE	GTP cyclohydrolase I [EC:3.5.4.16]	ko00790 Folate biosynthesis	0.70	0.0068	0.322942
K01487	E3.5.4.3, guaD	guanine deaminase [EC:3.5.4.3]	ko00230 Purine metabolism	0.79	0.0037	0.322942
K03283	HSPA1_8	heat shock 70kDa protein 1/8	ko03040 Spliceosome; ko04010 MAPK signaling pathway; ko04141 Protein processing in endopl	0.53	0.0173	0.34213
K00510	HMOX, hmuO, ho	heme oxygenase [EC:1.14.99.3]	ko00860 Porphyrin and chlorophyll metabolism; ko04978 Mineral absorption	1.28	0.0052	0.322942
K02503	HINT1, hinT, hit	histidine triad (HIT) family protein	NA	0.52	0.0417	0.361087
K11253	H3	histone H3	ko05034 Alcoholism; ko05202 Transcriptional misregulation in cancer; ko05322 Systemic lupus e	0.41	0.0363	0.356921
K11424	WHSC1, MMSET, NSD2	histone-lysine N-methyltransferase NSD2 [EC:2.1.1.43]	ko00310 Lysine degradation; ko05202 Transcriptional misregulation in cancer	-0.51	0.0457	0.363386
K00451	HGD, hmgA	homogentisate 1,2-dioxygenase [EC:1.13.11.5]	ko00350 Tyrosine metabolism; ko00643 Styrene degradation	0.76	0.0280	0.356921
K16817	PLA2G16	HRAS-like suppressor 3 [EC:3.1.1.32 3.1.1.4]	ko00564 Glycerophospholipid metabolism; ko00565 Ether lipid metabolism; ko00590 Arachidor	-0.53	0.0032	0.322942
K06092	INADL, PATJ	InaD-like protein	ko04390 Hippo signaling pathway; ko04530 Tight junction	-0.60	0.0402	0.361087
K00463	INDO	indoleamine 2,3-dioxygenase [EC:1.13.11.52]	ko00380 Tryptophan metabolism; ko05143 African trypanosomiasis	0.56	0.0374	0.359115
K15046	NS1BP	influenza virus NS1A-binding protein	ko05164 Influenza A	0.51	0.0068	0.322942
K01107	INPP1	inositol polyphosphate 1-phosphatase [EC:3.1.3.57]	ko00562 Inositol phosphate metabolism; ko04070 Phosphatidylinositol signaling system	-0.41	0.0327	0.356921
K01109	INPP4	inositol polyphosphate-4-phosphatase [EC:3.1.3.66]	ko00562 Inositol phosphate metabolism; ko04070 Phosphatidylinositol signaling system	-0.71	0.0101	0.322942
K05459	IGF1	insulin-like growth factor 1	ko04066 HIF-1 signaling pathway; ko04114 Oocyte meiosis; ko04115 p53 signaling pathway; ko0	0.64	0.0242	0.355469
K05719	ITGB1	integrin beta 1	ko04145 Phagosome; ko04151 PI3K-Akt signaling pathway; ko04360 Axon guidance; ko04510 Fo	-0.42	0.0205	0.348275
K05132	IFNGR1, CD119	interferon gamma receptor 1	ko04060 Cytokine-cytokine receptor interaction; ko04066 HIF-1 signaling pathway; ko04380 Ost	-0.72	0.0044	0.322942
K05076	IL13RA1	interleukin 13 receptor alpha-1	ko04060 Cytokine-cytokine receptor interaction; ko04630 Jak-STAT signaling pathway	-0.47	0.0403	0.361087
K05055	IL6R	interleukin 6 receptor	ko04060 Cytokine-cytokine receptor interaction; ko04066 HIF-1 signaling pathway; ko04151 PI3	-0.50	0.0093	0.322942
K05050	IL8RB, CXCR2	interleukin 8 receptor beta	ko04060 Cytokine-cytokine receptor interaction; ko04062 Chemokine signaling pathway; ko041	-0.51	0.0144	0.333013
K01823	idi, IDI	isopentenyl-diphosphate delta-isomerase [EC:5.3.3.2]	ko00900 Terpenoid backbone biosynthesis	-0.91	0.0232	0.353307
K00253	IVD, ivd	isovaleryl-CoA dehydrogenase [EC:1.3.8.4]	ko00280 Valine, leucine and isoleucine degradation	0.53	0.0176	0.34213
K03898	KNG	kininogen	ko04610 Complement and coagulation cascades	-0.41	0.0156	0.337954
K09228	KRAB	KRAB domain-containing zinc finger protein	NA	-0.72	0.0035	0.322942
K09208	KLF9S, BTEB	krueppel-like factor 9/13/14/16	NA	0.99	0.0049	0.322942
K01852	E5.4.99.7, LSS, ERG7	lanosterol synthase [EC:5.4.99.7]	ko00100 Steroid biosynthesis	-0.42	0.0410	0.361087
K00227	SC5DL, ERG3	lathosterol oxidase [EC:1.14.21.6]	ko00100 Steroid biosynthesis	-0.42	0.0355	0.356921
K02431	fucU, FUOM	L-fucose mutarotase [EC:5.1.3.29]	NA	-0.39	0.0372	0.359115
K15013	ACSBG	long-chain-fatty-acid--CoA ligase ACSBG [EC:6.2.1.3]	ko00071 Fatty acid degradation; ko03320 PPAR signaling pathway; ko04920 Adipocytokine signa	1.34	0.0022	0.320209
K03159	TNFRSF3, LTBR	lymphotoxin beta receptor TNFR superfamily member 3	ko04060 Cytokine-cytokine receptor interaction; ko04064 NF-kappa B signaling pathway; ko040	-0.49	0.0457	0.363326
K04294	LPAR3, EDG7	lysophosphatidic acid receptor 3	ko04080 Neuroactive ligand-receptor interaction; ko04151 PI3K-Akt signaling pathway	-0.99	0.0182	0.34213
K12387	LAPTM	lysosomal-associated transmembrane protein	ko04142 Lysosome	-0.38	0.0314	0.356921
K13646	PLOD3	lysyl hydroxylase/galactosyltransferase/glucosyltransferase [EC:1.14.11.4 2.4	ko00310 Lysine degradation; ko00514 Other types of O-glycan biosynthesis	-1.29	0.0028	0.322942
K04679	MADHIP, SARA	MAD, mothers against decapentaplegic interacting protein	ko04144 Endocytosis; ko04350 TGF-beta signaling pathway	-0.45	0.0226	0.351668
K09262	MEF2D	MADS-box transcription enhancer factor 2D	NA	-0.68	0.0049	0.322942
K00029	E1.1.1.40, maeB	malate dehydrogenase (oxaloacetate-decarboxylating)(NADP+) [EC:1.1.	ko00620 Pyruvate metabolism; ko00710 Carbon fixation in photosynthetic organisms	0.94	0.0158	0.337954
K00140	mmsA, iolA, ALDH6A1	malonate-semialdehyde dehydrogenase (acetylating) / methylmalon	ko00280 Valine, leucine and isoleucine degradation; ko00410 beta-Alanine metabolism; ko005	0.76	0.0019	0.320209
K06560	MRC	mannose receptor, C type	ko04145 Phagosome; ko05152 Tuberculosis	-0.52	0.0233	0.353307
K07994	MMP13	matrix metalloproteinase-13 (collagenase 3) [EC:3.4.24.-]	NA	-1.35	0.0263	0.356414
K08001	MMP23	matrix metalloproteinase-23 (CA-MMP) [EC:3.4.24.-]	NA	0.50	0.0313	0.356921
K01394	MMP3	matrix metalloproteinase-3 (stromelysin 1, progelatinase) [EC:3.4.24.17]	ko04668 TNF signaling pathway; ko05202 Transcriptional misregulation in cancer; ko05323 Rheu	-1.32	0.0232	0.353307
K01403	MMP9	matrix metalloproteinase-9 (gelatinase B) [EC:3.4.24.35]	ko04668 TNF signaling pathway; ko04670 Leukocyte transendothelial migration; ko04915 Estrog	-1.31	0.0164	0.339247
K05607	AUH	methylglutaconyl-CoA hydratase [EC:4.2.1.18]	ko00280 Valine, leucine and isoleucine degradation	0.42	0.0386	0.359621
K00869	E2.7.1.36, MVK, mvaK1	mevalonate kinase [EC:2.7.1.36]	ko00900 Terpenoid backbone biosynthesis; ko04146 Peroxisome	-0.71	0.0024	0.322942
K14463	MTTP, MTP	microsomal triglyceride transfer protein large subunit	ko04975 Fat digestion and absorption	0.79	0.0117	0.327913
K17885	MTCH	mitochondrial carrier	NA	0.42	0.0344	0.356921
K17781	TIM13	mitochondrial import inner membrane translocase subunit TIM13	NA	-0.40	0.0360	0.356921
K17804	TIM44	mitochondrial import inner membrane translocase subunit TIM44	NA	0.64	0.0193	0.343412
K17732	PMPCB, MAS1	mitochondrial-processing peptidase subunit beta [EC:3.4.24.64]	NA	0.59	0.0111	0.327913
K02539	MCL1	myeloid leukemia cell differntiation protein MCL-1	ko04151 PI3K-Akt signaling pathway; ko05206 MicroRNAs in cancer	0.68	0.0001	0.285374
K12751	MYL6	myosin light chain 6	ko04270 Vascular smooth muscle contraction	-0.53	0.0090	0.322942
K12757	MYL12	myosin regulatory light chain 12	ko04510 Focal adhesion; ko04530 Tight junction; ko04670 Leukocyte transendothelial migration	0.56	0.0129	0.328024
K03375	SIAT7E, ST6GalNAc V	N-acetylgalactosaminide alpha-2,6-sialyltransferase (sialyltran	ko00604 Glycosphingolipid biosynthesis - ganglio series	-0.44	0.0124	0.327913
K00781	SIAT6	N-acetyllactosaminide alpha-2,3-sialyltransferase (sialyltransferase 6) [EC:2	ko00513 Various types of N-glycan biosynthesis; ko00514 Other types of O-glycan biosynthesis;	-0.59	0.0038	0.322942
K18458	ACY3	N-acyl-aromatic-L-amino acid amidohydrolase [EC:3.5.1.114]	NA	0.47	0.0172	0.34213
K00775	E2.4.2.31, ART	NAD(P)-arginine ADP-ribosyltransferase [EC:2.4.2.31]	NA	-0.56	0.0214	0.348275
K00858	ppnK, NADK	NAD+ kinase [EC:2.7.1.23]	ko00760 Nicotinate and nicotinamide metabolism	-0.60	0.0056	0.322942
K03957	NDUFB1	NADH dehydrogenase (ubiquinone) 1 beta subcomplex subunit 1	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NAFLD); ko0501	-0.43	0.0342	0.356921
K03963	NDUFB7	NADH dehydrogenase (ubiquinone) 1 beta subcomplex subunit 7	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NAFLD); ko0501	0.38	0.0356	0.356921
K03968	NDUFC2	NADH dehydrogenase (ubiquinone) 1 subunit C2	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NAFLD); ko0501	-0.47	0.0423	0.361087
K03936	NDUFS3	NADH dehydrogenase (ubiquinone) Fe-S protein 3 [EC:1.6.5.3 1.6.99.3]	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NAFLD); ko0501	0.47	0.0314	0.356921
K08008	NOX, GP91	NADPH oxidase	ko04066 HIF-1 signaling pathway; ko04145 Phagosome; ko04380 Osteoclast differentiation; ko0	-0.44	0.0157	0.337954
K05750	NCKAP1, NAP125	NCK-associated protein 1	ko04810 Regulation of actin cytoskeleton	-0.43	0.0102	0.322942
K06757	NFASC	neurofascin	ko04514 Cell adhesion molecules (CAMs)	-0.44	0.0194	0.343412
K08011	NCF1, P47PHOX	neutrophil cytosolic factor 1	ko04062 Chemokine signaling pathway; ko04145 Phagosome; ko04380 Osteoclast differentiatic	-1.11	0.0077	0.322942
K00767	nadC, QPRT	nicotinate-nucleotide pyrophosphorylase (carboxylating) [EC:2.4.2.19]	ko00760 Nicotinate and nicotinamide metabolism	-0.56	0.0010	0.320209
K14461	NPC1L1	Niemann-Pick C1-like protein 1	ko04975 Fat digestion and absorption	-0.48	0.0320	0.356921
K18764	CCRN4L	nocturnin [EC:3.1.13.4]	NA	-0.50	0.0243	0.355469
K17108	GBA2	non-lysosomal glucosylceramidase [EC:3.2.1.45]	ko00511 Other glycan degradation; ko00600 Sphingolipid metabolism	-0.57	0.0338	0.356921
K14537	NUG2, GNL2	nuclear GTP-binding protein	ko03008 Ribosome biogenesis in eukaryotes	-0.39	0.0286	0.356921
K14302	NUP37	nuclear pore complex protein Nup37	ko03013 RNA transport	-0.50	0.0384	0.359115
K08064	NFYA	nuclear transcription factor Y, alpha	ko04612 Antigen processing and presentation; ko05152 Tuberculosis	-0.50	0.0035	0.322942
K03768	PPIB, ppiB	peptidyl-prolyl cis-trans isomerase B (cyclophilin B) [EC:5.2.1.8]	NA	-0.44	0.0452	0.363326
K13279	PRDX1	peroxiredoxin 1 [EC:1.11.1.15]	ko04146 Peroxisome	0.45	0.0093	0.322942
K17594	PHACTR3	phosphatase and actin regulator 3	NA	-1.66	0.0073	0.322942
K19404	LIPH_I	phosphatidic acid-selective&#160	NA	0.42	0.0304	0.356921
K01079	serB, PSPH	phosphoserine phosphatase [EC:3.1.3.3]	ko00260 Glycine, serine and threonine metabolism; ko00680 Methane metabolism	0.53	0.0432	0.361087

K01062	PAFAH	platelet-activating factor acetylhydrolase [EC:3.1.1.47]	ko00565 Ether lipid metabolism	🟥 0.39	0.0316	0.356921
K12862	PLRG1, PRL1, PRP46	pleiotropic regulator 1	ko03040 Spliceosome	🟩 -0.41	0.0354	0.356921
K04917	KCNK6	potassium channel subfamily K member 6	NA	🟥 0.43	0.0275	0.356921
K00318	PRODH	proline dehydrogenase [EC:1.5.-.-]	ko00330 Arginine and proline metabolism	🟩 -0.62	0.0120	0.327913
K14443	TOB	protein Tob/BTG	ko03018 RNA degradation	🟥 0.46	0.0044	0.322942
K18041	PTP4A	protein tyrosine phosphatase type IVA [EC:3.1.3.48]	NA	🟩 -0.44	0.0033	0.322942
K00573	E2.1.1.77, pcm	protein-L-isoaspartate(D-aspartate) O-methyltransferase [EC:2.1.1.77	NA	🟥 0.60	0.0480	0.366158
K01021	TPST	protein-tyrosine sulfotransferase [EC:2.8.2.20]	NA	🟥 0.60	0.0060	0.322942
K05762	RDX	radixin	ko04810 Regulation of actin cytoskeleton; ko05205 Proteoglycans in cancer; ko05206 MicroRNA	🟥 0.72	0.0206	0.348275
K07855	RERG	Ras-related and estrogen-regulated growth inhibitor	NA	🟥 0.46	0.0237	0.354448
K06109	RAB13	Ras-related protein Rab-13	ko04530 Tight junction	🟩 -0.39	0.0469	0.366052
K08847	RIPK3	receptor-interacting serine/threonine-protein kinase 3 [EC:2.7.11.1]	ko04623 Cytosolic DNA-sensing pathway; ko04668 TNF signaling pathway	🟩 -0.45	0.0104	0.322942
K06778	PTPRS	receptor-type tyrosine-protein phosphatase S [EC:3.1.3.48]	NA	🟩 -0.43	0.0105	0.322942
K10754	RFC1	replication factor C subunit 1	ko03030 DNA replication; ko03420 Nucleotide excision repair; ko03430 Mismatch repair	🟩 -0.45	0.0184	0.34213
K08526	NR2B3, RXRG	retinoid X receptor gamma	ko03320 PPAR signaling pathway; ko04920 Adipocytokine signaling pathway; ko05200 Pathways	🟥 0.54	0.0163	0.339247
K03539	RPP1, RPP30	ribonuclease P/MRP protein subunit RPP1 [EC:3.1.26.5]	ko03008 Ribosome biogenesis in eukaryotes; ko03013 RNA transport	🟥 0.63	0.0125	0.327913
K14000	RRBP1	ribosome-binding protein 1	ko04141 Protein processing in endoplasmic reticulum	🟩 -0.63	0.0204	0.348275
K15216	RRN3, TIFIA	RNA polymerase I-specific transcription initiation factor RRN3	NA	🟩 -0.60	0.0214	0.348275
K14411	MSI	RNA-binding protein Musashi	ko03015 mRNA surveillance pathway	🟩 -0.46	0.0090	0.322942
K00789	metK	S-adenosylmethionine synthetase [EC:2.5.1.6]	ko00270 Cysteine and methionine metabolism	🟩 -0.59	0.0177	0.34213
K00314	SARDH	sarcosine dehydrogenase [EC:1.5.8.3]	ko00260 Glycine, serine and threonine metabolism	🟥 0.65	0.0082	0.322942
K14381	SQSTM1	sequestosome 1	ko04380 Osteoclast differentiation	🟥 0.58	0.0195	0.343412
K00654	SPT	serine palmitoyltransferase [EC:2.3.1.50]	ko00600 Sphingolipid metabolism	🟩 -0.45	0.0134	0.328871
K16312	STK40, SHIK	serine/threonine-protein kinase 40 [EC:2.7.11.1]	NA	🟩 -0.61	0.0081	0.322942
K02977	RP-S27Ae, RPS27A	small subunit ribosomal protein S27Ae	ko03010 Ribosome	🟩 -0.45	0.0087	0.322942
K02978	RP-S27e, RPS27	small subunit ribosomal protein S27e	ko03010 Ribosome	🟩 -0.71	0.0128	0.328024
K17409	MRPS30	small subunit ribosomal protein S30	NA	🟥 0.41	0.0156	0.337954
K17412	MRPS34	small subunit ribosomal protein S34	NA	🟥 0.42	0.0249	0.355469
K02993	RP-S7e, RPS7	small subunit ribosomal protein S7e	ko03010 Ribosome	🟥 0.54	0.0291	0.356921
K05855	SYK	spleen tyrosine kinase [EC:2.7.10.2]	ko04064 NF-kappa B signaling pathway; ko04151 PI3K-Akt signaling pathway; ko04380 Osteocla	🟩 -0.40	0.0081	0.322942
K13219	SFPQ, PSF	splicing factor, proline- and glutamine-rich	NA	🟩 -0.70	0.0080	0.322942
K00511	SQLE, ERG1	squalene monooxygenase [EC:1.14.13.132]	ko00909 Sesquiterpenoid and triterpenoid biosynthesis	🟩 -0.44	0.0068	0.322942
K00507	SCD, desC	stearoyl-CoA desaturase (delta-9 desaturase) [EC:1.14.19.1]	ko01040 Biosynthesis of unsaturated fatty acids; ko03320 PPAR signaling pathway	🟥 1.04	0.0013	0.320209
K05917	CYP51	sterol 14-demethylase [EC:1.14.13.70]	ko00100 Steroid biosynthesis	🟩 -0.89	0.0105	0.322942
K06669	SMC3, CSPG6	structural maintenance of chromosome 3 (chondroitin sulfate proteoglyca	ko04110 Cell cycle; ko04111 Cell cycle - yeast; ko04113 Meiosis - yeast; ko04114 Oocyte meiosis	🟩 -0.65	0.0078	0.322942
K00237	SDHD, SDH4	succinate dehydrogenase (ubiquinone) membrane anchor subunit	ko00020 Citrate cycle (TCA cycle); ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic f	🟥 0.48	0.0222	0.351668
K17254	SDCBP	syntenin-1	NA	🟩 -0.67	0.0111	0.327913
K00384	trxB	thioredoxin reductase (NADPH) [EC:1.8.1.9]	ko00240 Pyrimidine metabolism; ko00450 Selenocompound metabolism	🟥 0.68	0.0001	0.285374
K07754	DIO3	thyroxine 5-deiodinase [EC:1.97.1.11]	NA	🟥 0.65	0.0338	0.356921
K12567	TTN	titin [EC:2.7.11.1]	ko05410 Hypertrophic cardiomyopathy (HCM); ko05414 Dilated cardiomyopathy	🟩 -0.92	0.0364	0.356921
K00616	E2.2.1.2, talA, talB	transaldolase [EC:2.2.1.2]	ko00030 Pentose phosphate pathway	🟥 0.56	0.0492	0.36668
K09275	TFCP2	transcription factor CP2 and related proteins	NA	🟥 0.42	0.0356	0.356921
K16796	SOX2	transcription factor SOX2 (SOX group B)	ko04390 Hippo signaling pathway	🟩 -0.40	0.0260	0.356414
K00615	E2.2.1.1, tktA, tktB	transketolase [EC:2.2.1.1]	ko00030 Pentose phosphate pathway; ko00710 Carbon fixation in photosynthetic organisms; ko	🟥 0.61	0.0016	0.320209
K03113	EIF1, SUI1	translation initiation factor 1	ko03013 RNA transport	🟩 -0.48	0.0263	0.356414
K03254	EIF3A	translation initiation factor 3 subunit A	ko03013 RNA transport	🟩 -0.49	0.0347	0.356921
K03247	EIF3H	translation initiation factor 3 subunit H	ko03013 RNA transport; ko05162 Measles	🟥 0.87	0.0264	0.356414
K03262	EIF5	translation initiation factor 5	ko03013 RNA transport	🟥 0.52	0.0098	0.322942
K01046	E3.1.1.3	triacylglycerol lipase [EC:3.1.1.3]	ko00561 Glycerolipid metabolism	🟩 -0.99	0.0049	0.322942
K12015	TRIM39	tripartite motif-containing protein 39 [EC:6.3.2.19]	NA	🟩 -0.50	0.0427	0.361087
K12034	TRIM69	tripartite motif-containing protein 69 [EC:6.3.2.19]	NA	🟩 -0.72	0.0097	0.322942
K10375	TPM4	tropomyosin 4	ko04260 Cardiac muscle contraction; ko05410 Hypertrophic cardiomyopathy (HCM); ko05414 Dil	🟥 0.44	0.0207	0.348275
K05865	TNNC1	troponin C, slow skeletal and cardiac muscles	ko04020 Calcium signaling pathway; ko04260 Cardiac muscle contraction; ko05410 Hypertrophic	🟩 -0.39	0.0004	0.285374
K17262	TBCB, CKAP1, ALF1	tubulin-folding cofactor B	NA	🟥 0.47	0.0091	0.322942
K05147	CD265, TNFRSF11A	tumor necrosis factor receptor superfamily, member 11a, activator	ko04060 Cytokine-cytokine receptor interaction; ko04064 NF-kappa B signaling pathway; ko043	🟩 -0.87	0.0019	0.320209
K06737	TACSTD1	tumor-associated calcium signal transducer 1	NA	🟥 0.38	0.0251	0.355469
K12842	SR140	U2-associated protein SR140	ko03040 Spliceosome	🟩 -0.45	0.0267	0.356414
K12626	LSM7	U6 snRNA-associated Sm-like protein LSm7	ko03018 RNA degradation; ko03040 Spliceosome	🟩 -0.54	0.0198	0.346585
K08770	UBC	ubiquitin C	ko03320 PPAR signaling pathway	🟩 -0.57	0.0180	0.34213
K10596	UBE4A	ubiquitin conjugation factor E4 A [EC:6.3.2.19]	ko04120 Ubiquitin mediated proteolysis	🟩 -0.50	0.0158	0.337954
K14016	UFD1	ubiquitin fusion degradation protein 1	ko04141 Protein processing in endoplasmic reticulum	🟥 0.38	0.0372	0.359115
K06689	UBE2D_E, UBC4, UBC5	ubiquitin-conjugating enzyme E2 D/E [EC:6.3.2.19]	ko04120 Ubiquitin mediated proteolysis; ko04141 Protein processing in endoplasmic reticulum	🟩 -0.44	0.0075	0.322942
K14012	SHP1, UBX1, NSFL1C	UBX domain-containing protein 1	ko04141 Protein processing in endoplasmic reticulum	🟥 0.40	0.0364	0.356921
K00365	uaZ	urate oxidase [EC:1.7.3.3]	ko00230 Purine metabolism; ko00232 Caffeine metabolism	🟥 0.77	0.0326	0.356921
K00757	udp, UPP	uridine phosphorylase [EC:2.4.2.3]	ko00240 Pyrimidine metabolism; ko00983 Drug metabolism - other enzymes	🟥 0.88	0.0451	0.363326
K01348	PLAU	urokinase plasminogen activator [EC:3.4.21.73]	ko04064 NF-kappa B signaling pathway; ko04610 Complement and coagulation cascades; ko052	🟩 -0.50	0.0090	0.322942
K15040	VDAC2	voltage-dependent anion channel protein 2	ko04020 Calcium signaling pathway; ko05012 Parkinson's disease; ko05016 Huntington's diseas	🟥 0.52	0.0488	0.36668
K02144	ATPeV1H	V-type H+-transporting ATPase subunit H	ko00190 Oxidative phosphorylation; ko04142 Lysosome; ko04145 Phagosome; ko04721 Synapti	🟥 0.38	0.0350	0.356921
K13128	ZCCHC8	zinc finger CCHC domain-containing protein 8	NA	🟩 -0.62	0.0365	0.356921

Diploid L3 vs L1

KOID	Gene Abbreviation	KEGG Annotation	Class	Log Fold Change	P Value	adj P Val
K00725	B4GALNT1, GALGT	(N-Acetylneuraminyl)-galactosylglucosylceramide N-acetylgalactosami	ko00604 Glycosphingolipid biosynthesis - ganglio series	1.00	0.0194	0.401932
K11517	HAO	(S)-2-hydroxy-acid oxidase [EC:1.1.3.15]	ko00630 Glyoxylate and dicarboxylate metabolism; ko04146 Peroxisome	-0.48	0.0166	0.398783
K02731	PSMA7	20S proteasome subunit alpha 4 [EC:3.4.25.1]	ko03050 Proteasome	0.39	0.0370	0.437297
K02741	PSMB9, LMP2	20S proteasome subunit beta 9 [EC:3.4.25.1]	ko03050 Proteasome	-2.05	0.0062	0.398783
K06692	PSMD5	26S proteasome non-ATPase regulatory subunit 5	NA	-0.59	0.0093	0.398783
K03030	PSMD14, RPN11, POH1	26S proteasome regulatory subunit N11	ko03050 Proteasome; ko05169 Epstein-Barr virus infection	0.49	0.0133	0.398783
K05692	ACTB_G1	actin beta/gamma 1	ko04145 Phagosome; ko04390 Hippo signaling pathway; ko04391 Hippo signaling pat	0.53	0.0250	0.422862
K05756	ARPC3	actin related protein 2/3 complex, subunit 3	ko04666 Fc gamma R-mediated phagocytosis; ko04810 Regulation of actin cytoskele	0.67	0.0022	0.382122
K05699	ACTN	actinin alpha	ko04510 Focal adhesion; ko04520 Adherens junction; ko04530 Tight junction; ko0467	0.70	0.0033	0.382122
K12417	ACOT11	acyl-CoA thioesteraes 11 [EC:3.1.2.-]	NA	-0.52	0.0275	0.436634
K01512	acyP	acylphosphatase [EC:3.6.1.7]	ko00620 Pyruvate metabolism; ko00627 Aminobenzoate degradation	-0.46	0.0057	0.398783
K08047	ADCY7	adenylate cyclase 7 [EC:4.6.1.1]	ko00230 Purine metabolism; ko04020 Calcium signaling pathway; ko04062 Chemokir	0.38	0.0223	0.411219
K18532	AK6, FAP7	adenylate kinase [EC:2.7.4.3]	NA	-0.65	0.0019	0.382122
K07296	ACDC	adiponectin	ko03320 PPAR signaling pathway; ko04920 Adipocytokine signaling pathway; ko0493	-0.88	0.0188	0.401932
K01242	CD38	ADP-ribosyl cyclase 1 [EC:3.2.2.6 2.4.99.20]	ko00760 Nicotinate and nicotinamide metabolism; ko04020 Calcium signaling pathw	-0.41	0.0001	0.357271
K01872	AARS, alaS	alanyl-tRNA synthetase [EC:6.1.1.7]	ko00970 Aminoacyl-tRNA biosynthesis	0.55	0.0483	0.457001
K03910	A2M	alpha-2-macroglobulin	ko04610 Complement and coagulation cascades	0.64	0.0032	0.382122
K10331	ASB9	ankyrin repeat and SOCS box protein 9	NA	0.43	0.0275	0.436634
K17092	ANXA2	annexin A2	NA	-0.70	0.0061	0.398783
K19502	ANO8, TMEM16H	anoctamin-8	NA	0.62	0.0118	0.398783
K01887	RARS, argS	arginyl-tRNA synthetase [EC:6.1.1.19]	ko00970 Aminoacyl-tRNA biosynthesis	0.43	0.0189	0.401932
K01893	NARS, asnS	asparaginyl-tRNA synthetase [EC:6.1.1.22]	ko00970 Aminoacyl-tRNA biosynthesis	0.58	0.0382	0.440055
K05655	ABCB8	ATP-binding cassette, subfamily B (MDR/TAP), member 8	ko02010 ABC transporters	0.41	0.0142	0.398783
K12823	DDX5, DBP2	ATP-dependent RNA helicase DDX5/DBP2 [EC:3.6.4.13]	ko03040 Spliceosome; ko05202 Transcriptional misregulation in cancer; ko05205 Pro	1.05	0.0136	0.398783
K11481	AURKA	aurora kinase A [EC:2.7.11.1]	ko04114 Oocyte meiosis	0.59	0.0399	0.442356
K08331	ATG13	autophagy-related protein 13	ko04140 Regulation of autophagy	-0.40	0.0398	0.442356
K03766	B3GNT5	beta-1,3-N-acetylglucosaminyltransferase 5 [EC:2.4.1.206]	ko00601 Glycosphingolipid biosynthesis - lacto and neolacto series	0.87	0.0193	0.401932
K06712	BTN	butyrophilin	NA	-0.99	0.0238	0.41936
K01948	CPS1	carbamoyl-phosphate synthase (ammonia) [EC:6.3.4.16]	ko00250 Alanine, aspartate and glutamate metabolism; ko00330 Arginine and prolir	0.49	0.0027	0.382122
K03927	CES2	carboxylesterase 2 [EC:3.1.1.1 3.1.1.84 3.1.1.56]	ko00983 Drug metabolism - other enzymes	-0.45	0.0335	0.436634
K13049	PM20D1	carboxypeptidase PM20D1 [EC:3.4.17.-]	NA	-0.42	0.0251	0.422862
K08766	CPT2	carnitine O-palmitoyltransferase 2 [EC:2.3.1.21]	ko00071 Fatty acid degradation; ko03320 PPAR signaling pathway	0.40	0.0194	0.401932
K04396	CASP6	caspase 6 [EC:3.4.22.59]	ko04210 Apoptosis	0.50	0.0149	0.398783
K06454	CD4	CD4 antigen	ko04514 Cell adhesion molecules (CAMs); ko04612 Antigen processing and presenta	-0.62	0.0264	0.432607
K15360	STRA13, CENPX, MHF2	centromere protein X	ko03460 Fanconi anemia pathway	0.39	0.0314	0.436634
K03998	C8B	complement component 8 subunit beta	ko04610 Complement and coagulation cascades; ko05020 Prion diseases; ko05146 Ar	0.55	0.0261	0.432086
K06626	CCNE	cyclin E	ko04110 Cell cycle; ko04114 Oocyte meiosis; ko04115 p53 signaling pathway; ko0415	0.40	0.0080	0.398783
K01697	E4.2.1.22, CBS	cystathionine beta-synthase [EC:4.2.1.22]	ko00260 Glycine, serine and threonine metabolism; ko00270 Cysteine and methioni	-0.53	0.0076	0.398783
K02266	COX6A	cytochrome c oxidase subunit 6a	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932 N	-0.65	0.0057	0.398783
K07408	CYP1A1	cytochrome P450, family 1, subfamily A, polypeptide 1 [EC:1.14.14.1]	ko00140 Steroid hormone biosynthesis; ko00380 Tryptophan metabolism; ko00830 F	-1.03	0.0149	0.398783
K17854	CYP2K	cytochrome P450, family 2, subfamily K	NA	-0.52	0.0219	0.410937
K17951	CYP27C	cytochrome P450, family 27, subfamily C	NA	0.41	0.0119	0.398783
K00058	serA, PHGDH	D-3-phosphoglycerate dehydrogenase [EC:1.1.1.95]	ko00260 Glycine, serine and threonine metabolism; ko00680 Methane metabolism	1.55	0.0035	0.382122
K13989	DERL2_3	Derlin-2/3	ko04141 Protein processing in endoplasmic reticulum	0.55	0.0495	0.457001
K01277	DPP3	dipeptidyl-peptidase III [EC:3.4.14.4]	NA	0.51	0.0214	0.409019
K05125	DDR2, TKT	discoidin domain receptor family member 2 [EC:2.7.10.1]	NA	0.43	0.0146	0.398783
K03509	POLH	DNA polymerase eta [EC:2.7.7.7]	ko03460 Fanconi anemia pathway	0.69	0.0168	0.398783
K02333	POLG2	DNA polymerase gamma 2	NA	-0.43	0.0297	0.436634
K02331	POL5, MYBBP1A	DNA polymerase phi [EC:2.7.7.7]	NA	0.51	0.0108	0.398783
K03015	RPB7, POLR2G	DNA-directed RNA polymerase II subunit RPB7	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polyme	0.42	0.0115	0.398783
K09504	DNAJA3	DnaJ homolog subfamily A member 3	ko05203 Viral carcinogenesis	-0.40	0.0329	0.436634
K12232	HECTD2	E3 ubiquitin-protein ligase HECTD2 [EC:6.3.2.19]	NA	-0.50	0.0454	0.457001
K17277	EPS8	epidermal growth factor receptor kinase substrate 8	NA	0.43	0.0280	0.436634
K15592	ETV4	ets translocation variant 4	ko05202 Transcriptional misregulation in cancer	0.43	0.0290	0.436634
K06110	EXOC3, SEC6L1	exocyst complex component 3	ko04530 Tight junction	-0.46	0.0208	0.406265
K10292	FBXO5, EMI1	F-box protein 5	ko04114 Oocyte meiosis	0.53	0.0122	0.398783
K00522	FTH1	ferritin heavy chain [EC:1.16.3.2]	ko00860 Porphyrin and chlorophyll metabolism; ko04978 Mineral absorption	-0.53	0.0379	0.440055
K03904	FGB	fibrinogen beta chain	ko04610 Complement and coagulation cascades	0.92	0.0368	0.437297
K09571	FKBP4_5	FK506-binding protein 4/5 [EC:5.2.1.8]	ko04915 Estrogen signaling pathway	0.52	0.0139	0.398783
K03841	FBP, fbp	fructose-1,6-bisphosphatase I [EC:3.1.3.11]	ko00010 Glycolysis / Gluconeogenesis; ko00030 Pentose phosphate pathway; ko000	-0.96	0.0383	0.440055
K02132	ATPeF1A, ATP5A1, ATP1	F-type H+-transporting ATPase subunit alpha	ko00190 Oxidative phosphorylation; ko05010 Alzheimer's disease; ko05012 Parkinsc	-0.44	0.0110	0.398783
K00849	galK	galactokinase [EC:2.7.1.6]	ko00052 Galactose metabolism; ko00520 Amino sugar and nucleotide sugar metabol	0.51	0.0046	0.398783
K00699	UGT	glucuronosyltransferase [EC:2.4.1.17]	ko00040 Pentose and glucuronate interconversions; ko00053 Ascorbate and aldarate	0.59	0.0305	0.436634
K00261	GLUD1_2, gdhA	glutamate dehydrogenase (NAD(P)+) [EC:1.4.1.3]	ko00250 Alanine, aspartate and glutamate metabolism; ko00330 Arginine and prolir	-0.45	0.0140	0.398783
K11204	GCLC	glutamate--cysteine ligase catalytic subunit [EC:6.3.2.2]	ko00480 Glutathione metabolism	-0.46	0.0028	0.382122
K01915	glnA, GLUL	glutamine synthetase [EC:6.3.1.2]	ko00250 Alanine, aspartate and glutamate metabolism; ko00330 Arginine and prolir	0.73	0.0005	0.382122
K00252	GCDH, gcdH	glutaryl-CoA dehydrogenase [EC:1.3.8.6]	ko00071 Fatty acid degradation; ko00310 Lysine degradation; ko00380 Tryptophan m	-0.73	0.0318	0.436634
K15839	GPSM1, AGS3	G-protein signaling modulator 1	ko05030 Cocaine addiction	-0.39	0.0092	0.398783
K04534	GNAO, G-ALPHA-O	guanine nucleotide-binding protein G(o) subunit alpha	ko04713 Circadian entrainment; ko04723 Retrograde endocannabinoid signaling; ko	-0.44	0.0025	0.382122
K04538	GNB4	guanine nucleotide-binding protein subunit beta-4	ko04062 Chemokine signaling pathway; ko04151 PI3K-Akt signaling pathway; ko0471	-0.50	0.0183	0.401388
K16142	HP	haptoglobin	NA	0.90	0.0403	0.443212
K09489	HSPA4	heat shock 70kDa protein 4	ko04612 Antigen processing and presentation	0.49	0.0345	0.437297
K13159	HNRNPL	heterogeneous nuclear ribonucleoprotein L	NA	0.61	0.0035	0.382122
K00844	HK	hexokinase [EC:2.7.1.1]	ko00010 Glycolysis / Gluconeogenesis; ko00051 Fructose and mannose metabolism;	-0.38	0.0002	0.357271
K11303	HAT1, KAT1	histone acetyltransferase 1 [EC:2.3.1.48]	ko05034 Alcoholism	0.68	0.0029	0.382122
K11424	WHSC1, MMSET, NSD2	histone-lysine N-methyltransferase NSD2 [EC:2.1.1.43]	ko00310 Lysine degradation; ko05202 Transcriptional misregulation in cancer	0.69	0.0079	0.398783
K14966	HCFC	host cell factor	ko05168 Herpes simplex infection	-0.47	0.0109	0.398783
K09562	HSPBP1	hsp70-interacting protein	ko04141 Protein processing in endoplasmic reticulum	0.48	0.0028	0.382122
K06092	INADL, PATJ	InaD-like protein	ko04390 Hippo signaling pathway; ko04530 Tight junction	0.71	0.0171	0.398783
K05459	IGF1	insulin-like growth factor 1	ko04066 HIF-1 signaling pathway; ko04114 Oocyte meiosis; ko04115 p53 signaling pa	-0.64	0.0254	0.423939
K18264	ITM2B	integral membrane protein 2B	NA	-0.44	0.0080	0.398783
K05414	IFNA	interferon alpha	ko04060 Cytokine-cytokine receptor interaction; ko04140 Regulation of autophagy;	0.57	0.0145	0.398783
K09228	KRAB	KRAB domain-containing zinc finger protein	NA	0.72	0.0032	0.382122
K17845	KLF2	krueppel-like factor 2	NA	-0.43	0.0018	0.382122
K02920	RP-L36e, RPL36	large subunit ribosomal protein L36e	ko03010 Ribosome	-0.46	0.0382	0.440055
K17989	SDS, SDH, CHA1	L-serine/L-threonine ammonia-lyase [EC:4.3.1.17 4.3.1.19]	NA	-0.44	0.0033	0.382122
K09262	MEF2D	MADS-box transcription enhancer factor 2D	NA	0.56	0.0171	0.398783
K06751	MHC1	major histocompatibility complex, class I	ko04144 Endocytosis; ko04145 Phagosome; ko04514 Cell adhesion molecules (CAMs	-0.55	0.0016	0.382122
K09660	MPDU1	mannose-P-dolichol utilization defect 1	NA	0.45	0.0312	0.436634
K17291	MARVELD2	MARVEL domain-containing protein 2	NA	-0.45	0.0161	0.398783
K14737	STEAP1	metalloreductase STEAP1 [EC:1.16.1.-]	ko04978 Mineral absorption	0.47	0.0024	0.382122
K08199	SLC22A2, OCT2	MFS transporter, OCT family, solute carrier family 22 (organic cation	NA	-0.61	0.0171	0.398783
K17656	MSS51	mitochondrial splicing suppressor protein 51	NA	0.39	0.0067	0.398783
K04431	MAP2K7, MKK7	mitogen-activated protein kinase kinase 7 [EC:2.7.12.2]	ko04010 MAPK signaling pathway; ko04012 ErbB signaling pathway; ko04141 Protein	0.76	0.0121	0.398783
K04676	SMAD1	mothers against decapentaplegic homolog 1	ko04350 TGF-beta signaling pathway; ko04390 Hippo signaling pathway; ko04391 Hip	-0.57	0.0093	0.398783
K04729	MYD88	myeloid differentiation primary response protein MyD88	ko04064 NF-kappa B signaling pathway; ko04210 Apoptosis; ko04620 Toll-like recept	0.44	0.0098	0.398783
K10352	MYH	myosin heavy chain	ko04530 Tight junction; ko05416 Viral myocarditis	0.71	0.0018	0.382122
K10356	MYO1	myosin I	NA	-0.49	0.0116	0.398783
K12800	NLRP3, PYPAF1	NACHT, LRR and PYD domains-containing protein 3	ko04621 NOD-like receptor signaling pathway; ko05133 Pertussis; ko05164 Influenza	0.93	0.0014	0.382122

K01097	NANP	N-acylneuraminate-9-phosphatase [EC:3.1.3.29]	ko00520 Amino sugar and nucleotide sugar metabolism	0.39	0.0029	0.382122
K00323	NNT	NAD(P) transhydrogenase [EC:1.6.1.2]	ko00760 Nicotinate and nicotinamide metabolism	0.40	0.0194	0.401932
K12347	SLC11A, NRAMP	natural resistance-associated macrophage protein	ko04142 Lysosome; ko04978 Mineral absorption	-0.46	0.0486	0.457001
K05750	NCKAP1, NAP125	NCK-associated protein 1	ko04810 Regulation of actin cytoskeleton	-0.41	0.0137	0.398783
K04573	NEF3, NF-M	neurofilament medium polypeptide (neurofilament 3)	ko05014 Amyotrophic lateral sclerosis (ALS)	0.75	0.0133	0.398783
K04469	NFKB2	nuclear factor of kappa light polypeptide gene enhancer in B-cells 2	ko04010 MAPK signaling pathway; ko04064 NF-kappa B signaling pathway; ko04380	0.45	0.0066	0.398783
K08126	OGN	osteoglycin (osteoinductive factor, mimecan)	NA	-0.54	0.0057	0.398783
K04441	P38	p38 MAP kinase [EC:2.7.11.24]	ko04010 MAPK signaling pathway; ko04011 MAPK signaling pathway - yeast; ko0437	-0.39	0.0089	0.398783
K13239	PECI	peroxisomal 3,2-trans-enoyl-CoA isomerase [EC:5.3.3.8]	ko00071 Fatty acid degradation; ko04146 Peroxisome	-0.48	0.0226	0.411219
K08530	NR1C3, PPARG	peroxisome proliferator-activated receptor gamma	ko03320 PPAR signaling pathway; ko04380 Osteoclast differentiation; ko05016 Hunti	-0.55	0.0367	0.437297
K01890	FARSB, pheT	phenylalanyl-tRNA synthetase beta chain [EC:6.1.1.20]	ko00970 Aminoacyl-tRNA biosynthesis	0.50	0.0098	0.398783
K07253	MIF	phenylpyruvate tautomerase [EC:5.3.2.1]	ko00350 Tyrosine metabolism; ko00360 Phenylalanine metabolism	-0.49	0.0088	0.398783
K17594	PHACTR3	phosphatase and actin regulator 3	NA	-1.28	0.0340	0.437297
K02649	PIK3R	phosphoinositide-3-kinase, regulatory subunit	ko04012 ErbB signaling pathway; ko04062 Chemokine signaling pathway; ko04066 HI	-0.39	0.0383	0.440055
K01922	PPCS, coaB	phosphopantothenate-cysteine ligase [EC:6.3.2.5]	ko00770 Pantothenate and CoA biosynthesis	0.39	0.0171	0.398783
K01952	purL, PFAS	phosphoribosylformylglycinamidine synthase [EC:6.3.5.3]	ko00230 Purine metabolism	0.41	0.0062	0.398783
K13114	PNN	pinin	ko03013 RNA transport; ko03015 mRNA surveillance pathway	-0.59	0.0107	0.398783
K03982	SERPINE1, PAI1	plasminogen activator inhibitor-1	ko04066 HIF-1 signaling pathway; ko04115 p53 signaling pathway; ko04390 Hippo sig	0.41	0.0066	0.398783
K13126	PABPC	polyadenylate-binding protein	ko03013 RNA transport; ko03015 mRNA surveillance pathway; ko03018 RNA degrada	-0.49	0.0239	0.41936
K14399	CLP1, HERB	polyribonucleotide 5'-hydroxyl-kinase [EC:2.7.1.78]	ko03015 mRNA surveillance pathway	-0.42	0.0490	0.457001
K05003	KCNJ10	potassium inwardly-rectifying channel subfamily J member 10	ko04971 Gastric acid secretion	0.54	0.0313	0.436634
K12850	PRPF38B	pre-mRNA-splicing factor 38B	ko03040 Spliceosome	0.42	0.0411	0.444617
K04727	PDCD8, AIF	programmed cell death 8 (apoptosis-inducing factor) [EC:1.-.-.-]	ko04210 Apoptosis	0.63	0.0121	0.398783
K01322	PREP	prolyl oligopeptidase [EC:3.4.21.26]	NA	0.39	0.0256	0.425293
K15719	NCOAT, MGEA5	protein O-GlcNAcase / histone acetyltransferase [EC:3.2.1.169 2.3.1.48	NA	-0.39	0.0477	0.457001
K12328	PPP1R14A, CPI17	protein phosphatase 1 regulatory subunit 14A	ko04270 Vascular smooth muscle contraction	0.66	0.0300	0.436634
K04461	PPM1B, PP2CB	protein phosphatase 1B [EC:3.1.3.16]	ko04010 MAPK signaling pathway	0.43	0.0250	0.422862
K14004	SEC13	protein transport protein SEC13	ko03013 RNA transport; ko04141 Protein processing in endoplasmic reticulum	0.42	0.0296	0.436634
K14005	SEC31	protein transport protein SEC31	ko04141 Protein processing in endoplasmic reticulum	0.41	0.0109	0.398783
K07342	SEC61G, SSS1, secE	protein transport protein SEC61 subunit gamma and related protei	ko03060 Protein export; ko04141 Protein processing in endoplasmic reticulum; ko04	0.41	0.0444	0.452402
K08773	RALBP1	RalA-binding protein 1	ko05200 Pathways in cancer; ko05212 Pancreatic cancer	0.42	0.0081	0.398783
K07874	RAB1A	Ras-related protein Rab-1A	ko05134 Legionellosis	0.40	0.0022	0.382122
K10740	RPA3	replication factor A3	ko03030 DNA replication; ko03420 Nucleotide excision repair; ko03430 Mismatch re	0.74	0.0370	0.437297
K06618	RB1	retinoblastoma-associated protein	ko04110 Cell cycle; ko05161 Hepatitis B; ko05166 HTLV-I infection; ko05169 Epstein-	0.41	0.0068	0.398783
K10808	RRM2	ribonucleoside-diphosphate reductase subunit M2 [EC:1.17.4.1]	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko00480 Glutathione	0.57	0.0138	0.398783
K12822	RBM25, S164	RNA-binding protein 25	ko03040 Spliceosome	0.77	0.0109	0.398783
K04499	RUVBL1, RVB1, INO80H	RuvB-like protein 1 (pontin 52)	ko04310 Wnt signaling pathway	-0.49	0.0245	0.422862
K12382	PSAP, SGP1	saposin	ko04142 Lysosome	-0.58	0.0016	0.382122
K06841	SEMA5	semaphorin 5	ko04360 Axon guidance	-0.69	0.0033	0.382122
K09646	SCPEP1	serine carboxypeptidase 1 [EC:3.4.16.-]	NA	-0.43	0.0110	0.398783
K16311	SIK2	serine/threonine-protein kinase SIK2 [EC:2.7.11.1]	NA	-0.39	0.0496	0.457001
K08269	ULK1_2_3, ATG1	serine/threonine-protein kinase ULK/ATG1 [EC:2.7.11.1]	ko04140 Regulation of autophagy; ko04150 mTOR signaling pathway	0.63	0.0113	0.398783
K04382	PPP2C	serine/threonine-protein phosphatase 2A catalytic subunit [EC:3.1.3.16]	ko03015 mRNA surveillance pathway; ko04111 Cell cycle - yeast; ko04113 Meiosis -	-0.41	0.0022	0.382122
K01875	SARS, serS	seryl-tRNA synthetase [EC:6.1.1.11]	ko00970 Aminoacyl-tRNA biosynthesis	0.51	0.0111	0.398783
K10141	SESN	sestrin	ko04115 p53 signaling pathway	-0.72	0.0089	0.398783
K01070	frmB, ESD, fghA	S-formylglutathione hydrolase [EC:3.1.2.12]	ko00680 Methane metabolism	-0.65	0.0054	0.398783
K02977	RP-S27Ae, RPS27A	small subunit ribosomal protein S27Ae	ko03010 Ribosome	-0.43	0.0116	0.398783
K13151	SNUPN, RNUT1	snurportin-1	ko03013 RNA transport	-0.38	0.0212	0.409019
K00802	SMS	spermine synthase [EC:2.5.1.22]	ko00270 Cysteine and methionine metabolism; ko00330 Arginine and proline meta	-0.56	0.0110	0.398783
K04404	MAP3K7IP2, TAB2	TAK1-binding protein 2	ko04010 MAPK signaling pathway; ko04064 NF-kappa B signaling pathway; ko04380	0.38	0.0367	0.437297
K12652	TBKBP1	TANK-binding kinase 1-binding protein	ko04622 RIG-I-like receptor signaling pathway	0.43	0.0184	0.401388
K06451	CD3E	T-cell surface glycoprotein CD3 epsilon chain	ko04640 Hematopoietic cell lineage; ko04660 T cell receptor signaling pathway; ko0	-0.39	0.0318	0.436634
K04659	THBS2S	thrombospondin 2/3/4/5	ko04145 Phagosome; ko04151 PI3K-Akt signaling pathway; ko04510 Focal adhesion;	0.86	0.0133	0.398783
K00857	tdk, TK	thymidine kinase [EC:2.7.1.21]	ko00240 Pyrimidine metabolism; ko00983 Drug metabolism - other enzymes	1.00	0.0251	0.422862
K10170	TLR8	toll-like receptor 8	ko04620 Toll-like receptor signaling pathway	0.51	0.0025	0.382122
K10161	TLR9	toll-like receptor 9	ko04620 Toll-like receptor signaling pathway; ko05142 Chagas disease (American tr	0.38	0.0025	0.382122
K16796	SOX2	transcription factor SOX2 (SOX group B)	ko04390 Hippo signaling pathway	0.49	0.0081	0.398783
K13525	VCP, CDC48	transitional endoplasmic reticulum ATPase	ko04141 Protein processing in endoplasmic reticulum; ko05134 Legionellosis	0.39	0.0415	0.444822
K03254	EIF3A	translation initiation factor 3 subunit A	ko03013 RNA transport	0.67	0.0053	0.398783
K03257	EIF4A	translation initiation factor 4A	ko03013 RNA transport	-0.56	0.0178	0.401388
K09540	SEC63, DNAJC23	translocation protein SEC63	ko03060 Protein export; ko04141 Protein processing in endoplasmic reticulum	-0.38	0.0127	0.398783
K12015	TRIM39	tripartite motif-containing protein 39 [EC:6.3.2.19]	NA	0.57	0.0213	0.409019
K01867	WARS, trpS	tryptophanyl-tRNA synthetase [EC:6.1.1.2]	ko00970 Aminoacyl-tRNA biosynthesis	0.72	0.0137	0.398783
K07374	TUBA	tubulin alpha	ko04145 Phagosome; ko04540 Gap junction; ko05130 Pathogenic Escherichia coli inf	0.48	0.0336	0.436634
K07604	KRT1	type I keratin, acidic	NA	-0.43	0.0017	0.382122
K01866	YARS, tyrS	tyrosyl-tRNA synthetase [EC:6.1.1.1]	ko00970 Aminoacyl-tRNA biosynthesis	0.82	0.0084	0.398783
K17492	UBN	ubinuclein	NA	0.40	0.0104	0.398783
K00412	CYTB, petB	ubiquinol-cytochrome c reductase cytochrome b subunit	ko00190 Oxidative phosphorylation; ko02020 Two-component system; ko04260 Car	-0.67	0.0173	0.400261
K11849	USP25_28, UBP2	ubiquitin carboxyl-terminal hydrolase 25/28 [EC:3.4.19.12]	NA	-0.43	0.0200	0.40587
K14012	SHP1, UBX1, NSFL1C	UBX domain-containing protein 1	ko04141 Protein processing in endoplasmic reticulum	0.39	0.0432	0.452056
K06793	VCAN, CSPG2	versican core protein	ko04514 Cell adhesion molecules (CAMs)	0.44	0.0260	0.431588
K07436	CYP24A1	vitamin D3 24-hydroxylase [EC:1.14.13.126]	ko00100 Steroid biosynthesis; ko05206 MicroRNAs in cancer	1.71	0.0002	0.382122

Triploids L2 vs L1

KOID	Gene Abbreviation	KEGG Annotation	Class	Log Fold Change	P Value	adj P Val
K02731	PSMA7	20S proteasome subunit alpha 4 [EC:3.4.25.1]	ko03050 Proteasome	-0.46	0.0009	0.366431979
K00643	E2.3.1.37, ALAS	5-aminolevulinate synthase [EC:2.3.1.37]	ko00260 Glycine, serine and threonine metabolism; ko00860 Porphyrin and ch	1.53	0.0130	0.406108274
K01081	E3.1.3.5	5'-nucleotidase [EC:3.1.3.5]	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko00760 Nicotir	0.41	0.0047	0.406108274
K19028	PFKFB1	6-phosphofructo-2-kinase / fructose-2,6-biphosphatase 1 [EC:2.7.1.105	NA	0.47	0.0387	0.4226574
K05757	ARPC1A_B	actin related protein 2/3 complex, subunit 1A/1B	ko04666 Fc gamma R-mediated phagocytosis; ko04810 Regulation of actin cyto	0.79	0.0024	0.406108274
K03910	A2M	alpha-2-macroglobulin	ko04610 Complement and coagulation cascades	0.61	0.0172	0.406108274
K01176	E3.2.1.1, amyA, malS	alpha-amylase [EC:3.2.1.1]	ko00500 Starch and sucrose metabolism; ko04973 Carbohydrate digestion and	0.57	0.0079	0.406108274
K11140	ANPEP	aminopeptidase N [EC:3.4.11.2]	ko00480 Glutathione metabolism; ko04614 Renin-angiotensin system; ko0464	-0.67	0.0039	0.406108274
K03359	APC12, CDC26	anaphase-promoting complex subunit 12	ko04110 Cell cycle; ko04111 Cell cycle - yeast; ko04113 Meiosis - yeast; ko0411	-0.41	0.0370	0.4226574
K10380	ANK	ankyrin	ko05205 Proteoglycans in cancer	0.71	0.0146	0.406108274
K17095	ANXA7_11	annexin A7/11	NA	0.49	0.0037	0.406108274
K09864	AQP1	aquaporin-1	ko04964 Proximal tubule bicarbonate reclamation; ko04976 Bile secretion	0.75	0.0108	0.406108274
K09866	AQP4	aquaporin-4	ko04962 Vasopressin-regulated water reabsorption; ko04976 Bile secretion	0.40	0.0398	0.424389339
K09034	BATF	ATF-like basic leucine zipper transcriptional factor	NA	-0.64	0.0072	0.406108274
K07820	B3GALT2	beta-1,3-galactosyltransferase 2 [EC:2.4.1.-]	ko00601 Glycosphingolipid biosynthesis - lacto and neolacto series	0.39	0.0224	0.406108274
K04726	BID	BH3 interacting domain death agonist	ko04115 p53 signaling pathway; ko04210 Apoptosis; ko04650 Natural killer cell	0.65	0.0237	0.406108274
K05901	BLVRB	biliverdin reductase / flavin reductase [EC:1.3.1.24 1.5.1.30]	ko00740 Riboflavin metabolism; ko00860 Porphyrin and chlorophyll metabolis	0.79	0.0131	0.406108274
K01435	BTD	biotinidase [EC:3.5.1.12]	ko00780 Biotin metabolism; ko04977 Vitamin digestion and absorption	0.59	0.0482	0.426599288
K04739	PRKAR	cAMP-dependent protein kinase regulator	ko04210 Apoptosis; ko04910 Insulin signaling pathway	0.45	0.0120	0.406108274
K18245	CA2	carbonic anhydrase 2 [EC:4.2.1.1]	NA	1.05	0.0146	0.406108274
K01379	CTSD	cathepsin D [EC:3.4.23.5]	ko04142 Lysosome; ko05152 Tuberculosis	0.57	0.0456	0.426599288
K01365	CTSL	cathepsin L [EC:3.4.22.15]	ko04142 Lysosome; ko04145 Phagosome; ko04612 Antigen processing and pres	-0.51	0.0063	0.406108274
K06454	CD4	CD4 antigen	ko04514 Cell adhesion molecules (CAMs); ko04612 Antigen processing and pre	0.42	0.0444	0.426599288
K05022	CLIC2	chloride intracellular channel protein 2	NA	0.39	0.0034	0.406108274
K03899	F8	coagulation factor VIII	ko04610 Complement and coagulation cascades	0.50	0.0089	0.406108274
K06236	COL1AS	collagen, type I/II/III/V/XI/XXIV/XXVII, alpha	ko04151 PI3K-Akt signaling pathway; ko04510 Focal adhesion; ko04512 ECM-re	0.50	0.0493	0.428391933
K01331	C1S	complement component 1, s subcomponent [EC:3.4.21.42]	ko04610 Complement and coagulation cascades; ko05133 Pertussis; ko05150 St	0.44	0.0208	0.406108274
K03997	C8A	complement component 8 subunit alpha	ko04610 Complement and coagulation cascades; ko05020 Prion diseases; ko05	0.40	0.0262	0.406108274
K01335	CFB	component factor B [EC:3.4.21.47]	ko04610 Complement and coagulation cascades; ko05150 Staphylococcus aure	0.68	0.0471	0.426599288
K01334	CFD	component factor D [EC:3.4.21.46]	ko04610 Complement and coagulation cascades; ko05150 Staphylococcus aure	0.45	0.0075	0.406108274
K10059	CLEC4E	C-type lectin domain family 4 member E	ko05152 Tuberculosis	0.67	0.0148	0.406108274
K05416	CXCL9	C-X-C motif chemokine 9	ko04060 Cytokine-cytokine receptor interaction; ko04062 Chemokine signaling	0.39	0.0375	0.4226574
K04685	CDKN2B, P15, INK4B	cyclin-dependent kinase inhibitor 2B	ko04110 Cell cycle; ko04350 TGF-beta signaling pathway; ko05166 HTLV-I infect	0.90	0.0078	0.406108274
K17494	CSRNP	cysteine/serine-rich nuclear protein	NA	0.40	0.0027	0.406108274
K01883	CARS, cysS	cysteinyl-tRNA synthetase [EC:6.1.1.16]	ko00970 Aminoacyl-tRNA biosynthesis	-0.70	0.0250	0.406108274
K01489	cdd, CDA	cytidine deaminase [EC:3.5.4.5]	ko00240 Pyrimidine metabolism; ko00983 Drug metabolism - other enzymes	0.70	0.0306	0.410911565
K18184	COX20	cytochrome c oxidase assembly protein subunit 20	NA	-0.56	0.0017	0.366431979
K02265	COX5B	cytochrome c oxidase subunit 5b	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04	0.62	0.0061	0.406108274
K02270	COX7A	cytochrome c oxidase subunit 7a	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04	-0.42	0.0179	0.406108274
K11995	DNASE1L	deoxyribonuclease-1-like protein [EC:3.1.21.-]	NA	0.59	0.0346	0.411688642
K10413	DYNC1H	dynein heavy chain 1, cytosolic	ko04145 Phagosome; ko04962 Vasopressin-regulated water reabsorption; ko0	0.48	0.0165	0.406108274
K10614	HERC3	E3 ubiquitin-protein ligase HERC3 [EC:6.3.2.19]	ko04120 Ubiquitin mediated proteolysis	0.55	0.0155	0.406108274
K10615	HERC4	E3 ubiquitin-protein ligase HERC4 [EC:6.3.2.19]	ko04120 Ubiquitin mediated proteolysis	0.70	0.0055	0.406108274
K03522	fixB, etfA	electron transfer flavoprotein alpha subunit	NA	-0.59	0.0244	0.406108274
K10205	ELOVL2	elongation of very long chain fatty acids protein 2 [EC:2.3.1.199]	ko00062 Fatty acid elongation; ko01040 Biosynthesis of unsaturated fatty acids	-0.46	0.0180	0.406108274
K17286	STOM	erythrocyte band 7 integral membrane protein	NA	0.43	0.0251	0.406108274
K05079	EPOR	erythropoietin receptor	ko04060 Cytokine-cytokine receptor interaction; ko04151 PI3K-Akt signaling pa	1.07	0.0123	0.406108274
K08751	FABP2	fatty acid-binding protein 2, intestinal	ko03320 PPAR signaling pathway; ko04975 Fat digestion and absorption	1.45	0.0342	0.411688642
K05097	FLT4, VEGFR3	FMS-like tyrosine kinase 4 [EC:2.7.10.1]	ko04060 Cytokine-cytokine receptor interaction; ko04151 PI3K-Akt signaling pa	0.43	0.0154	0.406108274
K09409	FOXP	forkhead box protein P	NA	0.52	0.0328	0.410911565
K02133	ATPeF1B, ATP5B, ATP	F-type H+-transporting ATPase subunit beta [EC:3.6.3.14]	ko00190 Oxidative phosphorylation; ko05010 Alzheimer's disease; ko05012 Pa	0.49	0.0066	0.406108274
K12900	FUSIP1	FUS-interacting serine-arginine-rich protein 1	ko03040 Spliceosome	-0.53	0.0266	0.406108274
K17894	GATA2	GATA-binding protein 2	NA	0.94	0.0249	0.406108274
K02377	TSTA3, fcl	GDP-L-fucose synthase [EC:1.1.1.271]	ko00051 Fructose and mannose metabolism; ko00520 Amino sugar and nucleo	1.16	0.0143	0.406108274
K00799	GST, gst	glutathione S-transferase [EC:2.5.1.18]	ko00480 Glutathione metabolism; ko00980 Metabolism of xenobiotics by cyto	0.67	0.0092	0.406108274
K00049	GRHPR	glyoxylate/hydroxypyruvate reductase [EC:1.1.1.79 1.1.1.81]	ko00260 Glycine, serine and threonine metabolism; ko00620 Pyruvate metabo	0.50	0.0412	0.424612243
K09223	GFI1	growth factor independent 1	NA	0.50	0.0177	0.406108274
K00542	GAMT	guanidinoacetate N-methyltransferase [EC:2.1.1.2]	ko00260 Glycine, serine and threonine metabolism; ko00330 Arginine and prol	1.20	0.0407	0.424612243
K03283	HSPA1_8	heat shock 70kDa protein 1/8	ko03040 Spliceosome; ko04010 MAPK signaling pathway; ko04141 Protein proc	0.88	0.0258	0.406108274
K09414	HSF1	heat shock transcription factor 1	ko05134 Legionellosis	0.62	0.0485	0.426599288
K11295	HMGB2	high mobility group protein B2	NA	0.42	0.0109	0.406108274
K11251	H2A	histone H2A	ko05034 Alcoholism; ko05322 Systemic lupus erythematosus	-0.51	0.0014	0.366431979
K01109	INPP4	inositol polyphosphate-4-phosphatase [EC:3.1.3.66]	ko00562 Inositol phosphate metabolism; ko04070 Phosphatidylinositol signali	0.75	0.0054	0.406108274
K06566	IFITM	interferon induced transmembrane protein	NA	0.42	0.0013	0.366431979
K05076	IL13RA1	interleukin 13 receptor alpha-1	ko04060 Cytokine-cytokine receptor interaction; ko04630 Jak-STAT signaling pa	0.43	0.0266	0.406108274
K05433	IL15	interleukin 15	ko04060 Cytokine-cytokine receptor interaction; ko04630 Jak-STAT signaling pa	0.42	0.0038	0.406108274
K07934	IFT27, RAYL, RABL4	intraflagellar transport protein 27 homolog	NA	-0.42	0.0077	0.406108274
K05636	LAMB1	laminin, beta 1	ko04151 PI3K-Akt signaling pathway; ko04510 Focal adhesion; ko04512 ECM-re	0.43	0.0167	0.406108274
K02873	RP-L13e, RPL13	large subunit ribosomal protein L13e	ko03010 Ribosome	-0.61	0.0182	0.406108274
K02899	RP-L27, MRPL27, rpmA	large subunit ribosomal protein L27	ko03010 Ribosome	-0.39	0.0216	0.406108274
K10080	LMAN1, ERGIC53	lectin, mannose-binding 1	ko04141 Protein processing in endoplasmic reticulum	0.48	0.0175	0.406108274
K19363	LITAF	lipopolysaccharide-induced tumor necrosis factor-alpha factor	NA	0.55	0.0136	0.406108274
K01059	LPL	lipoprotein lipase [EC:3.1.1.34]	ko00561 Glycerolipid metabolism; ko03320 PPAR signaling pathway; ko05010 A	0.40	0.0114	0.406108274
K15013	ACSBG	long-chain-fatty-acid--CoA ligase ACSBG [EC:6.2.1.3]	ko00071 Fatty acid degradation; ko03320 PPAR signaling pathway; ko04920 Adi	0.63	0.0054	0.406108274
K12387	LAPTM	lysosomal-associated transmembrane protein	ko04142 Lysosome	-0.42	0.0223	0.406108274
K06751	MHC1	major histocompatibility complex, class I	ko04144 Endocytosis; ko04145 Phagosome; ko04514 Cell adhesion molecules (	0.66	0.0014	0.366431979
K08888	MATK	megakaryocyte-associated tyrosine kinase [EC:2.7.10.2]	ko04722 Neurotrophin signaling pathway	0.69	0.0093	0.406108274
K17772	TOM6	mitochondrial import receptor subunit TOM6	NA	-0.43	0.0400	0.424612243
K17771	TOM7	mitochondrial import receptor subunit TOM7	NA	-0.38	0.0196	0.406108274
K04079	htpG, HSP90A	molecular chaperone HtpG	ko04141 Protein processing in endoplasmic reticulum; ko04151 PI3K-Akt signal	-0.49	0.0126	0.406108274
K15626	NUPR1, COM1	nuclear protein, 1	ko05202 Transcriptional misregulation in cancer	0.90	0.0472	0.426599288
K11797	PHIP, WDR11	PH-interacting protein	NA	0.43	0.0015	0.366431979
K01530	E3.6.3.1	phospholipid-translocating ATPase [EC:3.6.3.1]	NA	-0.39	0.0281	0.407707745
K06263	GP9	platelet glycoprotein IX	ko04512 ECM-receptor interaction; ko04640 Hematopoietic cell lineage	0.51	0.0330	0.410911565
K08672	PCSK6	proprotein convertase subtilisin/kexin type 6 [EC:3.4.21.-]	NA	0.75	0.0203	0.406108274
K09649	PRSS16	protease, serine, 16 (thymus) [EC:3.4.-.-]	NA	0.93	0.0171	0.406108274
K09667	OGT	protein O-GlcNAc transferase [EC:2.4.1.255]	ko00514 Other types of O-glycan biosynthesis	0.40	0.0319	0.410911565
K17566	PPP1R27	protein phosphatase 1 regulatory subunit 27	NA	0.42	0.0156	0.406108274
K00573	E2.1.1.77, pcm	protein-L-isoaspartate(D-aspartate) O-methyltransferase [EC:2.1.1.77	NA	1.18	0.0025	0.406108274
K03783	punA	purine-nucleoside phosphorylase [EC:2.4.2.1]	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko00760 Nicotir	0.50	0.0396	0.424389339
K00773	tgt, QTRT1	queuine tRNA-ribosyltransferase [EC:2.4.2.29]	NA	0.38	0.0003	0.366431979
K15045	RSAD2	radical S-adenosyl methionine domain-containing protein 2	ko05164 Influenza A	0.62	0.0063	0.406108274
K06478	PTPRC, CD45	receptor-type tyrosine-protein phosphatase C [EC:3.1.3.48]	ko04514 Cell adhesion molecules (CAMs); ko04660 T cell receptor signaling pat	0.42	0.0151	0.406108274
K11220	STAT1	signal transducer and activator of transcription 1	ko04062 Chemokine signaling pathway; ko04380 Osteoclast differentiation; ko	0.47	0.0134	0.406108274
K04692	STAT3	signal transducer and activator of transcription 3	ko04062 Chemokine signaling pathway; ko04066 HIF-1 signaling pathway; ko04	0.58	0.0446	0.426599288
K11099	SNRPG, SMG	small nuclear ribonucleoprotein G	ko03040 Spliceosome	-0.40	0.0258	0.406108274
K02989	RP-S5e, RPS5	small subunit ribosomal protein S5e	ko03010 Ribosome	-0.52	0.0123	0.406108274
K02993	RP-S7e, RPS7	small subunit ribosomal protein S7e	ko03010 Ribosome	-0.53	0.0249	0.406108274
K05863	SLC25A4S, ANT	solute carrier family 25 (mitochondrial adenine nucleotide translocat	ko04020 Calcium signaling pathway; ko05012 Parkinson's disease; ko05016 Hur	-0.40	0.0356	0.415769902

K06573	SLC4A1, AE1	solute carrier family 4 (anion exchanger), member 1	ko04966 Collecting duct acid secretion	1.15	0.0178	0.406108274
K12827	SF3A3, SAP61, PRP9	splicing factor 3A subunit 3	ko03040 Spliceosome	0.42	0.0136	0.406108274
K12892	SFRS3	splicing factor, arginine/serine-rich 3	ko03040 Spliceosome; ko05168 Herpes simplex infection	-0.50	0.0090	0.406108274
K10345	SPSB3, SSB3	SPRY domain-containing SOCS box protein 3	NA	-0.55	0.0201	0.406108274
K09497	CCT5	T-complex protein 1 subunit epsilon	NA	-0.38	0.0399	0.424389339
K09585	TXNDC10	thioredoxin domain-containing protein 10 [EC:5.3.4.1]	NA	0.65	0.0064	0.406108274
K10168	TLR5	toll-like receptor 5	ko04620 Toll-like receptor signaling pathway; ko05130 Pathogenic Escherichia	1.18	0.0445	0.426599288
K14736	TF	transferrin	ko04066 HIF-1 signaling pathway; ko04978 Mineral absorption	1.04	0.0088	0.406108274
K01312	PRSS	trypsin [EC:3.4.21.4]	ko04080 Neuroactive ligand-receptor interaction; ko04972 Pancreatic secretio	0.67	0.0132	0.406108274
K07375	TUBB	tubulin beta	ko04145 Phagosome; ko04540 Gap junction; ko05130 Pathogenic Escherichia c	1.01	0.0225	0.406108274
K00815	TAT	tyrosine aminotransferase [EC:2.6.1.5]	ko00130 Ubiquinone and other terpenoid-quinone biosynthesis; ko00270 Cyst	0.98	0.0004	0.366431979
K12621	LSM2	U6 snRNA-associated Sm-like protein LSm2	ko03018 RNA degradation; ko03040 Spliceosome	-0.41	0.0280	0.407707745
K08770	UBC	ubiquitin C	ko03320 PPAR signaling pathway	0.47	0.0052	0.406108274
K12161	URM1	ubiquitin related modifier 1	ko04122 Sulfur relay system	-0.39	0.0046	0.406108274
K02207	UBE2R, UBC3, CDC34	ubiquitin-conjugating enzyme E2 R [EC:6.3.2.19]	ko04120 Ubiquitin mediated proteolysis; ko05168 Herpes simplex infection	0.47	0.0057	0.406108274
K00757	udp, UPP	uridine phosphorylase [EC:2.4.2.3]	ko00240 Pyrimidine metabolism; ko00983 Drug metabolism - other enzymes	0.79	0.0230	0.406108274
K01719	hemD, UROS	uroporphyrinogen-III synthase [EC:4.2.1.75]	ko00860 Porphyrin and chlorophyll metabolism	0.63	0.0162	0.406108274
K02149	ATPeV1D, ATP6M	V-type H+-transporting ATPase subunit D	ko00190 Oxidative phosphorylation; ko04145 Phagosome; ko04721 Synaptic ve	-0.50	0.0327	0.410911565

Triploids L3 vs L1

KOID	Gene Abbreviation	KEGG Annotation	Class	Log Fold Change	P Value	adj P Val
K13373	HSD17B7	17beta-estradiol 17-dehydrogenase / 3beta-hydroxysteroid 3-dehydrogenase [E	ko00100 Steroid biosynthesis; ko00140 Steroid hormone biosynthesis; ko04913 Ov	-1.55	0.0001	0.097393314
K02730	PSMA6	20S proteasome subunit alpha 1 [EC:3.4.25.1]	ko03050 Proteasome	-0.43	0.0031	0.15204453
K02731	PSMA7	20S proteasome subunit alpha 4 [EC:3.4.25.1]	ko03050 Proteasome	-0.60	0.0000	0.092606071
K02732	PSMB1	20S proteasome subunit beta 6 [EC:3.4.25.1]	ko03050 Proteasome	-0.54	0.0186	0.200624952
K06692	PSMD5	26S proteasome non-ATPase regulatory subunit 5	NA	-0.38	0.0088	0.172884702
K03029	PSMD4, RPN10	26S proteasome regulatory subunit N10	ko03050 Proteasome; ko05169 Epstein-Barr virus infection	-0.38	0.0086	0.172822126
K03033	PSMD3, RPN3	26S proteasome regulatory subunit N3	ko03050 Proteasome; ko05169 Epstein-Barr virus infection	-0.45	0.0195	0.203851854
K03035	PSMD12, RPN5	26S proteasome regulatory subunit N5	ko03050 Proteasome; ko05169 Epstein-Barr virus infection	-0.46	0.0279	0.224952262
K03062	PSMC1, RPT2	26S proteasome regulatory subunit T2	ko03050 Proteasome; ko05169 Epstein-Barr virus infection; ko05203 Viral carcinog	-0.49	0.0221	0.212426584
K03063	PSMC4, RPT3	26S proteasome regulatory subunit T3	ko03050 Proteasome; ko05169 Epstein-Barr virus infection	-0.60	0.0022	0.14321829
K03064	PSMC6, RPT4	26S proteasome regulatory subunit T4	ko03050 Proteasome; ko05169 Epstein-Barr virus infection	-0.79	0.0062	0.165190087
K03066	PSMC5, RPT6	26S proteasome regulatory subunit T6	ko03050 Proteasome; ko05169 Epstein-Barr virus infection	-0.42	0.0125	0.18692096
K14458	MOGAT1, MGAT1	2-acylglycerol O-acyltransferase 1 [EC:2.3.1.22]	NA	1.15	0.0097	0.18029481
K14457	MOGAT2, MGAT2	2-acylglycerol O-acyltransferase 2 [EC:2.3.1.22]	ko04975 Fat digestion and absorption	0.86	0.0034	0.152539243
K00457	HPD, hppD	4-hydroxyphenylpyruvate dioxygenase [EC:1.13.11.27]	ko00130 Ubiquinone and other terpenoid-quinone biosynthesis; ko00350 Tyrosine	0.43	0.0195	0.203851854
K00213	DHCR7	7-dehydrocholesterol reductase [EC:1.3.1.21]	ko00100 Steroid biosynthesis	-1.33	0.0055	0.165190087
K17816	NUDT1, MTH1	8-oxo-dGTP diphosphatase / 2-hydroxy-dATP diphosphatase [EC:3.6.1.55 3.	NA	-0.43	0.0495	0.266543434
K01895	ACSS, acs	acetyl-CoA synthetase [EC:6.2.1.1]	ko00010 Glycolysis / Gluconeogenesis; ko00620 Pyruvate metabolism; ko00640 Pro	0.69	0.0020	0.143042222
K12348	ASAH1	acid ceramidase [EC:3.5.1.23]	ko00600 Sphingolipid metabolism; ko04142 Lysosome	0.44	0.0328	0.237164916
K05757	ARPC1A_B	actin related protein 2/3 complex, subunit 1A/1B	ko04666 Fc gamma R-mediated phagocytosis; ko04810 Regulation of actin cytoskel	0.70	0.0064	0.165190087
K12314	ACTC1	actin, alpha cardiac muscle	ko04260 Cardiac muscle contraction; ko05410 Hypertrophic cardiomyopathy (HCM	0.43	0.0115	0.186859932
K11340	ACTL6A, INO80K	actin-like protein 6A	NA	-0.39	0.0314	0.232265167
K04675	ACVR1, ALK2	activin receptor type-1 [EC:2.7.11.30]	ko04060 Cytokine-cytokine receptor interaction; ko04350 TGF-beta signaling pathw	0.51	0.0031	0.15204453
K17362	ACOT13	acyl-coenzyme A thioesterase 13 [EC:3.1.2.-]	NA	-0.50	0.0062	0.165190087
K00814	GPT, ALT	alanine transaminase [EC:2.6.1.2]	ko00250 Alanine, aspartate and glutamate metabolism; ko00710 Carbon fixation ir	0.45	0.0063	0.165190087
K15537	AGMO	alkylglycerol monooxygenase [EC:1.14.16.5]	NA	0.76	0.0138	0.187508268
K09516	RETSAT	all-trans-retinol 13,14-reductase [EC:1.3.99.23]	ko00830 Retinol metabolism	0.38	0.0168	0.196890943
K15734	SDR16C5	all-trans-retinol dehydrogenase (NAD+) [EC:1.1.1.105]	ko00830 Retinol metabolism	0.43	0.0051	0.165133463
K01176	E3.2.1.1, amyA, malS	alpha-amylase [EC:3.2.1.1]	ko00500 Starch and sucrose metabolism; ko04973 Carbohydrate digestion and abs	0.92	0.0001	0.097393314
K11140	ANPEP	aminopeptidase N [EC:3.4.11.2]	ko00480 Glutathione metabolism; ko04614 Renin-angiotensin system; ko04640 He	-0.58	0.0113	0.186740724
K03349	APC2	anaphase-promoting complex subunit 2	ko04110 Cell cycle; ko04111 Cell cycle - yeast; ko04113 Meiosis - yeast; ko04114 Oc	-0.45	0.0005	0.143042222
K08767	ANGPTL4, PGAR	angiopoietin-like 4	ko03320 PPAR signaling pathway	0.79	0.0047	0.165133463
K10327	ASB5	ankyrin repeat and SOCS box protein 5	NA	-0.43	0.0100	0.18100852
K17091	ANXA1	annexin A1	NA	0.57	0.0158	0.193046798
K17093	ANXA4	annexin A4	NA	0.48	0.0224	0.212626738
K16646	ANXA5	annexin A5	NA	0.97	0.0057	0.165190087
K17095	ANXA7_11	annexin A7/11	NA	0.51	0.0029	0.15204453
K14462	APOB	apolipoprotein B	ko04975 Fat digestion and absorption; ko04977 Vitamin digestion and absorption	0.45	0.0111	0.186618503
K02434	gatB, PET112	aspartyl-tRNA(Asn)/glutamyl-tRNA(Gln) amidotransferase subunit B [EC:6	ko00970 Aminoacyl-tRNA biosynthesis	-0.41	0.0134	0.187355725
K13184	DHX9	ATP-dependent RNA helicase A [EC:3.6.4.13]	NA	-0.45	0.0033	0.152539243
K18655	DDX19, DBP5	ATP-dependent RNA helicase DDX19/DBP5 [EC:3.6.4.13]	NA	0.48	0.0240	0.216901595
K13182	DDX39	ATP-dependent RNA helicase DDX39 [EC:3.6.4.13]	NA	-0.53	0.0037	0.157088272
K14777	DDX47, RRP3	ATP-dependent RNA helicase DDX47/RRP3 [EC:3.6.4.13]	NA	-0.46	0.0137	0.187355725
K14810	DDX56, DBP9	ATP-dependent RNA helicase DDX56/DBP9 [EC:3.6.4.13]	NA	-0.45	0.0291	0.226747861
K16914	NO66	bifunctional lysine-specific demethylase and histidyl-hydroxylase NO66 [EC:1.1	NA	-0.45	0.0376	0.249525502
K12409	GNE	bifunctional UDP-N-acetylglucosamine 2-epimerase / N-acetylmannosamine kinas	ko00520 Amino sugar and nucleotide sugar metabolism	0.40	0.0351	0.24365317
K01435	BTD	biotinidase [EC:3.5.1.12]	ko00780 Biotin metabolism; ko04977 Vitamin digestion and absorption	0.78	0.0109	0.186087782
K04663	BMP5	bone morphogenetic protein 5	ko04350 TGF-beta signaling pathway; ko04390 Hippo signaling pathway	0.45	0.0180	0.198691113
K12332	CALCA	calcitonin	ko04270 Vascular smooth muscle contraction	1.23	0.0416	0.254344055
K17274	S100A10	calpactin-1 light chain	NA	0.58	0.0393	0.251981833
K03927	CES2	carboxylesterase 2 [EC:3.1.1.1 3.1.1.84 3.1.1.56]	ko00983 Drug metabolism - other enzymes	0.45	0.0085	0.172822126
K01294	CPE	carboxypeptidase E [EC:3.4.17.10]	ko04940 Type I diabetes mellitus	-0.54	0.0014	0.143042222
K13022	CPZ	carboxypeptidase Z [EC:3.4.17.-]	NA	0.53	0.0033	0.152539243
K08765	CPT1A	carnitine O-palmitoyltransferase 1, liver isoform [EC:2.3.1.21]	ko00071 Fatty acid degradation; ko03320 PPAR signaling pathway; ko04920 Adipoc	0.62	0.0028	0.15204453
K12801	CARD8, CARDINAL	caspase recruitment domain-containing protein 8	ko04621 NOD-like receptor signaling pathway	-0.54	0.0030	0.15204453
K03781	katE, CAT, catB, srpA	catalase [EC:1.11.1.6]	ko00380 Tryptophan metabolism; ko00630 Glyoxylate and dicarboxylate metaboli	0.52	0.0107	0.184946192
K00545	COMT	catechol O-methyltransferase [EC:2.1.1.6]	ko00140 Steroid hormone biosynthesis; ko00350 Tyrosine metabolism; ko00965 Be	0.56	0.0156	0.191823694
K01371	CTSK	cathepsin K [EC:3.4.22.38]	ko04142 Lysosome; ko04380 Osteoclast differentiation; ko04620 Toll-like receptor	0.40	0.0015	0.143042222
K05512	CCL19, ELC	C-C motif chemokine 19	ko04060 Cytokine-cytokine receptor interaction; ko04062 Chemokine signaling pa	-1.23	0.0387	0.25121965
K10050	CEBPD	CCAAT/enhancer binding protein (C/EBP), delta	NA	0.44	0.0427	0.254716933
K06454	CD4	CD4 antigen	ko04514 Cell adhesion molecules (CAMs); ko04612 Antigen processing and presen	0.57	0.0076	0.168745194
K04393	CDC42	cell division control protein 42	ko04010 MAPK signaling pathway; ko04011 MAPK signaling pathway - yeast; ko040	-0.44	0.0019	0.143042222
K04710	CERS	ceramide synthetase [EC:2.3.1.24]	ko00600 Sphingolipid metabolism	0.46	0.0048	0.165133463
K13624	CP	ceruloplasmin [EC:1.16.3.1]	ko00860 Porphyrin and chlorophyll metabolism	0.58	0.0417	0.254344055
K04077	groEL, HSPD1	chaperonin GroEL	ko03018 RNA degradation; ko04940 Type I diabetes mellitus; ko05134 Legionellosi	-0.68	0.0022	0.14321829
K05022	CLIC2	chloride intracellular channel protein 2	NA	0.44	0.0012	0.143042222
K07440	CYP46A1	cholesterol 24(S)-hydroxylase [EC:1.14.13.98]	ko00120 Primary bile acid biosynthesis	0.48	0.0370	0.247118814
K00489	CYP7A1	cholesterol 7alpha-monooxygenase [EC:1.14.13.17]	ko00120 Primary bile acid biosynthesis; ko00140 Steroid hormone biosynthesis; kc	2.61	0.0002	0.112669745
K11586	CBX3, HP1G	chromobox protein 3	NA	-0.43	0.0055	0.165190087
K17252	CLU	clusterin	NA	0.41	0.0064	0.165190087
K03899	F8	coagulation factor VIII	ko04610 Complement and coagulation cascades	0.60	0.0022	0.14321829
K13195	CIRBP	cold-inducible RNA-binding protein	NA	-0.54	0.0118	0.186859932
K06236	COL1AS	collagen, type I/II/III/V/XI/XXIV/XXVII, alpha	ko04151 PI3K-Akt signaling pathway; ko04510 Focal adhesion; ko04512 ECM-recept	1.00	0.0003	0.143042222
K06237	COL4A	collagen, type IV, alpha	ko04151 PI3K-Akt signaling pathway; ko04510 Focal adhesion; ko04512 ECM-recept	0.45	0.0041	0.161328781
K04011	CR1, CD35	complement component (3b/4b) receptor 1	ko04610 Complement and coagulation cascades; ko04640 Hematopoietic cell linea	0.38	0.0277	0.223998206
K01331	C1S	complement component 1, s subcomponent [EC:3.4.21.42]	ko04610 Complement and coagulation cascades; ko05133 Pertussis; ko05150 Staph	0.39	0.0389	0.251981833
K04002	C4BPA	complement component 4 binding protein, alpha	ko04610 Complement and coagulation cascades; ko05133 Pertussis	0.50	0.0123	0.186859932
K01334	CFD	component factor D [EC:3.4.21.46]	ko04610 Complement and coagulation cascades; ko05150 Staphylococcus aureus ir	1.05	0.0000	0.001870843
K06677	YCS4, CNAP1, CAPD2	condensin complex subunit 1	ko04111 Cell cycle - yeast	0.56	0.0011	0.143042222
K07213	ATOX1, ATX1, copZ	copper chaperone	ko04978 Mineral absorption	-0.47	0.0160	0.193753298
K00933	E2.7.3.2	creatine kinase [EC:2.7.3.2]	ko00330 Arginine and proline metabolism	0.41	0.0018	0.143042222
K17495	CSMD	CUB and sushi domain-containing protein	NA	0.48	0.0021	0.143042222
K09054	ATF6A	cyclic AMP-dependent transcription factor ATF-6 alpha	ko04141 Protein processing in endoplasmic reticulum; ko05010 Alzheimer's diseas	0.49	0.0397	0.252610475
K00456	CDO1	cysteine dioxygenase [EC:1.13.11.20]	ko00270 Cysteine and methionine metabolism; ko00430 Taurine and hypotaurine	0.54	0.0005	0.143042222
K08738	CYC	cytochrome c	ko00920 Sulfur metabolism; ko02020 Two-component system; ko04115 p53 signali	-0.38	0.0179	0.198691113
K18182	COX16	cytochrome c oxidase assembly protein subunit 16	NA	-0.54	0.0068	0.168745194
K02260	COX17	cytochrome c oxidase assembly protein subunit 17	ko00190 Oxidative phosphorylation	-0.47	0.0098	0.180472394
K18184	COX20	cytochrome c oxidase assembly protein subunit 20	NA	-0.61	0.0007	0.143042222
K02256	COX1	cytochrome c oxidase subunit 1 [EC:1.9.3.1]	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	0.40	0.0131	0.187355725
K02261	COX2	cytochrome c oxidase subunit 2	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	0.41	0.0335	0.239193287
K02262	COX3	cytochrome c oxidase subunit 3	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	0.55	0.0262	0.223131579
K02264	COX5A	cytochrome c oxidase subunit 5a	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	-0.54	0.0125	0.18692096
K02266	COX6A	cytochrome c oxidase subunit 6a	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	-0.42	0.0157	0.193046798
K02270	COX7A	cytochrome c oxidase subunit 7a	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	-0.53	0.0036	0.157088272
K02272	COX7C	cytochrome c oxidase subunit 7c	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	-0.38	0.0222	0.212506754
K07416	CYP2F	cytochrome P450, family 2, subfamily F [EC:1.14.14.1]	ko00980 Metabolism of xenobiotics by cytochrome P450	0.40	0.0178	0.198691113
K17858	CYP2X	cytochrome P450, family 2, subfamily X	NA	0.68	0.0360	0.246238756
K07424	CYP3A	cytochrome P450, family 3, subfamily A [EC:1.14.14.1]	ko00140 Steroid hormone biosynthesis; ko00591 Linoleic acid metabolism; ko0062	0.39	0.0422	0.254635449
K07427	CYP4V	cytochrome P450, family 4, subfamily V	NA	0.51	0.0300	0.22837528

K15730	PTGES3	cytosolic prostaglandin-E synthase [EC:5.3.99.3]	ko00590 Arachidonic acid metabolism	🟩	-0.47	0.0222	0.212506754
K00222	TM7SF2, ERG24	delta14-sterol reductase [EC:1.3.1.70]	ko00100 Steroid biosynthesis	🟩	-0.87	0.0110	0.186503889
K11995	DNASE1L	deoxyribonuclease-1-like protein [EC:3.1.21.-]	NA	🟥	0.73	0.0108	0.185417043
K11160	DGAT2	diacylglycerol O-acyltransferase 2 [EC:2.3.1.20 2.3.1.75]	ko00561 Glycerolipid metabolism; ko04975 Fat digestion and absorption	🟥	0.42	0.0257	0.221905228
K07766	E3.6.1.52	diphosphoinositol-polyphosphate diphosphatase [EC:3.6.1.52]	NA	🟩	-0.45	0.0078	0.168745194
K01597	MVD, mvaD	diphosphomevalonate decarboxylase [EC:4.1.1.33]	ko00900 Terpenoid backbone biosynthesis	🟩	-0.69	0.0029	0.15204453
K12475	DAB2	disabled homolog 2	ko04144 Endocytosis	🟥	0.47	0.0374	0.249020182
K02540	MCM2	DNA replication licensing factor MCM2 [EC:3.6.4.12]	ko03030 DNA replication; ko04110 Cell cycle; ko04111 Cell cycle - yeast; ko04113 M	🟩	-0.40	0.0460	0.258205427
K02209	MCM5, CDC46	DNA replication licensing factor MCM5 [EC:3.6.4.12]	ko03030 DNA replication; ko04110 Cell cycle; ko04111 Cell cycle - yeast; ko04113 M	🟩	-0.64	0.0156	0.191823694
K02542	MCM6	DNA replication licensing factor MCM6 [EC:3.6.4.12]	ko03030 DNA replication; ko04110 Cell cycle; ko04111 Cell cycle - yeast; ko04113 M	🟩	-0.87	0.0104	0.182571981
K17693	ID2	DNA-binding protein inhibitor ID2	NA	🟥	0.58	0.0393	0.251981833
K03015	RPB7, POLR2G	DNA-directed RNA polymerase II subunit RPB7	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polym	🟩	-0.44	0.0213	0.20698367
K03017	RPB9, POLR2I	DNA-directed RNA polymerase II subunit RPB9	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polym	🟩	-0.44	0.0060	0.165190087
K03019	RPC11, POLR3K	DNA-directed RNA polymerase III subunit RPC11	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polym	🟩	-0.39	0.0203	0.205722905
K03020	RPC19, POLR1D	DNA-directed RNA polymerases I and III subunit RPAC2	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polym	🟩	-0.58	0.0010	0.143042222
K03013	RPB5, POLR2E	DNA-directed RNA polymerases I, II, and III subunit RPABC1	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polym	🟩	-0.52	0.0074	0.168745194
K03007	RPB10, POLR2L	DNA-directed RNA polymerases I, II, and III subunit RPABC5	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko03020 RNA polym	🟩	-0.50	0.0018	0.143042222
K10880	XRCC3	DNA-repair protein XRCC3	ko03440 Homologous recombination	🟩	-0.46	0.0000	0.063123807
K10415	DYNC1I, DNCI	dynein intermediate chain, cytosolic	ko04145 Phagosome; ko04962 Vasopressin-regulated water reabsorption; ko0513	🟩	-0.44	0.0042	0.161328781
K10660	Mar-05	E3 ubiquitin-protein ligase MARCH5 [EC:6.3.2.19]	NA	🟩	-0.42	0.0033	0.152539243
K10601	SYVN1, HRD1	E3 ubiquitin-protein ligase synoviolin [EC:6.3.2.19]	ko04120 Ubiquitin mediated proteolysis; ko04141 Protein processing in endoplas	🟥	0.42	0.0362	0.246238756
K15901	CGI121, TPRKB	EKC/KEOPS complex subunit CGI121/TPRKB	NA	🟩	-0.50	0.0007	0.143042222
K15902	PCC1, LAGE3	EKC/KEOPS complex subunit PCC1/LAGE3	NA	🟩	-0.39	0.0085	0.172822126
K03522	fixB, etfA	electron transfer flavoprotein alpha subunit	NA	🟩	-0.95	0.0007	0.143042222
K10205	ELOVL2	elongation of very long chain fatty acids protein 2 [EC:2.3.1.199]	ko00062 Fatty acid elongation; ko01040 Biosynthesis of unsaturated fatty acids	🟩	-0.45	0.0194	0.203851854
K01173	ENDOG	endonuclease G, mitochondrial	ko04210 Apoptosis	🟩	-0.51	0.0133	0.187355725
K14286	AGXT2L1, ETNPPL	ethanolamine-phosphate phospho-lyase [EC:4.2.3.2]	NA	🟥	0.49	0.0117	0.186859932
K03681	RRP40, EXOSC3	exosome complex component RRP40	ko03018 RNA degradation	🟩	-0.61	0.0003	0.143042222
K00787	FDPS	farnesyl diphosphate synthase [EC:2.5.1.1 2.5.1.10]	ko00900 Terpenoid backbone biosynthesis; ko05164 Influenza A; ko05166 HTLV-I i	🟩	-1.03	0.0030	0.15204453
K02373	FADD	FAS-associated death domain protein	ko04210 Apoptosis; ko04620 Toll-like receptor signaling pathway; ko04622 RIG-I-li	🟩	-0.43	0.0164	0.195337521
K08751	FABP2	fatty acid-binding protein 2, intestinal	ko03320 PPAR signaling pathway; ko04975 Fat digestion and absorption	🟥	1.70	0.0141	0.187641673
K08752	FABP3	fatty acid-binding protein 3, muscle and heart	ko03320 PPAR signaling pathway	🟥	0.46	0.0211	0.206767944
K08755	FABP6	fatty acid-binding protein 6, ileal (gastrotropin)	ko03320 PPAR signaling pathway	🟥	0.40	0.0040	0.161328781
K10285	FBXL19	F-box and leucine-rich repeat protein 19	NA	🟥	0.49	0.0293	0.226747861
K00522	FTH1	ferritin heavy chain [EC:1.16.3.2]	ko00860 Porphyrin and chlorophyll metabolism; ko04978 Mineral absorption	🟥	0.42	0.0097	0.18029481
K09570	FKBP3	FK506-binding protein 3 [EC:5.2.1.8]	NA	🟩	-0.54	0.0135	0.187355725
K09409	FOXP	forkhead box protein P	NA	🟥	0.53	0.0306	0.229821398
K02133	ATPeF1B, ATP5B, ATP2	F-type H+-transporting ATPase subunit beta [EC:3.6.3.14]	ko00190 Oxidative phosphorylation; ko05010 Alzheimer's disease; ko05012 Parkin	🟥	0.60	0.0013	0.143042222
K02128	ATPeF0C, ATP5G, ATP9	F-type H+-transporting ATPase subunit c	ko00190 Oxidative phosphorylation; ko05010 Alzheimer's disease; ko05012 Parkin	🟩	-1.05	0.0019	0.143042222
K12900	FUSIP1	FUS-interacting serine-arginine-rich protein 1	ko03040 Spliceosome	🟩	-0.49	0.0378	0.249741275
K08266	GBL	G protein beta subunit-like	ko04150 mTOR signaling pathway; ko04151 PI3K-Akt signaling pathway	🟩	-0.44	0.0040	0.161328781
K08426	GPR132	G protein-coupled receptor 132	NA	🟥	0.96	0.0010	0.143042222
K11257	FUT11	galactoside 3-L-fucosyltransferase 11 [EC:2.4.1.-]	NA	🟥	0.42	0.0199	0.205299668
K17300	LGALS3BP	galectin-3-binding protein	NA	🟥	0.54	0.0099	0.180472394
K00699	UGT	glucuronosyltransferase [EC:2.4.1.17]	ko00040 Pentose and glucuronate interconversions; ko00053 Ascorbate and aldara	🟥	0.64	0.0019	0.143042222
K13990	FTCD	glutamate formiminotransferase / formiminotetrahydrofolate cyclodeaminase [E	ko00340 Histidine metabolism; ko00670 One carbon pool by folate	🟥	0.75	0.0191	0.203435986
K00252	GCDH, gcdH	glutaryl-CoA dehydrogenase [EC:1.3.8.6]	ko00071 Fatty acid degradation; ko00310 Lysine degradation; ko00380 Tryptophan	🟩	-0.78	0.0001	0.097393314
K00432	E1.11.1.9	glutathione peroxidase [EC:1.11.1.9]	ko00480 Glutathione metabolism; ko00590 Arachidonic acid metabolism; ko04918	🟥	0.75	0.0367	0.246725736
K00600	glyA, SHMT	glycine hydroxymethyltransferase [EC:2.1.2.1]	ko00260 Glycine, serine and threonine metabolism; ko00460 Cyanoamino acid me	🟥	0.42	0.0133	0.187355725
K01196	AGL	glycogen debranching enzyme [EC:2.4.1.25 3.2.1.33]	ko00500 Starch and sucrose metabolism	🟥	0.65	0.0004	0.143042222
K00049	GRHPR	glyoxylate/hydroxypyruvate reductase [EC:1.1.1.79 1.1.1.81]	ko00260 Glycine, serine and threonine metabolism; ko00620 Pyruvate metabolis	🟥	0.55	0.0259	0.221989249
K06232	GAS1	growth arrest-specific 1	ko04340 Hedgehog signaling pathway	🟥	0.49	0.0100	0.18100852
K04630	GNAI	guanine nucleotide-binding protein G(i) subunit alpha	ko04062 Chemokine signaling pathway; ko04360 Axon guidance; ko04530 Tight jun	🟥	0.39	0.0044	0.165133463
K01139	spoT, HDDC3	guanosine-3',5'-bis(diphosphate) 3'-pyrophosphohydrolase [EC:3.1.7.2]	ko00230 Purine metabolism	🟩	-0.52	0.0094	0.178297363
K11128	GAR1, NOLA1	H/ACA ribonucleoprotein complex subunit 1	ko03008 Ribosome biogenesis in eukaryotes	🟩	-0.61	0.0185	0.200420738
K11129	NHP2, NOLA2	H/ACA ribonucleoprotein complex subunit 2	ko03008 Ribosome biogenesis in eukaryotes	🟩	-0.54	0.0469	0.260922686
K11130	NOP10, NOLA3	H/ACA ribonucleoprotein complex subunit 3	ko03008 Ribosome biogenesis in eukaryotes	🟩	-0.55	0.0064	0.165190087
K09414	HSF1	heat shock transcription factor 1	ko05134 Legionellosis	🟥	0.66	0.0363	0.246238756
K13044	HNRNPABD	heterogeneous nuclear ribonucleoprotein A/B/D	NA	🟩	-0.40	0.0176	0.198691113
K12894	HNRNPA0	heterogeneous nuclear ribonucleoprotein A0	NA	🟩	-0.56	0.0411	0.254344055
K12885	RBMX, HNRNPG	heterogeneous nuclear ribonucleoprotein G	ko03040 Spliceosome	🟩	-0.63	0.0459	0.258205427
K11296	HMGB3	high mobility group protein B3	NA	🟩	-0.63	0.0362	0.246238756
K11307	MYST2, HBO1, KAT7	histone acetyltransferase MYST2 [EC:2.3.1.48]	NA	🟩	-0.45	0.0016	0.143042222
K11251	H2A	histone H2A	ko05034 Alcoholism; ko05322 Systemic lupus erythematosus	🟩	-0.41	0.0077	0.168745194
K11252	H2B	histone H2B	ko05034 Alcoholism; ko05203 Viral carcinogenesis; ko05322 Systemic lupus erythe	🟩	-0.54	0.0172	0.197085215
K08024	HHEX, HEX, PRH	homeobox protein HEX	ko04950 Maturity onset diabetes of the young; ko05202 Transcriptional misregulat	🟥	0.44	0.0053	0.165190087
K09339	HLX1	homeobox protein HLX1	NA	🟥	0.48	0.0021	0.143042222
K08648	HABP2	hyaluronan binding protein 2 [EC:3.4.21.-]	NA	🟥	0.75	0.0471	0.261133498
K11394	PRODH2	hydroxyproline oxidase [EC:1.5.-.-]	ko00330 Arginine and proline metabolism	🟥	0.44	0.0141	0.187641673
K01507	ppa	inorganic pyrophosphatase [EC:3.6.1.1]	ko00190 Oxidative phosphorylation	🟩	-0.42	0.0335	0.239193287
K05719	ITGB1	integrin beta 1	ko04145 Phagosome; ko04151 PI3K-Akt signaling pathway; ko04360 Axon guidance	🟥	0.66	0.0001	0.097393314
K06566	IFITM	interferon induced transmembrane protein	NA	🟥	0.45	0.0008	0.143042222
K04387	IL1R2	interleukin 1 receptor type II	ko04010 MAPK signaling pathway; ko04060 Cytokine-cytokine receptor interactio	🟩	-0.39	0.0017	0.143042222
K05055	IL6R	interleukin 6 receptor	ko04060 Cytokine-cytokine receptor interaction; ko04066 HIF-1 signaling pathway;	🟥	0.52	0.0027	0.15204453
K13089	ILF2	interleukin enhancer-binding factor 2	NA	🟩	-0.68	0.0015	0.143042222
K01823	idi, IDI	isopentenyl-diphosphate delta-isomerase [EC:5.3.3.2]	ko00900 Terpenoid backbone biosynthesis	🟩	-1.17	0.0024	0.14835443
K17845	KLF2	krueppel-like factor 2	NA	🟥	0.41	0.0074	0.168745194
K05636	LAMB1	laminin, beta 1	ko04151 PI3K-Akt signaling pathway; ko04510 Focal adhesion; ko04512 ECM-recep	🟥	0.54	0.0037	0.157088272
K02873	RP-L13e, RPL13	large subunit ribosomal protein L13e	ko03010 Ribosome	🟩	-0.69	0.0078	0.168745194
K02888	RP-L21, MRPL21, rplU	large subunit ribosomal protein L21	ko03010 Ribosome	🟩	-0.41	0.0184	0.200096052
K02890	RP-L22, MRPL22, rplV	large subunit ribosomal protein L22	ko03010 Ribosome	🟩	-0.40	0.0051	0.165133463
K02891	RP-L22e, RPL22	large subunit ribosomal protein L22e	ko03010 Ribosome	🟩	-0.47	0.0180	0.198691113
K02893	RP-L23Ae, RPL23A	large subunit ribosomal protein L23Ae	ko03010 Ribosome	🟩	-0.48	0.0057	0.165190087
K02896	RP-L24e, RPL24	large subunit ribosomal protein L24e	ko03010 Ribosome	🟩	-0.39	0.0117	0.186859932
K02899	RP-L27, MRPL27, rpmA	large subunit ribosomal protein L27	ko03010 Ribosome	🟩	-0.41	0.0154	0.191417951
K02910	RP-L31e, RPL31	large subunit ribosomal protein L31e	ko03010 Ribosome	🟩	-0.43	0.0168	0.196890943
K02911	RP-L32, MRPL32, rpmF	large subunit ribosomal protein L32	ko03010 Ribosome	🟩	-0.53	0.0086	0.172822126
K02912	RP-L32e, RPL32	large subunit ribosomal protein L32e	ko03010 Ribosome	🟩	-0.46	0.0370	0.247118814
K02916	RP-L35, MRPL35, rpmI	large subunit ribosomal protein L35	ko03010 Ribosome	🟩	-0.55	0.0020	0.143042222
K02919	RP-L36, MRPL36, rpmJ	large subunit ribosomal protein L36	ko03010 Ribosome	🟩	-0.48	0.0017	0.143042222
K17422	MRPL41	large subunit ribosomal protein L41	NA	🟩	-0.50	0.0071	0.168745194
K17423	MRPL42	large subunit ribosomal protein L42	NA	🟩	-0.51	0.0034	0.152539243
K17427	MRPL46	large subunit ribosomal protein L46	NA	🟩	-0.73	0.0027	0.15204453
K17428	MRPL47, NCM1	large subunit ribosomal protein L47	NA	🟩	-0.50	0.0292	0.226747861
K17430	MRPL49, NOF1	large subunit ribosomal protein L49	NA	🟩	-0.44	0.0364	0.246332947
K17432	MRPL51	large subunit ribosomal protein L51	NA	🟩	-0.41	0.0152	0.190267528
K17433	MRPL52	large subunit ribosomal protein L52	NA	🟩	-0.54	0.0123	0.186859932
K02934	RP-L6e, RPL6	large subunit ribosomal protein L6e	ko03010 Ribosome	🟩	-1.58	0.0061	0.165190087
K02937	RP-L7e, RPL7	large subunit ribosomal protein L7e	ko03010 Ribosome	🟩	-0.41	0.0393	0.251981833
K00227	SC5DL, ERG3	lathosterol oxidase [EC:1.14.21.6]	ko00100 Steroid biosynthesis	🟩	-0.54	0.0020	0.143042222

K00650	LCAT	lecithin-cholesterol acyltransferase [EC:2.3.1.43]	ko00564 Glycerophospholipid metabolism	🟥	0.46	0.0274	0.223998206
K01059	LPL	lipoprotein lipase [EC:3.1.1.34]	ko00561 Glycerolipid metabolism; ko03320 PPAR signaling pathway; ko05010 Alzh	🟥	0.51	0.0017	0.143042222
K12384	SCARB2, LIMP2, CD36L2	lysosome membrane protein 2	ko04142 Lysosome	🟥	0.66	0.0007	0.143042222
K03991	MBL	mannose-binding lectin	ko04145 Phagosome; ko04610 Complement and coagulation cascades; ko05150 Sta	🟥	1.35	0.0029	0.15204453
K15159	MED16	mediator of RNA polymerase II transcription subunit 16	NA	🟥	0.59	0.0092	0.175549137
K15135	MED18	mediator of RNA polymerase II transcription subunit 18	NA	🟩	-0.42	0.0096	0.17983084
K04200	MC2R	melanocortin 2 receptor	ko04080 Neuroactive ligand-receptor interaction	🟥	0.43	0.0225	0.213229584
K14737	STEAP1	metalloreductase STEAP1 [EC:1.16.1.-]	ko04978 Mineral absorption	🟥	0.39	0.0009	0.143042222
K14618	MMACHC	methylmalonic aciduria homocystinuria type C protein	ko04977 Vitamin digestion and absorption	🟩	-0.43	0.0123	0.186859932
K00869	E2.7.1.36, MVK, mvaK1	mevalonate kinase [EC:2.7.1.36]	ko00900 Terpenoid backbone biosynthesis; ko04146 Peroxisome	🟩	-0.50	0.0048	0.165133463
K06258	SV2	MFS transporter, VNT family, synaptic vesicle glycoprotein 2	ko04512 ECM-receptor interaction	🟩	-0.41	0.0213	0.20698367
K05309	PTGES2	microsomal prostaglandin-E synthase 2 [EC:5.3.99.3]	ko00590 Arachidonic acid metabolism	🟥	0.46	0.0123	0.186859932
K14463	MTTP, MTP	microsomal triglyceride transfer protein large subunit	ko04975 Fat digestion and absorption	🟥	0.44	0.0139	0.187508268
K17780	TIM8	mitochondrial import inner membrane translocase subunit TIM8	NA	🟩	-0.44	0.0254	0.220819904
K17777	TIM9	mitochondrial import inner membrane translocase subunit TIM9	NA	🟩	-0.40	0.0386	0.25121965
K17770	TOM20	mitochondrial import receptor subunit TOM20	NA	🟩	-0.40	0.0248	0.218040876
K11518	TOM40	mitochondrial import receptor subunit TOM40	ko05014 Amyotrophic lateral sclerosis (ALS)	🟩	-0.64	0.0144	0.189571307
K17773	TOM5	mitochondrial import receptor subunit TOM5	NA	🟩	-0.47	0.0021	0.14321829
K17772	TOM6	mitochondrial import receptor subunit TOM6	NA	🟩	-0.49	0.0218	0.210559277
K03687	GRPE	molecular chaperone GrpE	NA	🟩	-0.45	0.0060	0.165190087
K15448	TRM112, TRMT112	multifunctional methyltransferase subunit TRM112	NA	🟩	-0.43	0.0237	0.216901595
K18458	ACY3	N-acyl-aromatic-L-amino acid amidohydrolase [EC:3.5.1.114]	NA	🟥	0.45	0.0299	0.22837528
K13985	NAPEPLD	N-acyl-phosphatidylethanolamine-hydrolysing phospholipase D [EC:3.1.4.54]	ko04723 Retrograde endocannabinoid signaling	🟥	0.38	0.0017	0.143042222
K03945	NDUFA1	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex subunit 1	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟩	-0.39	0.0078	0.168745194
K03956	NDUFA11	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex subunit 11	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟩	-0.38	0.0139	0.187508268
K03946	NDUFA2	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex subunit 2	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟩	-0.43	0.0115	0.186859932
K03955	NDUFAB1	NADH dehydrogenase (ubiquinone) 1 alpha/beta subcomplex 1	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟩	-0.60	0.0009	0.143042222
K03957	NDUFB1	NADH dehydrogenase (ubiquinone) 1 beta subcomplex subunit 1	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟩	-0.47	0.0044	0.165133463
K11351	NDUFB11	NADH dehydrogenase (ubiquinone) 1 beta subcomplex subunit 11	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟩	-0.40	0.0137	0.187355725
K03934	NDUFS1	NADH dehydrogenase (ubiquinone) Fe-S protein 1 [EC:1.6.5.3 1.6.99.3]	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟥	0.41	0.0130	0.187355725
K03938	NDUFS5	NADH dehydrogenase (ubiquinone) Fe-S protein 5	ko00190 Oxidative phosphorylation; ko04932 Non-alcoholic fatty liver disease (NA	🟩	-0.39	0.0102	0.181674235
K08011	NCF1, P47PHOX	neutrophil cytosolic factor 1	ko04062 Chemokine signaling pathway; ko04145 Phagosome; ko04380 Osteoclast	🟩	-1.15	0.0032	0.15204453
K04807	CHRNA5	nicotinic acetylcholine receptor alpha-5	ko04080 Neuroactive ligand-receptor interaction	🟩	-0.40	0.0136	0.187355725
K17972	NAA20, NAT3	N-terminal acetyltransferase B complex catalytic subunit [EC:2.3.1.88]	NA	🟩	-0.41	0.0080	0.168788939
K12883	NCBP2, CBP20	nuclear cap-binding protein subunit 2	ko03013 RNA transport; ko03015 mRNA surveillance pathway; ko03040 Spliceosom	🟩	-0.49	0.0031	0.15204453
K14302	NUP37	nuclear pore complex protein Nup37	ko03013 RNA transport	🟩	-0.44	0.0271	0.223618949
K14840	NOP53, GLTSCR2	nucleolar protein 53	ko05168 Herpes simplex infection	🟩	-0.51	0.0081	0.171859824
K13288	orn, REX2, REXO2	oligoribonuclease [EC:3.1.-.-]	ko03008 Ribosome biogenesis in eukaryotes	🟩	-0.42	0.0488	0.264832304
K14360	OSTALPHA, OSTA, SLC51A1	organic solute transporter subunit alpha	ko04976 Bile secretion	🟥	0.42	0.0057	0.165190087
K05215	P2RX1	P2X purinoceptor 1	ko04020 Calcium signaling pathway; ko04080 Neuroactive ligand-receptor interact	🟩	-0.40	0.0273	0.223998206
K17659	PTCD3	pentatricopeptide repeat domain-containing protein 3	NA	🟩	-0.64	0.0086	0.172822126
K12733	PPIL1	peptidyl-prolyl cis-trans isomerase-like 1 [EC:5.2.1.8]	ko03040 Spliceosome	🟩	-0.52	0.0225	0.213229584
K12734	PPIL3	peptidyl-prolyl cis-trans isomerase-like 3 [EC:5.2.1.8]	NA	🟩	-0.41	0.0079	0.168745194
K04794	PTH2	peptidyl-tRNA hydrolase, PTH2 family [EC:3.1.1.29]	NA	🟩	-0.44	0.0030	0.15204453
K14558	PWP2, UTP1	periodic tryptophan protein 2	ko03008 Ribosome biogenesis in eukaryotes	🟩	-0.68	0.0128	0.187355725
K00500	phhA, PAH	phenylalanine-4-hydroxylase [EC:1.14.16.1]	ko00360 Phenylalanine metabolism; ko00400 Phenylalanine, tyrosine and tryptop	🟥	0.71	0.0103	0.182571981
K01889	FARSA, pheS	phenylalanyl-tRNA synthetase alpha chain [EC:6.1.1.20]	ko00970 Aminoacyl-tRNA biosynthesis	🟩	-0.41	0.0056	0.165190087
K01080	PPAP2	phosphatidate phosphatase [EC:3.1.3.4]	ko00561 Glycerolipid metabolism; ko00564 Glycerophospholipid metabolism; ko0	🟩	-0.95	0.0060	0.165190087
K19404	LIPH_I	phosphatidic acid-selective&#160	NA	🟥	0.39	0.0297	0.227893755
K05929	E2.1.1.103, NMT	phosphoethanolamine N-methyltransferase [EC:2.1.1.103]	ko00564 Glycerophospholipid metabolism	🟥	0.56	0.0008	0.143042222
K01112	PHPT1	phosphohistidine phosphatase [EC:3.1.3.-]	ko00051 Fructose and mannose metabolism	🟩	-0.39	0.0007	0.143042222
K13618	PLA1A	phospholipase A1 member A [EC:3.1.1.-]	NA	🟥	0.54	0.0097	0.18029481
K01079	serB, PSPH	phosphoserine phosphatase [EC:3.1.3.3]	ko00260 Glycine, serine and threonine metabolism; ko00680 Methane metabolisn	🟩	-0.72	0.0257	0.221905228
K01315	PLG	plasminogen [EC:3.4.21.7]	ko04080 Neuroactive ligand-receptor interaction; ko04610 Complement and coagu	🟥	0.70	0.0405	0.254260306
K13126	PABPC	polyadenylate-binding protein	ko03013 RNA transport; ko03015 mRNA surveillance pathway; ko03018 RNA degra	🟩	-0.39	0.0410	0.254344055
K00710	GALNT	polypeptide N-acetylgalactosaminyltransferase [EC:2.4.1.41]	ko00512 Mucin type O-Glycan biosynthesis	🟥	0.79	0.0413	0.254344055
K12820	DHX15, PRP43	pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15/PRP43 [EC:3.	ko03040 Spliceosome	🟩	-0.39	0.0139	0.187508268
K00276	AOC3, AOC2, tynA	primary-amine oxidase [EC:1.4.3.21]	ko00260 Glycine, serine and threonine metabolism; ko00350 Tyrosine metabolism	🟥	0.43	0.0345	0.241701062
K04802	PCNA	proliferating cell nuclear antigen	ko03030 DNA replication; ko03410 Base excision repair; ko03420 Nucleotide excisi	🟩	-0.64	0.0102	0.181674235
K01830	E5.3.99.2, PTGDS	prostaglandin-H2 D-isomerase [EC:5.3.99.2]	ko00590 Arachidonic acid metabolism	🟥	0.48	0.0030	0.15204453
K11599	POMP, UMP1	proteasome maturation protein	ko03050 Proteasome	🟩	-0.40	0.0070	0.168745194
K02516	PRMT5, HSL7	protein arginine N-methyltransferase 5 [EC:2.1.1.125]	ko03013 RNA transport; ko04111 Cell cycle - yeast	🟩	-0.49	0.0091	0.175063798
K18266	NDRG1	protein NDRG1	NA	🟥	0.58	0.0360	0.246238756
K16219	METTL11, NTM1	protein N-terminal methyltransferase [EC:2.1.1.244]	NA	🟩	-0.44	0.0271	0.223618949
K17499	PPM1G, PP2CG	protein phosphatase 1G [EC:3.1.3.16]	NA	🟩	-0.39	0.0035	0.153325268
K00573	E2.1.1.77, pcm	protein-L-isoaspartate(D-aspartate) O-methyltransferase [EC:2.1.1.77	NA	🟥	0.88	0.0198	0.205299668
K03783	punA	purine-nucleoside phosphorylase [EC:2.4.2.1]	ko00230 Purine metabolism; ko00240 Pyrimidine metabolism; ko00760 Nicotinate	🟥	0.82	0.0015	0.143042222
K05762	RDX	radixin	ko04810 Regulation of actin cytoskeleton; ko05205 Proteoglycans in cancer; ko052	🟥	0.67	0.0095	0.179800348
K15306	RANBP1	Ran-binding protein 1	ko05166 HTLV-I infection; ko05203 Viral carcinogenesis	🟩	-0.42	0.0056	0.165190087
K07906	RAB25	Ras-related protein Rab-25	NA	🟥	0.58	0.0245	0.218040876
K08526	NR2B3, RXRG	retinoid X receptor gamma	ko03320 PPAR signaling pathway; ko04920 Adipocytokine signaling pathway; ko05	🟥	0.46	0.0097	0.18029481
K10743	RNASEH2A	ribonuclease H2 subunit A [EC:3.1.26.4]	ko03030 DNA replication	🟩	-0.42	0.0045	0.165133463
K00784	rnz	ribonuclease Z [EC:3.1.26.11]	ko03013 RNA transport	🟩	-0.61	0.0015	0.143042222
K14530	RPP40	ribonucleases P/MRP protein subunit RPP40 [EC:3.1.26.5]	ko03008 Ribosome biogenesis in eukaryotes; ko03013 RNA transport	🟩	-0.40	0.0086	0.172822126
K15433	CGI99, CLE7, RLLM1	RLL motif containing protein 1	NA	🟩	-0.42	0.0303	0.229821398
K13094	RBM5_10	RNA-binding protein 5/10	NA	🟥	0.39	0.0086	0.172822126
K00121	frmA, ADH5, adhC	S-(hydroxymethyl)glutathione dehydrogenase / alcohol dehydrogenase	ko00010 Glycolysis / Gluconeogenesis; ko00071 Fatty acid degradation; ko00350 Ty	🟥	0.80	0.0239	0.216901595
K12382	PSAP, SGP1	saposin	ko04142 Lysosome	🟥	0.39	0.0047	0.165133463
K16312	STK40, SHIK	serine/threonine-protein kinase 40 [EC:2.7.11.1]	NA	🟥	0.63	0.0136	0.187355725
K08269	ULK1_2_3, ATG1	serine/threonine-protein kinase ULK/ATG1 [EC:2.7.11.1]	ko04140 Regulation of autophagy; ko04150 mTOR signaling pathway	🟥	0.38	0.0103	0.182571981
K15637	PGAM5	serine/threonine-protein phosphatase PGAM5 [EC:3.1.3.16]	ko04668 TNF signaling pathway	🟩	-0.41	0.0021	0.143042222
K16141	ALB	serum albumin	NA	🟥	0.40	0.0087	0.172822126
K05304	NANS, SAS	sialic acid synthase [EC:2.5.1.56 2.5.1.57]	ko00520 Amino sugar and nucleotide sugar metabolism	🟩	-0.53	0.0061	0.165190087
K11220	STAT1	signal transducer and activator of transcription 1	ko04062 Chemokine signaling pathway; ko04380 Osteoclast differentiation; ko046	🟥	0.41	0.0277	0.223998206
K11096	SNRPD2, SMD2	small nuclear ribonucleoprotein D2	ko03040 Spliceosome	🟩	-0.49	0.0010	0.143042222
K11098	SNRPF, SMF	small nuclear ribonucleoprotein F	ko03040 Spliceosome	🟩	-0.57	0.0013	0.143042222
K11099	SNRPG, SMG	small nuclear ribonucleoprotein G	ko03040 Spliceosome	🟩	-0.49	0.0075	0.168745194
K02948	RP-S11, MRPS11, rpsK	small subunit ribosomal protein S11	ko03010 Ribosome	🟩	-0.68	0.0066	0.165190087
K02950	RP-S12, MRPS12, rpsL	small subunit ribosomal protein S12	ko03010 Ribosome	🟩	-0.53	0.0057	0.165190087
K02954	RP-S14, MRPS14, rpsN	small subunit ribosomal protein S14	ko03010 Ribosome	🟩	-0.47	0.0190	0.202958509
K02960	RP-S16e, RPS16	small subunit ribosomal protein S16e	ko03010 Ribosome	🟩	-0.39	0.0051	0.165133463
K02962	RP-S17e, RPS17	small subunit ribosomal protein S17e	ko03010 Ribosome	🟩	-0.42	0.0393	0.251981833
K16174	MRPS18B, MRPS18-2	small subunit ribosomal protein S18b, mitochondrial	ko05203 Viral carcinogenesis	🟩	-0.42	0.0112	0.186740724
K02969	RP-S20e, RPS20	small subunit ribosomal protein S20e	ko03010 Ribosome	🟩	-0.49	0.0060	0.165190087
K02970	RP-S21, MRPS21, rpsU	small subunit ribosomal protein S21	ko03010 Ribosome	🟩	-0.42	0.0099	0.180472394
K17404	MRPS25	small subunit ribosomal protein S25	NA	🟩	-0.52	0.0011	0.143042222
K02975	RP-S25e, RPS25	small subunit ribosomal protein S25e	ko03010 Ribosome	🟩	-0.50	0.0043	0.163642877
K02976	RP-S26e, RPS26	small subunit ribosomal protein S26e	ko03010 Ribosome	🟩	-0.56	0.0121	0.186859932
K17412	MRPS34	small subunit ribosomal protein S34	NA	🟩	-0.59	0.0051	0.165133463
K02989	RP-S5e, RPS5	small subunit ribosomal protein S5e	ko03010 Ribosome	🟩	-0.59	0.0050	0.165133463

K02990	RP-S6, MRPS6, rpsF	small subunit ribosomal protein S6	ko03010 Ribosome	🟩	-0.39	0.0348	0.242713867
K02991	RP-S6e, RPS6	small subunit ribosomal protein S6e	ko03010 Ribosome; ko04066 HIF-1 signaling pathway; ko04150 mTOR signaling pat	🟩	-0.47	0.0132	0.187355725
K02992	RP-S7, MRPS7, rpsG	small subunit ribosomal protein S7	ko03010 Ribosome	🟩	-0.44	0.0341	0.241125045
K02998	RP-SAe, RPSA	small subunit ribosomal protein SAe	ko03010 Ribosome	🟩	-0.56	0.0435	0.256044303
K12160	SUMO, SMT3	small ubiquitin-related modifier	ko03013 RNA transport	🟩	-0.63	0.0041	0.161328781
K05863	SLC25A4S, ANT	solute carrier family 25 (mitochondrial adenine nucleotide translocat	ko04020 Calcium signaling pathway; ko05012 Parkinson's disease; ko05016 Huntin	🟩	-0.38	0.0433	0.255943021
K08746	SLC27A2, FACVL1, FATP2	solute carrier family 27 (fatty acid transporter), member 2	ko03320 PPAR signaling pathway; ko04146 Peroxisome	🟥	0.56	0.0039	0.161227988
K06519	CD98, SLC3A2	solute carrier family 3 (activators of dibasic and neutral amino acid	ko04974 Protein digestion and absorption	🟥	0.52	0.0031	0.15204453
K00511	SQLE, ERG1	squalene monooxygenase [EC:1.14.13.132]	ko00909 Sesquiterpenoid and triterpenoid biosynthesis	🟩	-0.50	0.0121	0.186859932
K07431	CYP8B1	sterol 12-alpha-hydroxylase [EC:1.14.13.95 1.14.13.96]	ko00120 Primary bile acid biosynthesis; ko03320 PPAR signaling pathway	🟥	0.65	0.0028	0.15204453
K05917	CYP51	sterol 14-demethylase [EC:1.14.13.70]	ko00100 Steroid biosynthesis	🟩	-1.40	0.0010	0.143042222
K07748	E1.1.1.170, NSDHL, ERG26	sterol-4alpha-carboxylate 3-dehydrogenase (decarboxylating	ko00100 Steroid biosynthesis	🟩	-0.46	0.0047	0.165133463
K09494	CCT2	T-complex protein 1 subunit beta	NA	🟩	-0.41	0.0338	0.239980947
K10758	QSOX	thiol oxidase [EC:1.8.3.2]	NA	🟥	0.49	0.0133	0.187355725
K00758	deoA, TYMP	thymidine phosphorylase [EC:2.4.2.4]	ko00240 Pyrimidine metabolism; ko00983 Drug metabolism - other enzymes; ko05	🟥	0.78	0.0363	0.246238756
K09058	TEF	thyrotrophic embryonic factor	NA	🟥	1.02	0.0173	0.197085215
K07754	DIO3	thyroxine 5-deiodinase [EC:1.97.1.11]	NA	🟥	0.65	0.0093	0.177625461
K03909	TFPI	tissue factor pathway inhibitor	ko04610 Complement and coagulation cascades	🟥	0.65	0.0020	0.143042222
K14619	TCN2	transcobalamin-2	ko04977 Vitamin digestion and absorption	🟥	0.42	0.0180	0.198691113
K09036	MAFB	transcription factor MAFB	NA	🟥	0.44	0.0302	0.229640822
K03237	EIF2S1	translation initiation factor 2 subunit 1	ko03013 RNA transport; ko04141 Protein processing in endoplasmic reticulum; ko0	🟩	-0.50	0.0123	0.186859932
K03246	EIF3I	translation initiation factor 3 subunit I	ko03013 RNA transport	🟩	-0.42	0.0199	0.205547989
K15029	EIF3L	translation initiation factor 3 subunit L	NA	🟩	-0.39	0.0266	0.223618949
K03259	EIF4E	translation initiation factor 4E	ko03013 RNA transport; ko04066 HIF-1 signaling pathway; ko04150 mTOR signaling	🟩	-0.71	0.0067	0.168046036
K03264	EIF6	translation initiation factor 6	ko03008 Ribosome biogenesis in eukaryotes	🟩	-0.53	0.0021	0.143042222
K09637	TMPRSS6	transmembrane protease, serine 6 [EC:3.4.21.-]	NA	🟥	0.41	0.0087	0.172822126
K17599	TMEM132	transmembrane protein 132	NA	🟥	0.41	0.0172	0.197085215
K17966	TMEM70	transmembrane protein 70, mitochondrial	NA	🟩	-0.38	0.0066	0.165190087
K00555	TRMT1, trm1	tRNA (guanine26-N2/guanine27-N2)-dimethyltransferase [EC:2.1.1.215 2.1.	NA	🟩	-0.45	0.0002	0.112669745
K15429	TRM5, TRMT5	tRNA (guanine37-N1)-methyltransferase [EC:2.1.1.228]	NA	🟩	-0.41	0.0071	0.168745194
K06173	truA, PUS1	tRNA pseudouridine38-40 synthase [EC:5.4.99.12]	NA	🟩	-0.40	0.0245	0.218040876
K10375	TPM4	tropomyosin 4	ko04260 Cardiac muscle contraction; ko05410 Hypertrophic cardiomyopathy (HCM	🟥	0.40	0.0046	0.165133463
K12045	TNNT2	troponin T, cardiac muscle	ko04260 Cardiac muscle contraction; ko05410 Hypertrophic cardiomyopathy (HCM	🟥	0.39	0.0025	0.148961431
K17292	TBCA	tubulin-specific chaperone A	NA	🟩	-0.46	0.0212	0.206767944
K07604	KRT1	type I keratin, acidic	NA	🟥	0.68	0.0024	0.14835443
K01562	DIO1	type I thyroxine 5'-deiodinase [EC:1.97.1.10]	NA	🟥	0.46	0.0480	0.263205722
K00815	TAT	tyrosine aminotransferase [EC:2.6.1.5]	ko00130 Ubiquinone and other terpenoid-quinone biosynthesis; ko00270 Cysteine	🟥	0.90	0.0011	0.143042222
K18026	PTPN2, PTPT	tyrosine-protein phosphatase non-receptor type 2 [EC:3.1.3.48]	NA	🟩	-0.45	0.0152	0.190267528
K01866	YARS, tyrS	tyrosyl-tRNA synthetase [EC:6.1.1.1]	ko00970 Aminoacyl-tRNA biosynthesis	🟩	-0.57	0.0001	0.112669745
K11095	SNRPC	U1 small nuclear ribonucleoprotein C	ko03040 Spliceosome	🟩	-0.38	0.0198	0.205299668
K13153	SNRNP25	U11/U12 small nuclear ribonucleoprotein 25 kDa protein	NA	🟩	-0.42	0.0032	0.152539243
K11094	SNRPB2	U2 small nuclear ribonucleoprotein B''	ko03040 Spliceosome	🟩	-0.43	0.0019	0.143042222
K14566	UTP24, FCF1	U3 small nucleolar RNA-associated protein 24	ko03008 Ribosome biogenesis in eukaryotes	🟩	-0.46	0.0140	0.187641673
K12845	SNU13, NHP2L	U4/U6 small nuclear ribonucleoprotein SNU13	ko03008 Ribosome biogenesis in eukaryotes; ko03040 Spliceosome	🟩	-1.12	0.0020	0.143042222
K12620	LSM1	U6 snRNA-associated Sm-like protein LSm1	ko03018 RNA degradation	🟩	-0.54	0.0010	0.143042222
K12622	LSM3	U6 snRNA-associated Sm-like protein LSm3	ko03018 RNA degradation; ko03040 Spliceosome	🟩	-0.48	0.0051	0.165133463
K12623	LSM4	U6 snRNA-associated Sm-like protein LSm4	ko03018 RNA degradation; ko03040 Spliceosome	🟩	-0.48	0.0030	0.15204453
K00416	QCR6, UQCRH	ubiquinol-cytochrome c reductase subunit 6	ko00190 Oxidative phosphorylation; ko04260 Cardiac muscle contraction; ko04932	🟩	-0.51	0.0126	0.187355725
K12161	URM1	ubiquitin related modifier 1	ko04122 Sulfur relay system	🟩	-0.39	0.0041	0.161328781
K06689	UBE2D_E, UBC4, UBC5	ubiquitin-conjugating enzyme E2 D/E [EC:6.3.2.19]	ko04120 Ubiquitin mediated proteolysis; ko04141 Protein processing in endoplas	🟥	0.41	0.0130	0.187355725
K00365	uaZ	urate oxidase [EC:1.7.3.3]	ko00230 Purine metabolism; ko00232 Caffeine metabolism	🟥	0.59	0.0122	0.186859932
K00757	udp, UPP	uridine phosphorylase [EC:2.4.2.3]	ko00240 Pyrimidine metabolism; ko00983 Drug metabolism - other enzymes	🟥	0.93	0.0083	0.172822126
K00963	UGP2, galU, galF	UTP--glucose-1-phosphate uridylyltransferase [EC:2.7.7.9]	ko00040 Pentose and glucuronate interconversions; ko00052 Galactose metabolis	🟥	0.47	0.0247	0.218040876
K14208	XPNPEP2	Xaa-Pro aminopeptidase 2 [EC:3.4.11.9]	ko04974 Protein digestion and absorption	🟥	0.54	0.0091	0.175171915

Supplementary File 4.

Additive	Limit
Vitamin A	No limit (for fish)
Vitamin D3	3000 I.U/kg or 0.075 mg/kg
Vitamin E	No limit
Vitamin K3	No limit
Vitamin B1	No limit
Vitamin B2	No limit
Vitamin B6	No limit
Vitamin B12	No limit
Vitamin B3 /Vitamin PP/ Niacin	No limit
Vitamin B5 (Calcium d-pantothenate)	No limit
Folic acid (vitamin B9)	No limit
Biotin	No limit
Vitamin C	No limit
Cobalt	No longer approved
Iodide and iodate	20 mg/kg
Selenium	0.5 mg/kg
Iron	max. 750 mg/kg
Manganese sulphate	100 mg/kg
Copper sulphate	25 mg/kg
Zinc sulphate monohydrate	180 mg/kg for salmonids, 150 mg/kg for other fish species
Taurine	No information
Histidine	No limit