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Phenotype Delineation of *ZNF462* related syndrome

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ABSTRACT

Zinc finger protein 462 (ZNF462) is a relatively newly discovered vertebrate specific protein with known critical roles in embryonic development in animal models. Two case reports and a case series study have described the phenotype of 10 individuals with *ZNF462* loss of function variants. Herein, we present 14 new individuals with loss of function variants to the previous studies to delineate the syndrome of loss of function in *ZNF462*. Collectively, these 24 individuals present with recurring phenotypes that define a multiple congenital anomaly syndrome. Most have some form of developmental delay (79%) and a minority have autism spectrum disorder (33%). Characteristic facial features include ptosis (83%), down slanting palpebral fissures (58%), exaggerated Cupid's bow/wide philtrum (54%), and arched eyebrows (50%). Metopic ridging or craniosynostosis was found in a third of study participants and feeding problems in half. Other phenotype characteristics include dysgenesis of the corpus callosum in 25% of individuals, hypotonia in half, and structural heart defects in 21%. Using facial analysis technology, a computer algorithm applying deep learning was able to accurately differentiate individuals with *ZNF462* loss of function variants from individuals with Noonan syndrome and healthy controls. In summary, we describe a multiple congenital anomaly syndrome associated with haploinsufficiency of *ZNF462* that has distinct clinical characteristics and facial features.

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KEYWORDS

ZNF462, ptosis, developmental delay, autism spectrum disorders, corpus callosum, craniosynostosis

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INTRODUCTION

Heterozygous loss of function variants in *ZNF462* present with a recognizable pattern of phenotype characteristics (Weiss et al., 2017). The first reported case was a reciprocal translocation t(2;9)(p24;q32) that disrupted both *ZNF462* and *ASXL2* (Ramocki et al., 2003; Talisetti et al., 2003). This individual presented with ptosis, agenesis of the corpus callosum, ventricular septal defect, periventricular nodular heterotopia, retina and iris colobomas, and a dysplastic left ear and hearing loss. *ASXL2* was subsequently associated with Shashi-Pena syndrome which presents as macrocephaly, retrognathia, low set ears, hypertelorism, arched eyebrows, intellectual disability, scoliosis, congenital heart disease, and hypotonia (Shashi et al., 2016). The phenotype of the individual in this case report likely resulted from the loss of function of both *ZNF462* and *ASXL2.* Over a decade later, Weiss et al. described 6 individuals from four families with putative loss of function variants and two unrelated individuals with deletions involving adjacent genes (Weiss et al., 2017). The individuals described by Weiss et al. presented with ptosis (100%), trigonocephaly or metopic ridging (83%), and developmental delay or autism spectrum disorder (33%) (Weiss et al., 2017). Subsequently, Cosemans et al. described an individual with a *de novo* translocation that disrupted *ZNF462* and

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KLF12 who presented with clinical features similar to those described by Weiss et al. (Cosemans et al., 2018; Weiss et al., 2017).

Zinc finger protein 462 (ZNF462) is a C2H2 type zinc finger transcription factor of unknown function (Nagase, Nakayama, Nakajima, Kikuno, & Ohara, 2001). Although the specific function of this molecule is unknown, animal studies have shown that it plays a vital role in embryonic development. In *Xenopus laevis,* knockdown expression of *Zfp462* disturbs early embryonic development and results in altered cell division during the cleavage stage; this phenotype is rescued with human *ZNF462* mRNA (Laurent et al., 2009). In the mouse model, Zfp462 knockout (KO) mice were prenatal lethal and heterozygous knockout mice ($Zfp462^{+/-}$) had developmental delay, low body and brain weights, and anxiety-like behaviors with excessive self-grooming behavior (Wang et al., 2017).

In this report, we describe 14 new individuals in addition to the 10 previously reported cases in the medical literature with truncating variants in *ZNF462,* collectively review the clinical presentation of this syndrome, and test facial analysis technology's ability to diagnose this syndrome.

METHODS

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Clinical

The study was approved by National Human Genome Research Institute Institutional Review Board (IRB). Thirteen new individuals in this report with loss of function variants in *ZNF462* were diagnosed using whole exome sequencing (WES) in multiple research and commercial labs including GeneDx and Ambry, and one individual (patient 5) was diagnosed by whole genome sequencing. Nine of the fourteen individuals were ascertained through GeneMatcher (Sobreira, Schiettecatte, Valle, & Hamosh, 2015).

Facial analysis technology

We performed two binary classification experiments using the Face2Gene Research application (FDNA Inc., Boston, MA), as previously described (Gurovich et al., 2019). Frontal facial 2D images were collected for three cohorts: individuals with *ZNF462* loss of function variants, Noonan syndrome, and healthy controls. Noonan syndrome was used as a second control group due the overlapping facial features of ptosis, downslanting palpebral fissures, hypertelorism, and low set ears in a subset of individuals. All facial images were fully de-identified through the use of the DeepGestalt facial analysis (Gurovich et al., 2019). Controls were matched for age, gender, and ethnicity.

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RESULTS

Clinical

Figure 1 shows the single nucleotide variant and small insertion/deletion (indel) locations on *ZNF462* for both the 14 newly reported cases and previously reported cases. All variants are predicted to result in loss of function , including a canonical splice variant in patient 6 that is predicted to result in abnormal splicing (Table 1; Figure 1). Most of these variants are in exon 3, which makes up 54% of the coding region of *ZNF42.* .

Table 1 summarizes the clinical features of all 24 affected individuals with 96% of individuals being Caucasian. Seventeen of 21 families (86%) have *de novo* variants, the other four families include unknown, mosaic, and autosomal dominant inheritance (Table 1). The two families with autosomal dominant inheritance demonstrated that the *ZNF462* variant segregated with the phenotype characterized in this study: patient 5's father had ptosis surgery and patients 15-17 are from the same family, and previously described (Weiss et al., 2017). The one case of mosaicism was in the mother of patient 1 who had 175 reference reads and 35 alternate reads on WES from a peripheral blood sample [alternate allele frequency =

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35/(35+175) = 17%], compared to 120 reference reads and 79 alternate reads in the proband [alternate allele frequency = 79/(79+120) = 40%]. The majority of individuals had developmental delay (79%) and 33% reported autism spectrum disorders (Table 1). The most common facial features were ptosis (83%), down slanting palpebral fissures (58%), exaggerated Cupid's bow/wide philtrum (54%), arched eyebrows (50%), and short upturned nose with bulbous tip (46%). Feeding issues (50%) and hypotonia (50%) were common. Less than half of affected individuals reported metopic ridging or craniosynostosis (38%) or dysgenesis of the corpus callosum (25%). Less common characteristics included structural heart defects (21%) and minor limb anomalies (25%). The clinical analysis of the individuals in this study was heterogenous and not all individuals received brain and heart imaging (Supplementary Clinical Information), thus the above fractions may be an underestimation of brain and heart malformations. Figure 2 shows facial images of individuals with loss of function variants in *ZNF462.*

Facial analysis technology

Binary comparison between individuals with loss of function variants in *ZNF462* and controls was resulted in two statistics: the mean results involved the computation of the average of the AUC of each of the 10 results, and secondly, the aggregated results consist of a score distribution curve and a receiver-operating-characteristic (ROC) curve for the aggregated results for each photo used in the validation set.

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The binary comparison between *ZNF462* (n=21) and healthy controls (n=21) yielded an AUC of 0.96 (STD 0.03), demonstrating good separation between these two cohorts (Supplementary Table 1). Similarly, the comparison between the *ZNF462* cohort (n=21) and the Noonan syndrome cohort (n=16) yielded an AUC of 0.97 (STD 0.02) which is also good separation (Supplementary Table 1). The aggregated binary comparison for the *ZNF462* group versus health controls yielded an AUC of 0.955 (P=0.006) and for the *ZNF462* group versus health Noonan syndrome yielded an AUC of 0.972 (P=0.001) (Supplementary Figure 1).

Applying DeepGestalt, the confusion matrix/multi-class comparison of the 58 frontal images of the *ZNF462* group and both control groups yielded a mean accuracy of 82.88% (STD 11.79%) which is significantly better than randomly expected (36.21%).

DISCUSSION

We report 24 individuals with loss of function variants in *ZNF462* which includes 14 previously unpublished individuals and 10 individuals reported in the medical literature. Based on this larger assembled cohort of individuals, the phenotype of loss of function in *ZNF462* is now a distinct multiple congenital anomaly syndrome. We show that ptosis (83%), developmental delay (79%), and down slanting

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palpebral fissures (58%) are three most reported phenotypic features (Table 1). In the previous case series of 6 families and 8 individuals, metopic ridging/craniosynostosis (63%) was a major phenotypic feature. In this report, we show that metopic ridging/craniosynostosis is still important, but less prevalent (25%) in this syndrome. Consistent with the previous report by Weiss et al. 2017 (Table 1: patients 15-17), loss of function in *ZNF462* appears to have variable expressivity and complete penetrance as demonstrated by patient 5 in the present study with a paternally inherited variant and a father requiring surgery for his ptosis (Table 1; Supplementary Clinical Information). Facial analysis technology was able to accurately differentiate individuals with loss of function in *ZNF462* from Noonan syndrome and healthy controls. We predict that the widespread use of facial analysis technology will result in an increase in the number of cases diagnosed this syndrome.

Based on the prevalence of developmental delay, corpus callosum anomalies, congenital heart defects, and hearing loss, we recommend a comprehensive multidisciplinary evaluation of individuals with loss of function variants in *ZNF462*. This evaluation includes at a minimum: a developmental evaluation, a cardiac exam with echocardiography, brain imaging, hearing evaluation, and consultation with a clinical geneticist and genetic counselor. Other evaluations specific to an

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individual's presentation such as neurosurgery consultation for craniosynostosis may be appropriate. At this time, treatment of complications associated with *ZNF462* related syndrome are not different from the general population. As more individuals are studied, future specific management recommendations for *ZNF462* related syndrome may be needed.

Pathogenicity of variants in *ZNF462* is presumed to be haploinsufficiency based on individuals having loss of function variants only, and this is reinforced by theGenome Aggregation Database (gnomAD) constraint metric of observed/expected loss of function (o/e) value (Karczewski et al., 2019). Values less than 0.35 (o/e) are considered under selection against LOF (https://gnomad.broadinstitute.org) and *ZNF462* is well below this threshold with an o/e value of 0.03 (90%CI, 0.01-0.09). As noted in the introduction, *ZNF462* is important to embryonic development in multiple species. *ZNF462* contains 23 C2H2-type zinc finger domains, making DNA binding a likely function (Chang, Stoykova, Chowdhury, & Gruss, 2007). We now know that ZNF462 is involved in chromatin remodeling. Using histone peptide pull down assays in mouse brain and kidney, Eberl et al. showed that ZNF462 binds H3K9me3, identifying Znf462 as a chromatin reader involved in heterochromatin modification (Eberl, Spruijt, Kelstrup, Vermeulen, & Mann, 2013). Additionally, Eberl et al. report an interaction with Heterochromatin Protein 1α (HP1α) (Eberl et al.,

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2013). As hallmarks of heterochromatin, HP1α and H3K9me3 are critical for transcriptional silencing of gene and repetitive DNA and for the maintenance of genome integrity (Almouzni & Probst, 2011; Beisel & Paro, 2011; Ren & Martienssen, 2012), further supporting ZNF462's role in chromatin remodeling. Masse et al. used short hairpin RNA knockdown of pluripotent mouse cells, demonstrating a disruption of pericentromeric domains and redistribution of HP1α proteins, giving evidence that Znf462 is instrumental in maintaining heterochromatin in pluripotent cells (Masse et al., 2010).

In summary we present 24 individuals with loss of function variants in *ZNF462*, and we define a multiple congenital anomaly syndrome that is recognizable from phenotype elements and by using facial analysis technology.

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DATA SHARING

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Table 1. Phenotype characteristics of individuals with loss of function variants in *ZNF462*

Patient	Age	Sex	*ZNF462* variant (NM_021224.5)	Inheritance	DD	ASD	Ptosis	Down slanting palpebral fissures	Arched eyebrows	Short upturned nose with bulbous tip	Exaggerated cupid bow/wide philtrum	Feeding issues	Epicanthal folds	Ears	Craniosynostosis /metopic ridging	Hypotonia	Hypertelorism	Corpus callosum dysgenesis	CHD	Limb anomalies (minor)
1	16m	M	c.2590C>T p.(Arg864*)	maternal (mosaic)	motor/speech	-	+	-	+	-	+	+	+	low set	-	+	+	normal MRI	not reported	fifth finger clinodactyly
2	10y	M	c.2542del p.(Cys848Valfs*66)	*de novo*	motor/speech	+	+	+	+	+	+	+	+	-	-	-	+	normal MRI	not reported	not reported
3	6y	M	c.831_834del p.(Arg277Serfs*26)	*de novo*	motor/speech	-	-	-	-	+	-	+	-	inner ear malformation	-	+	+	normal MRI	bicuspid aoritc valve; VSD	not reported
4	2y 7m	M	c.6214_6215del p.(His2072Tyrfs*8)	*de novo*	speech	-	+	-	-	-	+	+	+	small, lowset	+	-	-	not tested	not reported	not reported
5	14y	F	c.763C>T p.(Arg255*)	paternal	IEP/special education	-	+	-	+	-	-	-	+	hearing loss	+	-	-	not tested	not reported	not reported
6	7m	F	c.7057-2A>G	*de novo*	early intervention for DD	-	+	+	+	+	+	+	+	horizontal crus helix	-	+	+	normal MRI	VSD	prominent creases on hands and feet
7	13y	M	c.6794dup p.(Tyr2265*)	*de novo*	cognitive impairment	+	-	-	+	-	+	-	-	prominent ears/ear pits/hearing loss	+	-	-	not tested	not reported	not reported
8	2y	M	c.882dup p.(Ser295Glnfs*64)	*de novo*	speech delay	-	+	+	-	-	-	-	-	-	-	-	-	ACC	not reported	not reported
9	15y	M	c.4165C>T p.(Gln1389*)	*de novo*	global	-	+	+	+	-	+	+	-	lowset	-	+	-	not tested	not reported	not reported
10	8y	M	c.1234_1235insAA; p.(Ser412*)	unknown	speech delay; motor apraxia; IEP	-	+	-	-	-	-	+		mildly cupped ears	-	-	-	normal MRI	not reported	not reported
11	2 y 5 m	F	c.6214_6215del p.(His2072Tyrfs*8)	*de novo*	-	-	+	-	-	-	-	+			-	+	-	not tested	not reported	not reported
12	9m	M	c.2049dup p.(Pro684Serfs*14)	*de novo*	motor	-	+	+	+	+	+	-	+	-	-	+	+	normal MRI	not reported	not reported
13	8y 7m	M	c.6631del p.(Arg2211Glyfs*59)	*de novo*	-	-	+	+	-	+	+	-	-	-	-	-	+	not tested	not reported	5th finger clinodactyly
14	8y	F	c.2695G>T; p.(Glu899*)	unknown	cognitive impairment	-	-	-	+	-	-	+	-	-	-	+	-	normal MRI	not reported	not reported
15[a]	2y	F	c.3787C>T p.(Arg1263*)	paternal	-	-	+	+	+	+	+	not reported	-	-	+	-	+	ACC; colpocephaly	not reported	not reported
16[a]	4y	F	c.3787C>T p.(Arg1263*)	paternal	-	-	+	+	-	+	+	not reported	+	-	+	-	-	normal prenatal ultrasound	not reported	not reported
17[a]	34y	M	c.3787C>T p.(Arg1263*)	maternal	-	-	+	-	-	-	-	not reported	-	-	+	-	-	not tested	not reported	not reported
18[a]	2y	M	c.2979_2980delinsA p.(Val994Trpfs*147)	*de novo*	speech	+	+	+	+	+	-	+	+	left overfolded ear	+	-	-	- normal MRI	not reported	single palmar crease ;5th finger clinodactyly
19[a]	32m	M	c.4263del p.(Glu1422Serfs*6)	*de novo*	motor/speech	+	+	+	-	+	-	-	+	lowset	+	+	+	hypoplastic corpus	D-TGA	not reported

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																		callosum and ventriculomegaly		
20[a]	5y	F	Chr9:g.(108940763-110561397)del (hg19)	*de novo*	-	-	+	+	+	+	+	not reported	+		-	+	-	hypoplastic corpus callosum	not tested	not reported
21[a]	15y	F	Chr9:g(108464368-110362345)del (hg19)	*de novo*	motor/intellectual	+	-	-	-	-	+	not reported	-		-	-	+	not tested	VSD	not reported
22[a]	9y	M	c.5145delC p.(Tyr1716Thrfs*28)	*de novo*	motor/speech delay	+	+	-	-	-	-	not reported	-	-	-	+	-	normal MRI	not reported	not reported
23[b]	5y	F	t(2;9)(p24;q32); disrupting *ZNF462* and *ASXL2*	*de novo*	intellectual disability	+	+	+	+	+	+	+	-	lowset; hearing loss	-	+	-	ACC; dilated venricles	VSD; left ventricular hypertrophy	single palmar crease; hypoplastic finger nails
24[c]	24y	M	t(9; 13)(q31.2; q22.1) disrupting *ZNF462* and *KLF12*	*de novo*	intellectual disability	+	+	+	-	-	-	+	+	lowset	+	+	-	hypoplastic corpus callosum	none reported	small hands and feet; proximally placed thumbs
Cohort prevalence[d]					79%	33%	83%	58%	50%	46%	54%	50%	46%	50%	38%	50%	25%	25%	21%	25%

[a]Weiss et al., 2017; [b]Talisetti et al., 2003; [c]Cosemans et al., 2018

[d]In order to avoid overestimating phenotype prevalence, we divided each positive phenotype report by the entire cohort (n=24).

Abbreviations: ACC (agenesis of the corpus callosum); ASD (autism spectrum disorder); CHD (congenital heart disease); DD (developmental delay); D-TGA (D-transposition of the great arteries); F (female); IEP (individualized education program); M (male); MRI (magnetic resonance imaging); ventricular septal defect (VSD);

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Kruszka Paul (Orcid ID: 0000-0003-4949-0875)
Bedeschi Maria Francesca (Orcid ID: 0000-0003-0174-3562)
Martinez-Agosto Julian (Orcid ID: 0000-0001-6776-6949)
Boycott Kym (Orcid ID: 0000-0003-4186-8052)

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FIGURE LEGENDS

Figure 1. *ZNF462* variant locations. Variants from the present study are in blue and variants from previous publications are shown in black. Thirteen of the seventeen variants are on exon 3 which makes up 54% of *ZNF462.* Note that there are two unrelated individuals with the p.(His2072Tyrfs*8) variant (patients 4 and 11 in Table 1).

Figure 2. A. Patient 1; B. Patient 2; C. Patient 3; D. Patient 4; E. Patient 5 at 8 years; F. Patient 6 at two and 7 months; G. Patient 7; H. Patient 8 at 3 months and 2.5 years; I. Patient 9 at ages 8 and 15 years; J. Patient 12; K. Patient 13; L. Patient 14; M. Patient 15; N. Patient 16; O. Patient 17; P. Patient 18; Q. Patient 19; R. Patient 20; S. Patient 21; T. Patient 22; U. Patient 24; (Figures M-T are from Weiss et al., 2017 and Figure U is from Cosemans et al., 2018)

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The Children's Hospital of Philadelphia

NAME SEX M F

MR#

AGE / DATE OF BIRTH

ACCOUNT#

(PATIENT PLATE IMPRINT)

CONSENT AND RELEASE FOR RECORDING OR FILMING (PAGE 1 OF 2)

I give permission for Clinical Genetics to take
Print Name of Department/Division

photographs, films and/or audiovisual recordings of Leah McEvoy 7mos
Print Name of Patient Age

for two years from the date this form is signed.

I allow the photographs, films or audiovisual recordings ("Images") taken of the patient, to be used and released by representatives of The Children's Hospital of Philadelphia and/or its affiliates ("CHOP") for purpose(s) I have initialed below. CHOP may use and release the Images (and other information I give permission for in this form) for the purposes I authorize below until CHOP no longer has the Images.

I give permission for CHOP to use and release these Images:

X **For treatment, payment and internal activities of CHOP, for example:**

- Diagnosis and/or treatment of the patient by clinicians.
- Providing information to insurance companies for purposes of supporting requests for payment.
- Internal activities such as staff training and improving the quality of care.

X **For educational activities outside of CHOP, for example:**

- Publications in medical textbooks and journals.
- Presentations to professional and/or medical boards/societies.

___ **For marketing and media relations activities of CHOP, for example:**

- Hospital publications and/or videos.
- Broadcast or print media, including television, radio, newspaper, magazines, and the Internet.
- Printed materials (brochures, posters, etc.).

___ **Other** *(describe any other purpose for which the Image will be used or released, including a description of who will use the Images within CHOP and/or receive the Images outside of CHOP):*

_____

_____

Permission to Use and Release Patient Name and Other Information with the Images: Some Images themselves may identify the patient (for example, pictures that show a patient's face). In some cases, CHOP may wish to use or release the patient's name along with the Images. Please initial one of the following for use of the patient's name with the Image:

____ **I agree** to the use and/or release of the patient's name with the Images.

X **I do not agree** to the use and/or release of the patient's name with the Images.

I also allow the following patient information to be used and/or released along with the Images:

_____

_____

AEL 1/2007

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NAME SEX M F

SITE

AGE/ DATE OF BIRTH

ACCOUNT#

(PATIENT PLATE IMPRINT)

The Children's Hospital of Philadelphia

CR-183
Rev. 10/98

CONSENT AND RELEASE FOR RECORDING OR FILMING
(PAGE 2 OF 2)

Understanding this Authorization:

- My decision to sign this authorization will not usually affect the patient's ability to get care at CHOP. At times, CHOP may be required to record or film the patient to provide medical services. If I do not agree to the recording or filming in these situations, services may not be provided.
- I understand that CHOP may use and release Images as the law requires or allows without further permission from the patient, even if I do not agree. See the CHOP Notice of Privacy Practices for details about how medical information, including Images, may be used and shared without further permission from the patient -- **http://www.chop.edu/about_chop/hipaa/npp.shtml**
- After signing this form, I can change my mind and ask that recording or filming stop. If I change my mind after recording or filming is done, I can notify the CHOP Department / Division indicated above in writing to ask that the Images not be used or released. This will not change any use or release of the Images by CHOP before receiving my notice. If the Images were released outside of CHOP, I understand the Images may continue to be used even after I withdraw my permission for CHOP to use or share them.
- If I allow CHOP to release Images to other individuals or organizations, I understand that the recipients could use, distribute, broadcast and/or publish them in ways that do not protect the patient's privacy and that CHOP cannot control.
- The Images belong to CHOP. I will not be paid for the use or release of the Images.

By signing, I understand that I am authorizing CHOP to take, use and release Images of the patient as described above.

V Gutierrez — Victoria Gutierrez — 11/21/2017

Signature **Print Name** **Date**

Relationship to Patient: ☐ Patient ☒ Parent ☐ Legal Guardian ☐ Other: _____

TO BE COMPLETED by CHOP STAFF

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Indicate type of Images taken: ☒ Photograph ☐ Film ☐ Audio Recording ☐ Other: _____

Print name of individual taking the Images and indicate affiliation with CHOP by checking below: Casey McDougall

☒ CHOP Employee ☐ Contractor ☐ News Media ☐ Other _____

Print name of Hospital representative supervising the recording:
Casey McDougall / Elaine Zacka, MD

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UNIVERSITAIRE DE NANTES

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MR. P. BOISSEAU
MR. F. AIRAUD

SECRETARIAT
Tél/Fax : 02 40 08 40 20
…ail : carine.huguenot@chu-nantes.fr

Je soussigné (e) Feray Fanny

~~Père,~~ mère de l'enfant Fonteneau Gabriel

Né (e) le 11 11/2011 autorisent

le Docteur Bertrand ISIDOR à faire usage des photographies de mon enfant pour une publication scientifique.

Fait à Nantes
Le 11/07/18

Signature (s) :

HOPITAL MERE ET ENFANT

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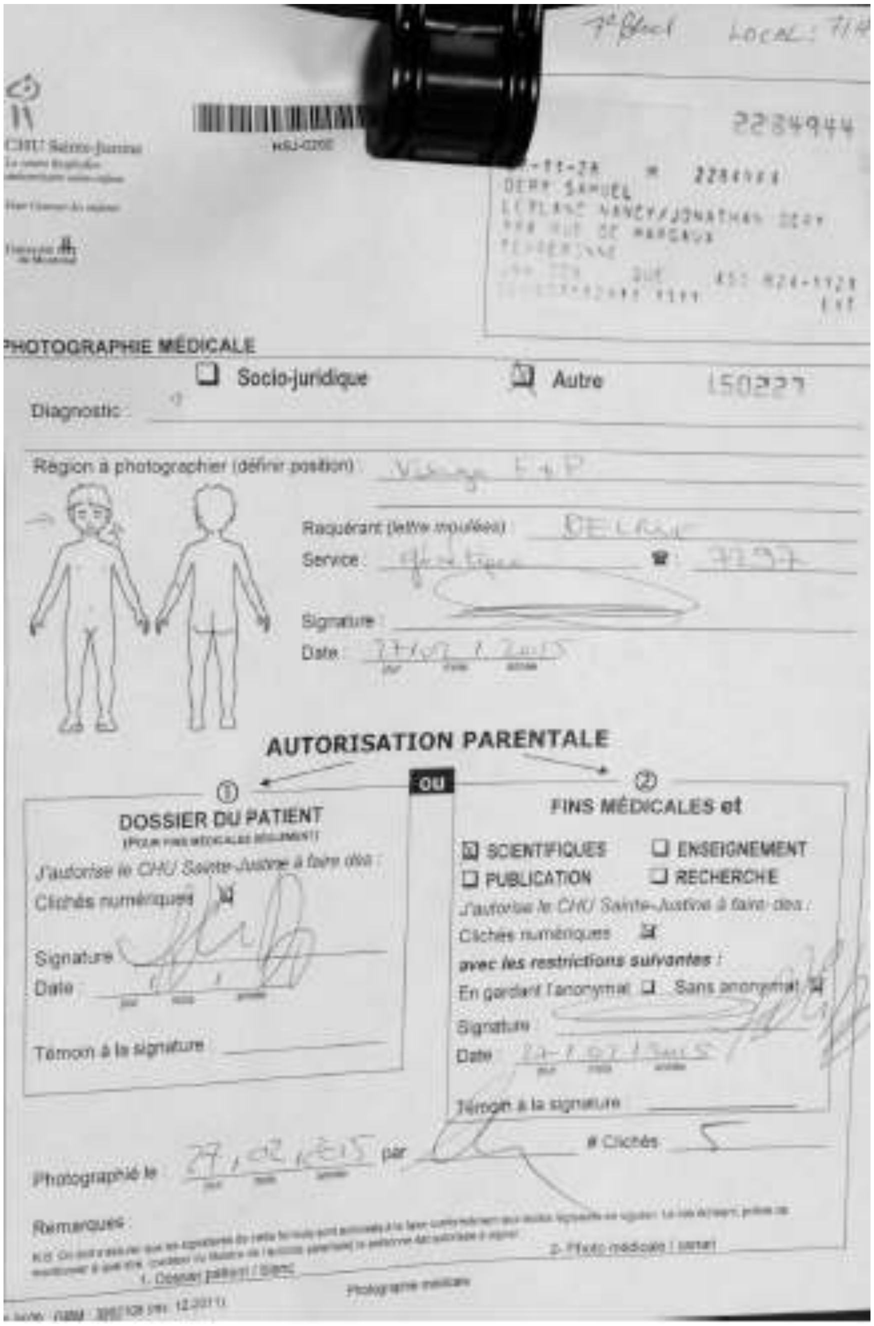

CHU Sainte-Justine

PHOTOGRAPHIE MÉDICALE

☐ Socio-juridique ☒ Autre

Diagnostic :

Région à photographier (définir position) :

Requérant (lettre moulées) :

Service :

Signature :

Date :

AUTORISATION PARENTALE

① DOSSIER DU PATIENT

J'autorise le CHU Sainte-Justine à faire des :

Clichés numériques ☒

Signature

Date

Témoin à la signature

OU

② FINS MÉDICALES et

☒ SCIENTIFIQUES ☐ ENSEIGNEMENT

☐ PUBLICATION ☐ RECHERCHE

J'autorise le CHU Sainte-Justine à faire des :

Clichés numériques ☒

avec les restrictions suivantes :

En gardant l'anonymat ☐ Sans anonymat ☒

Signature

Date

Témoin à la signature

Photographié le 27, 02, 2015 par

Clichés 5

Remarques :

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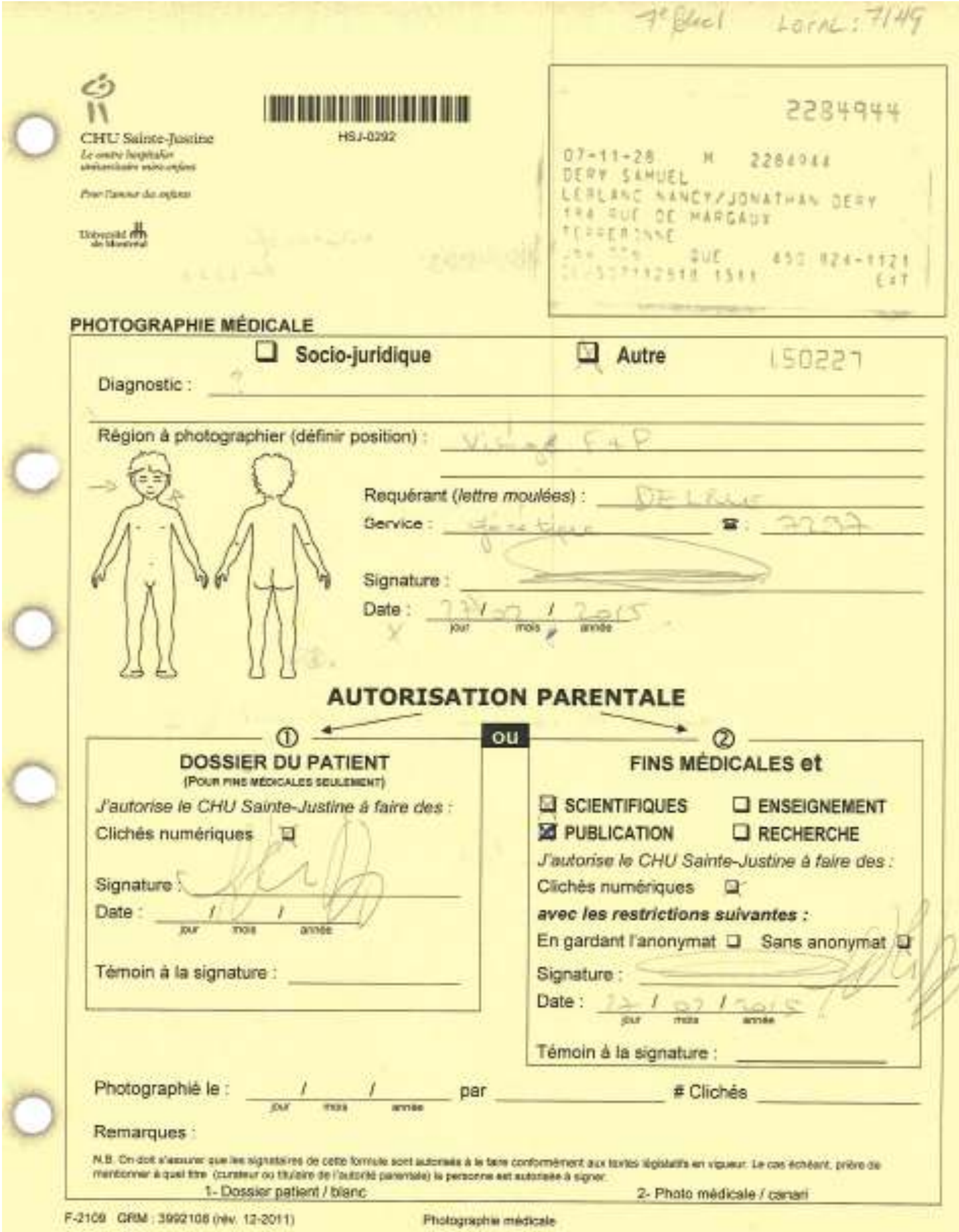

CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant
Pour l'amour des enfants
Université de Montréal

HSJ-0292

PHOTOGRAPHIE MÉDICALE

☐ Socio-juridique ☒ Autre

Diagnostic :

Région à photographier (définir position) :

Requérant (lettre moulées) :

Service :

Signature :

Date : jour / mois / année

AUTORISATION PARENTALE

① DOSSIER DU PATIENT (POUR FINS MÉDICALES SEULEMENT)

J'autorise le CHU Sainte-Justine à faire des :

Clichés numériques ☐

Signature :

Date : jour / mois / année

Témoin à la signature :

ou

② FINS MÉDICALES et

☒ SCIENTIFIQUES ☐ ENSEIGNEMENT
☒ PUBLICATION ☐ RECHERCHE

J'autorise le CHU Sainte-Justine à faire des :

Clichés numériques ☐

avec les restrictions suivantes :

En gardant l'anonymat ☐ Sans anonymat ☒

Signature :

Date : jour / mois / année

Témoin à la signature :

Photographié le : jour / mois / année par # Clichés

Remarques :

N.B. On doit s'assurer que les signataires de cette formule sont autorisés à le faire conformément aux textes législatifs en vigueur. Le cas échéant, prière de mentionner à quel titre (curateur ou titulaire de l'autorité parentale) la personne est autorisée à signer.

1- Dossier patient / blanc 2- Photo médicale / canari

F-2109 GRM : 3992108 (rév. 12-2011) Photographie médicale

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Acute Services Division
Diagnostics Directorate

West of Scotland Regional Genetic Service
Level 2A Laboratory Medicine
Queen Elizabeth University Hospital
1345 Govan Road
Glasgow
G51 4TF

3116

NHS
Greater Glasgow and Clyde

CONSENT FORM FOR PHOTOGRAPHY/AUDIO/VIDEO RECORDING OF PATIENTS

Parent/guardian

I consent to photograph(s)/~~audio/video~~ recording(s) being taken for ~~my~~/my child's personal medical record for diagnostic purposes only [LG]

I consent to photograph(s)/~~audio/video~~ recording(s) being taken for ~~my~~/my child's personal medical record for diagnostic purposes, and to shown to appropriate health professionals and students, in the UK and abroad, to aid medical teaching and research [LG]

~~I consent to photograph(s)/recordings being used at appropriate patient/public information events~~ [ ]

I understand that I have the right to withdraw consent any time by contacting the West of Scotland Genetic Services.

Name of Patient AIDAN TAYLOR CHI / D.O.B. 2/10/02 5735 Family No 3116

Signature [signature] Relation to patient (patient/parent/guardian)

Date 24/08/18

I consent to ~~my~~/my child's photograph(s) being published in an open access journal, textbook or other form of medical publication (which may include the internet), and therefore may be seen by the general public as well as medical professionals. [LG]

I understand that once published, it will not be possible to completely withdraw this consent.

Name of Patient AIDAN TAYLOR CHI /D.O.B. 2/10/2 5735 Family No. 3116

Signature [signature] Relation to patient (~~patient~~/parent/~~guardian~~)

Date 24/08/18

Name and signature of medical professional requesting illustrations/recording and obtaining consent

Name DR ESTHER KINNING Position CONSULTANT Department Genetics

Signature [signature] Date 22/8/18

Version 1 September 2016
For review March 2017

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Patient Consent for Medical Photography

Patient name: BRI-ANNA THOMPSON Date: Mar 13/19

☑ check here if minor or unable to provide consent

I consent for medical photographs to be made of me or my child (or person for whom I am legal guardian). I understand that the information may be used in my medical record, for purposes of medical teaching, or for publication in medical textbooks or journals as I have designated below. By consenting to these medical photographs I understand that I will not receive payment from any party. Refusal to consent to photographs will in no way affect the medical care I will receive. If I have any questions or wish to withdraw my consent in the future I may contact:

Dr. Paul Kruszka, NIH, 301-402-9654, paul.kruszka@nih.gov

By signing this form below I confirm that this consent form has been explained to me in terms which I understand.

1) I consent for these photographs to be used in medical publications, including medical journals, textbooks, and electronic publications. I understand that the image may be seen by members of the general public, in addition to scientists and medical researchers that regularly use these publications in their professional education. Although these photographs will be used without identifying information such as my name, I understand that it is possible that someone may recognize me. I also agree for my image to be shown for teaching purposes and to be used for my medical record.

Brianna Thompson (Signature) _____ (Witness)

2) I agree for my image to be shown for teaching purposes **AND** to be used for my medical record but **NOT FOR** medical publication:

_____ (Signature) _____ (Witness)

3) I agree to use of my image for medical records **ONLY**:

_____ (Signature) _____ (Witness)

For patients between ages 7 and 18 years, a signature below indicates that the information in this consent form has been explained to me, and I assent to use of my images as outlined above:

_____ (Signature of patient) _____ (Witness)

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WKZ - KC04.084.2
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The Netherlands
Tel. +31 88 75 53800
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7107691
26-01-2015 **M**
Elkerbout
Eden E.
Busken Huetstraat 27
2394 TD Hazerswoude-Rijndijk
06-53312465 moeder

The undersigned, parent(s) of:

name: ....

date of birth: ....

give(s) ....DR. GILFAN EN DR. KRUSZKA..........

permission to publish clinical photographs of their son / daughter* in a medical journal.

Place: Hazeerswoude Rijndijk..........

Date: 18 - 11 - 2018..........

Signature (father):

Signature (mother):

* Please delete as appropriate.

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F026-OD / Versie 6 / 31-03-2017

Betreft Toestemming publicatie gegevens kind in medisch tijdschrift

7107691
26-01-2015 **M**

Elkerbout

Eden E.
Busken Huetstraat 27
2394 TD Hazerswoude-Rijndijk
06-63312465 moeder
[illegible]
Huisarts: [illegible]
Afgedrukt op 07-11-2018 11:39:44

Divisie Biomedische Genetica

Afdeling Genetica

Tel 088 755 3800
Fax 088 755 3801
genetica@umcutrecht.nl

Ondergetekenden, ouders (verzorgers)

Naam: M. P. Elkerbout

Geboortedatum: 15-05-1981

geven toestemming aan DR SILFHY EN DR [illegible]

tot publicatie van foto(s) van hun zoon / dochter* in een medisch tijdschrift.

Handtekening (vader): [illegible]

Plaats: Hazerswoude

Datum: 18-11-18

Handtekening (moeder): [illegible]

Plaats: Hazerswoude

Datum: 18-11-2018

* s.v.p. doorhalen wat niet van toepassing is

Bezoekadres:
Lundlaan 6
3584 EA Utrecht

Postadres:
Huispostnummer KC4.084.2
Postbus 85090
3508 AB Utrecht

www.umcutrecht.nl

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Patient Consent for Medical Photography

Patient name: [illegible] RICARDO Date: 12/02/2019

☐ check here if minor or unable to provide consent

I consent for medical photographs to be made of me or my child (or person for whom I am legal guardian). I understand that the information may be used in my medical record, for purposes of medical teaching, or for publication in medical textbooks or journals as I have designated below. By consenting to these medical photographs I understand that I will not receive payment from any party. Refusal to consent to photographs will in no way affect the medical care I will receive. If I have any questions or wish to withdraw my consent in the future I may contact:

Dr. Paul Kruszka, NIH, 301-402-9654, paul.kruszka@nih.gov

By signing this form below I confirm that this consent form has been explained to me in terms which I understand.

1) I consent for these photographs to be used in medical publications, including medical journals, textbooks, and electronic publications. I understand that the image may be seen by members of the general public, in addition to scientists and medical researchers that regularly use these publications in their professional education. Although these photographs will be used without identifying information such as my name, I understand that it is possible that someone may recognize me. I also agree for my image to be shown for teaching purposes and to be used for my medical record.

[signature] (Signature) _____ (Witness)

2) I agree for my image to be shown for teaching purposes **AND** to be used for my medical record but **NOT FOR** medical publication:

[signature] (Signature) _____ (Witness)

3) I agree to use of my image for medical records **ONLY**:

[signature] (Signature) _____ (Witness)

For patients between ages 7 and 18 years, a signature below indicates that the information in this consent form has been explained to me, and I assent to use of my images as outlined above.

[signature] _____

(Signature of patient) (Witness)

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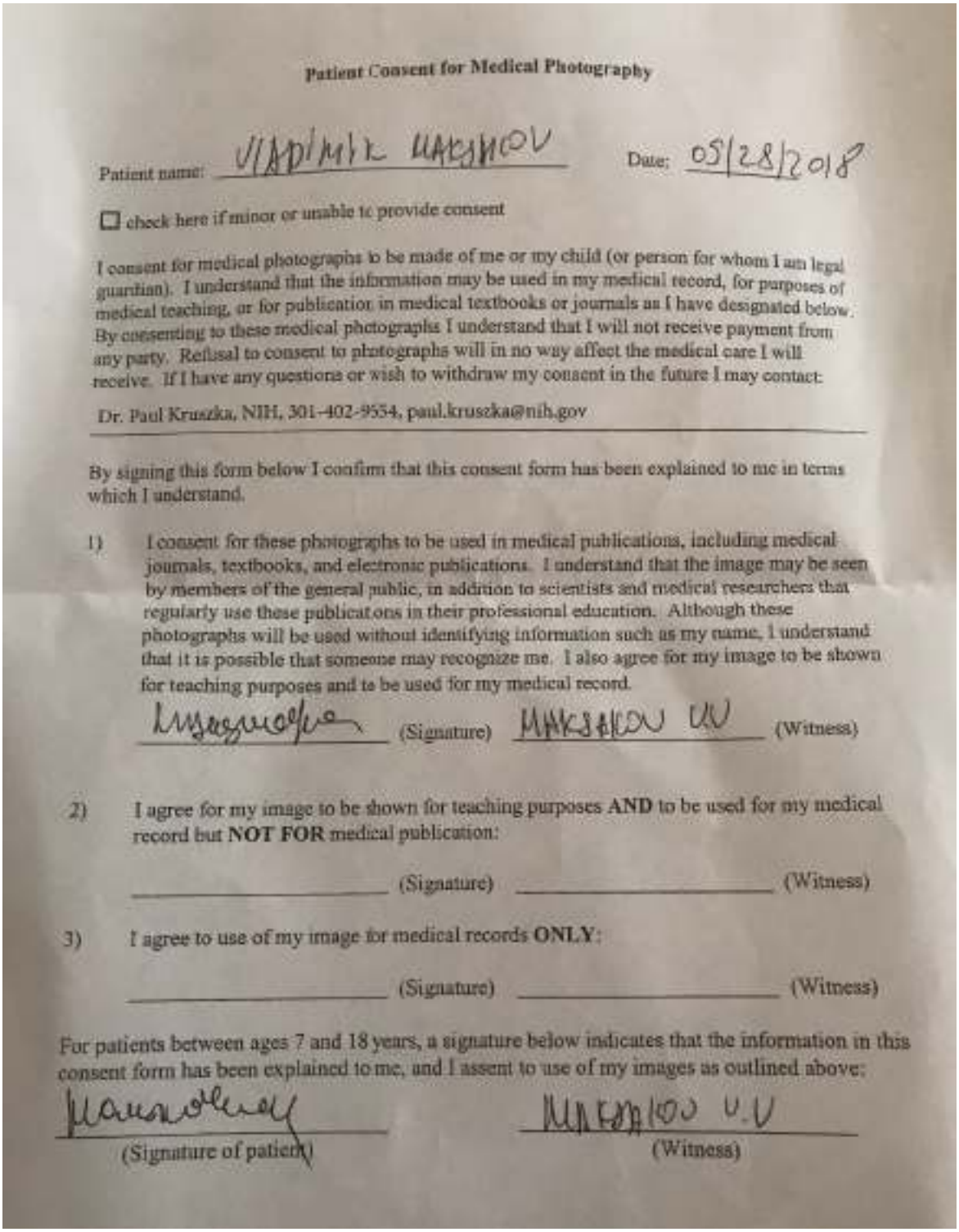

Patient Consent for Medical Photography

Patient name: VLADIMIR MAKSIMOV Date: 05/28/2018

☐ check here if minor or unable to provide consent

I consent for medical photographs to be made of me or my child (or person for whom I am legal guardian). I understand that the information may be used in my medical record, for purposes of medical teaching, or for publication in medical textbooks or journals as I have designated below. By consenting to these medical photographs I understand that I will not receive payment from any party. Refusal to consent to photographs will in no way affect the medical care I will receive. If I have any questions or wish to withdraw my consent in the future I may contact:

Dr. Paul Kruszka, NIH, 301-402-9554, paul.kruszka@nih.gov

By signing this form below I confirm that this consent form has been explained to me in terms which I understand.

1) I consent for these photographs to be used in medical publications, including medical journals, textbooks, and electronic publications. I understand that the image may be seen by members of the general public, in addition to scientists and medical researchers that regularly use these publications in their professional education. Although these photographs will be used without identifying information such as my name, I understand that it is possible that someone may recognize me. I also agree for my image to be shown for teaching purposes and to be used for my medical record.

_____ (Signature) MAKSIMOV VV (Witness)

2) I agree for my image to be shown for teaching purposes **AND** to be used for my medical record but **NOT FOR** medical publication:

_____ (Signature) _____ (Witness)

3) I agree to use of my image for medical records **ONLY**:

_____ (Signature) _____ (Witness)

For patients between ages 7 and 18 years, a signature below indicates that the information in this consent form has been explained to me, and I assent to use of my images as outlined above:

_____ (Signature of patient) MAKSIMOV V.V (Witness)

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UCLA Health

5228453

Patterson, Alexander

AUTHORIZATION FOR RELEASE OF PROTECTED HEALTH INFORMATION (PHI): COMMUNICATIONS | MARKETING

UCLA Health is committed to protecting the privacy of our patients. That is why we must obtain your written consent before we may reveal details about you, or your ward's, care.

Participant: Alexander Patterson Date of Birth: 1 / 30 / 2017

Address: 1714 Stoner Ave Apt 3 Los Angeles CA 90025

Phone Number: (310) 993-7821 Email (optional): _____

Guardian or Representative (if applicable): Karen Tsu Patterson

BRIEF DESCRIPTION OF PROJECT:
NIH researchers are publishing a paper documenting the clinical presentation and range of phenotypes in individuals with ZNF462 mutations. The authors would like the clinical information and if possible, photographs, for publication

HEALTH INFORMATION DISCLOSED MAY INCLUDE (check all that apply):
☒ Health History ☒ Medical and/or Photo Images ☒ Treatment Information ☒ Diagnosis
☐ Other: _____

PURPOSE OF PROJECT (check all that apply):
☐ Educational Material ☒ Publication ☐ Media Outreach ☐ Promotional Material
☐ Other: _____

INFORMATION REGARDING CARE WILL BE GATHERED FROM:
☒ UCLA Health employees involved in the patient's care.
☐ Other: _____

INFORMATION REGARDING CARE WILL BE DISCLOSED TO:
☐ UCLA Health ☐ Outside Media ☒ Other: National Institute of Health, Dr. Paul Kruszka

I SPECIFICALLY AUTHORIZE RELEASE OF THE FOLLOWING (if applicable):
☒ Not Applicable
☐ Mental health treatment information NOT including psychotherapy notes.
☐ HIV test results and/or HIV treatment information
☐ Alcohol and/or substance abuse treatment information.

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UCLA Health

5228453
Patterson, Alexandria

AUTHORIZATION FOR RELEASE OF PROTECTED HEALTH INFORMATION (PHI): COMMUNICATIONS | MARKETING

LIMITATIONS ON THE USE OF PARTICIPANT'S HEALTH INFORMATION (please be specific):

_____

_____

_____

_____

DURATION OF AUTHORIZATION

This authorization will remain in effect until: ____/____/____.

If no date is listed, this authorization will remain in effect for a period of five (5) years from the date of signature attached.

UCLA is required by law to keep health information confidential. If you have authorized the disclosure of health information to someone who is not legally required to keep it confidential, it may be subject to re-disclosure.

DO I HAVE TO SIGN THIS FORM?

Absolutely not! This authorization to release health information is voluntary. Declining to sign this authorization will not affect you, or your ward's, treatment, payment enrollment, or eligibility for benefits.

CAN I RECEIVE A COPY OF THIS AUTHORIZATION?

Yes! You have the right to request and receive a signed copy of this authorization.

WHAT IF I CHANGE MY MIND?

You may revoke this authorization at any time by writing to:

UCLAHealthNews@mednet.ucla.edu
OR
UCLA Health Sciences Media Relations
924 Westwood Boulevard, Suite 350
Los Angeles, CA 90024

Because UCLA Health puts a great deal of time and care into conceiving and developing communications and publications, we ask that you write to the address above as soon as possible after deciding to revoke your authorization.

Revocation will be effective upon receipt, except to the extent that UCLA or others have already relied on it. If the multimedia items have already been shared, it may not be possible to recall them.

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UCLA Health

MRN 5228453
Patient Name: Patterson, Alexander

AUTHORIZATION FOR RELEASE OF PROTECTED HEALTH INFORMATION (PHI): COMMUNICATIONS | MARKETING

I have read this form and all of my questions have been answered. My signature confirms that I understand and accept all of the above conditions, and approve the disclosure and use of health information by UCLA Health.

Signature of patient, parent or conservator | Date: 2/7/2018 | Time: 12:37 PM

If not signed by patient, indicate relationship or guardian: Mother

Rebecca Signer
UCLA Representative Name

UCLA Representative Signature

Date: 2/7/18 | Time: 8:09

I have accurately and completely read this consent to (patient or patient's legal representative) in the patient's or legal representative's primary language _____ (identify language). He/she understood all of the terms and conditions and acknowledged his/her agreement by signing the document in my presence.

Signature of Translator | Printed Name of Translator

Date | Time | Translator ID #

UCLA Form #10889 (Rev.11/17) Signed Chart Copy ☐ Patient Copy ☐ Page 3 of 3

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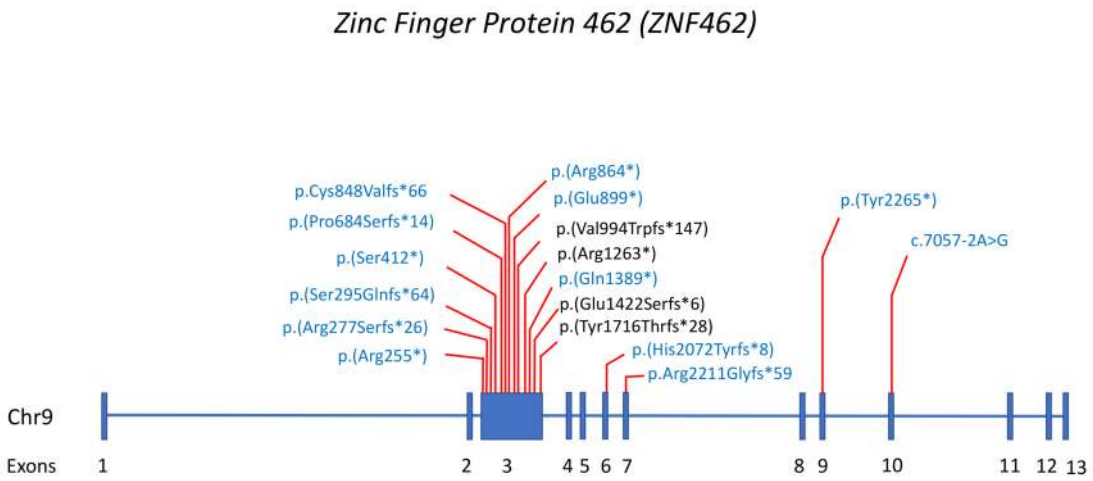

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Title:
Phenotype delineation of ZNF462 related syndrome

Date:
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