The human muscle proteome in aging

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Sarcopenia: the mystery of muscle loss

It account for

- a decrease of muscle mass
- a decrease in velocity
- a decrease in Po/CSA
- a decrease in strength

Factors involved:

- physical inactivity
- motor unit remodeling
- decrease of hormone levels
- decrease in protein synthesis

Human muscle structure

Fiber classification:

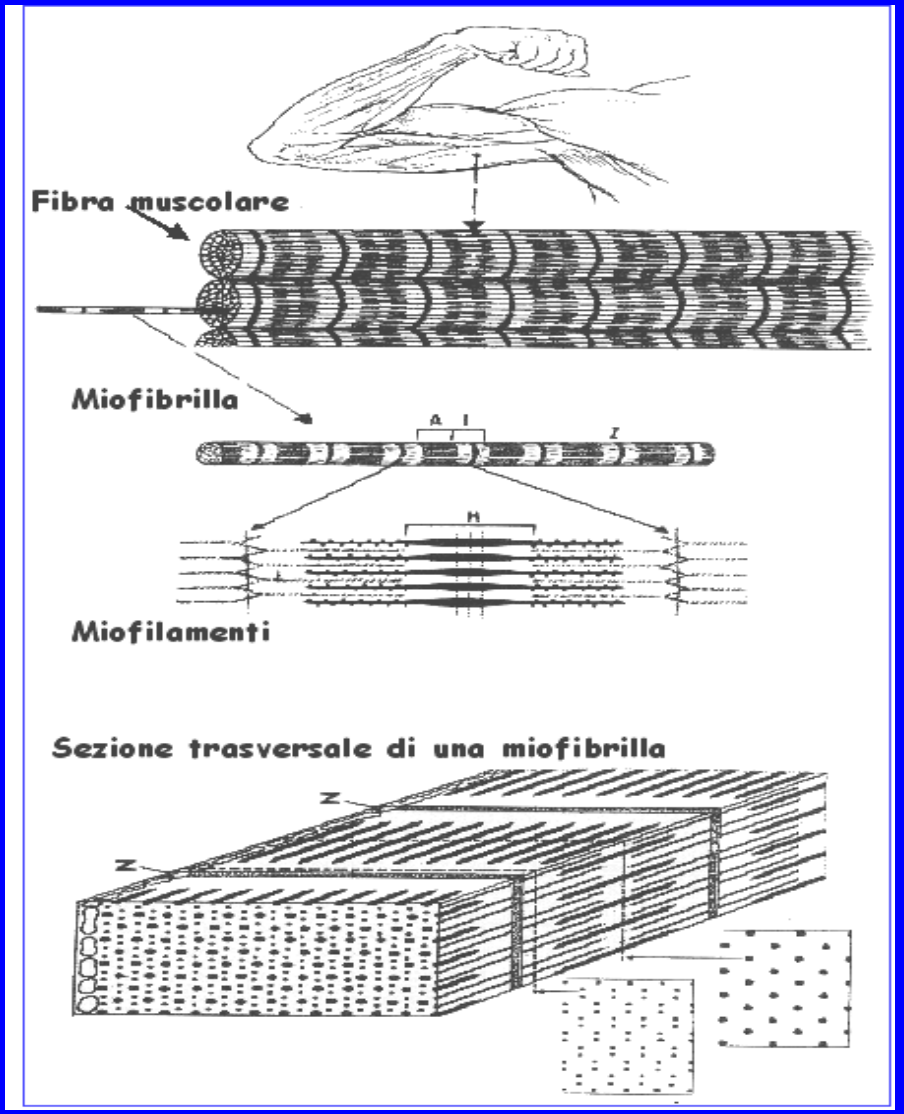
type 1 slow, oxidative

type 2A fast, oxidative

type 2X fast, glycolitic

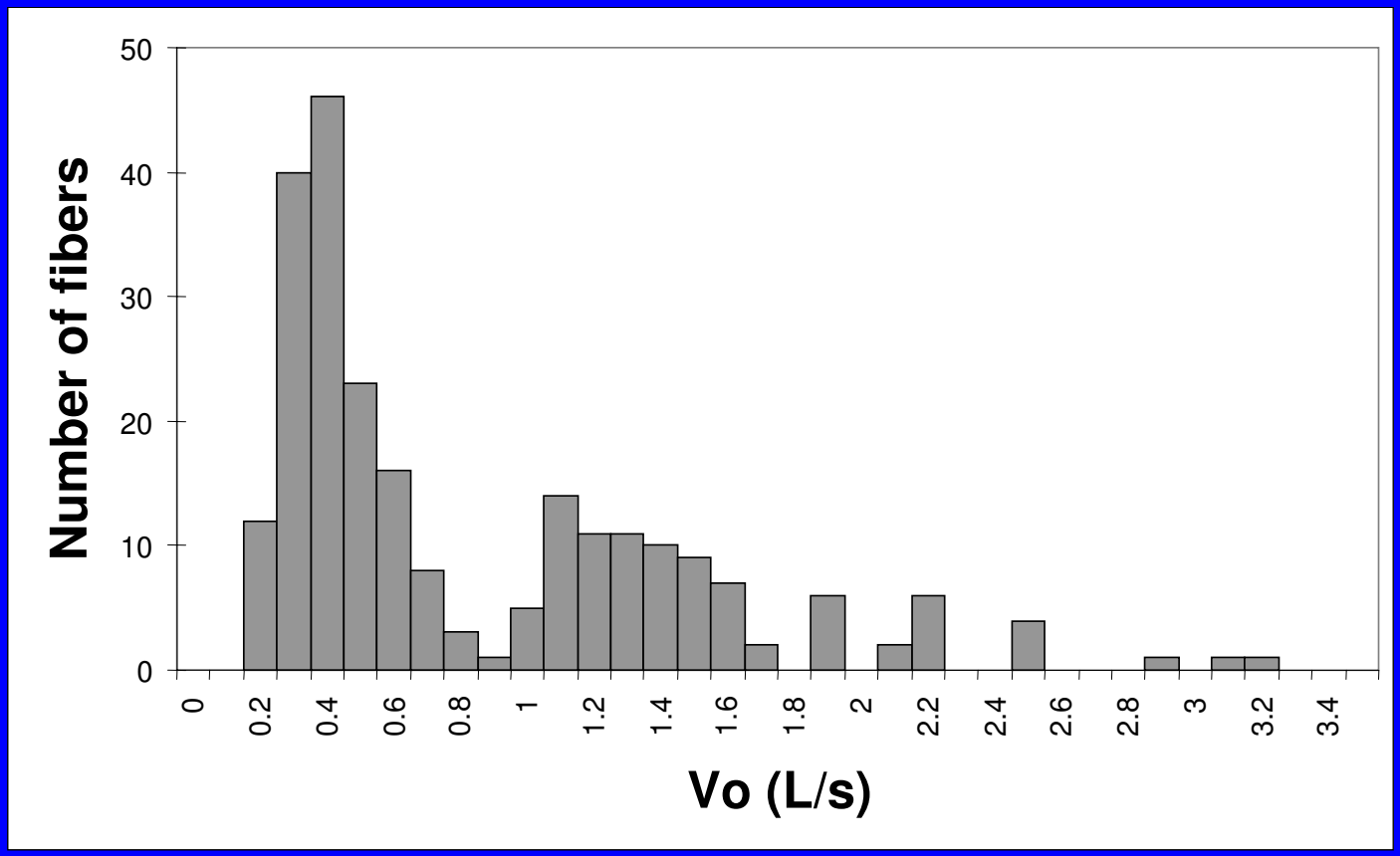
type 1-2A, mixed fiber

type 2A-2X, mixed fiber

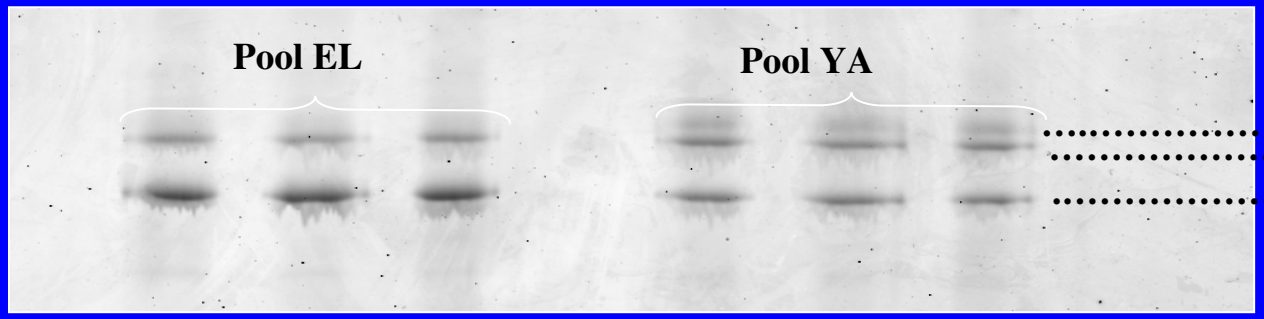


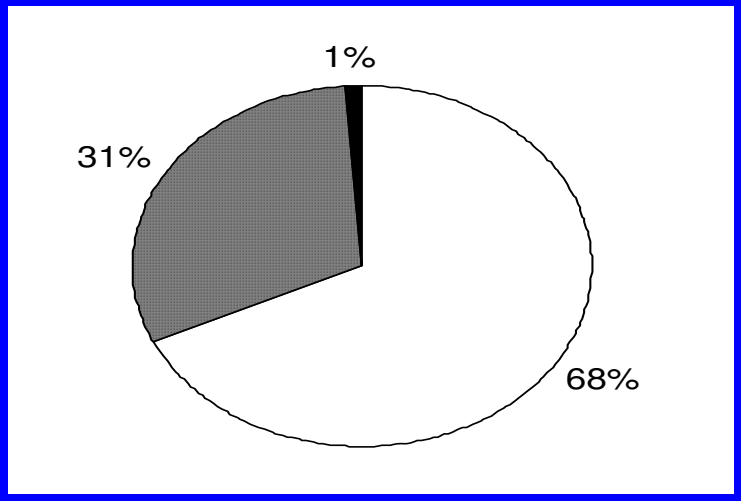
Functional parameters under debate

- Most contractile and energetic parameters show wide variations among fibers of the same muscle
- differences in velocity among different fiber types are actually related to myosin heavy chain isoforms but the variability in velocity within the same type remain unknown

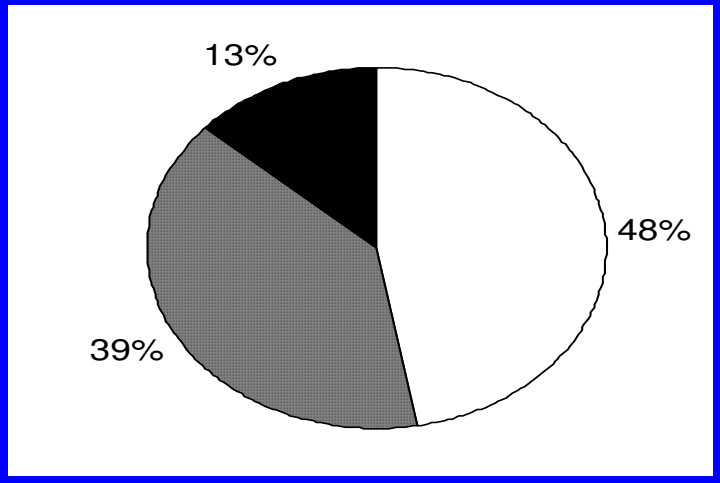


MHC Distribution





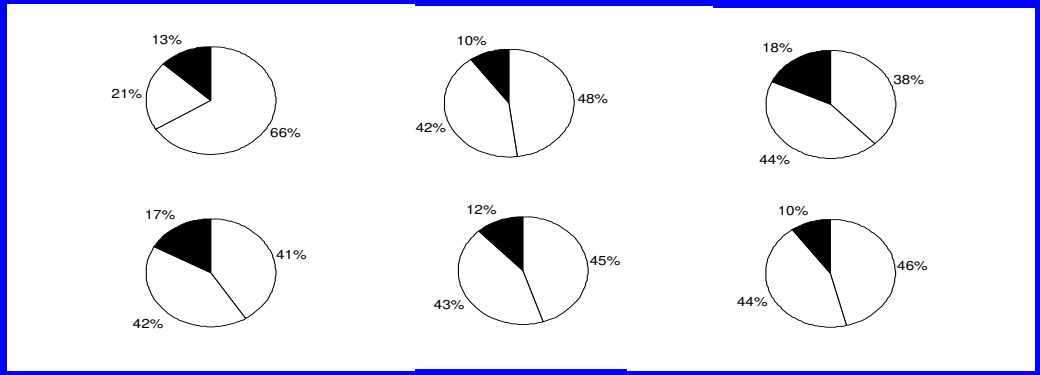
Pool EL



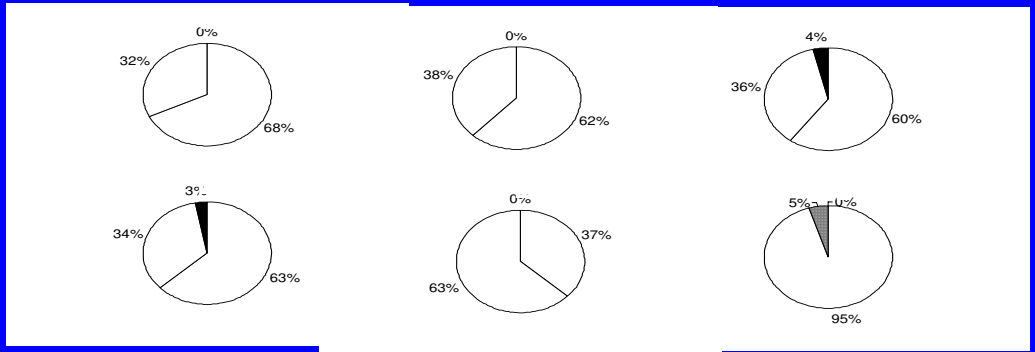
Pool YA

MHC 1
MHC 2A
MHC 2X

MHC Distribution



YA



EL

- MHC 1
- MHC 2A
- MHC 2X

MUSCOLO
VASTO LAT. UMANO

Mappa standard 3-10 NL
con divisione in classi funzionali
delle proteine identificate

Aggiornamento del: 31-03-05

Legenda:

+ Prot. contrattili-strutturali

+ Prot. metabolismo ossidativo
(TCA, Fosforilazione ox., β–ox.acidi grassi)

+ Prot. metabolismo anaerobico
(glicolisi, gluconeogenesi, high energy phosphate buff.)

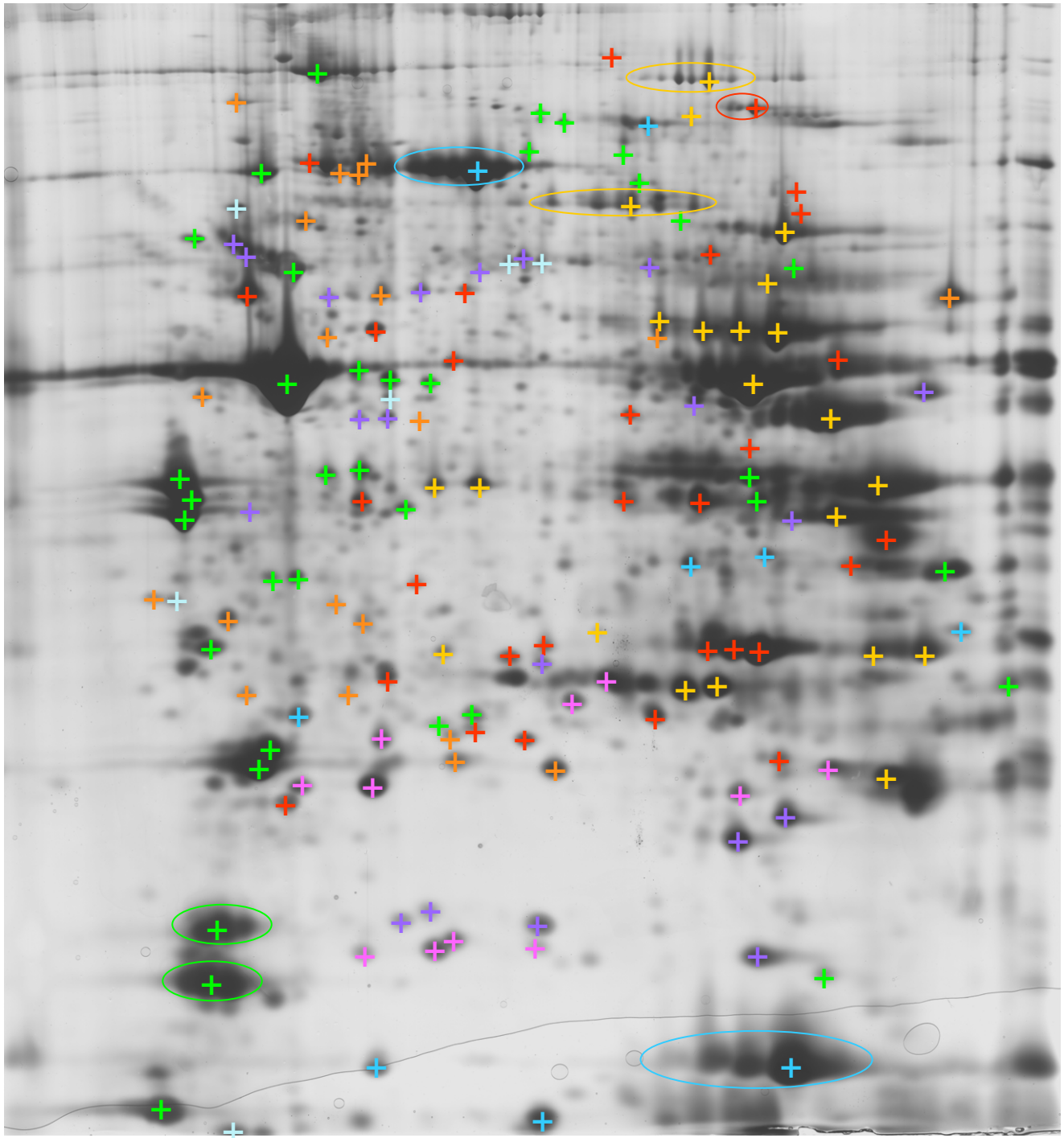
+ Prot. di trasporto

+ Prot. stress ossidativo

+ Prot. biosintesi-degradazione

+ Prot. cell signalling

+ Altre funzioni

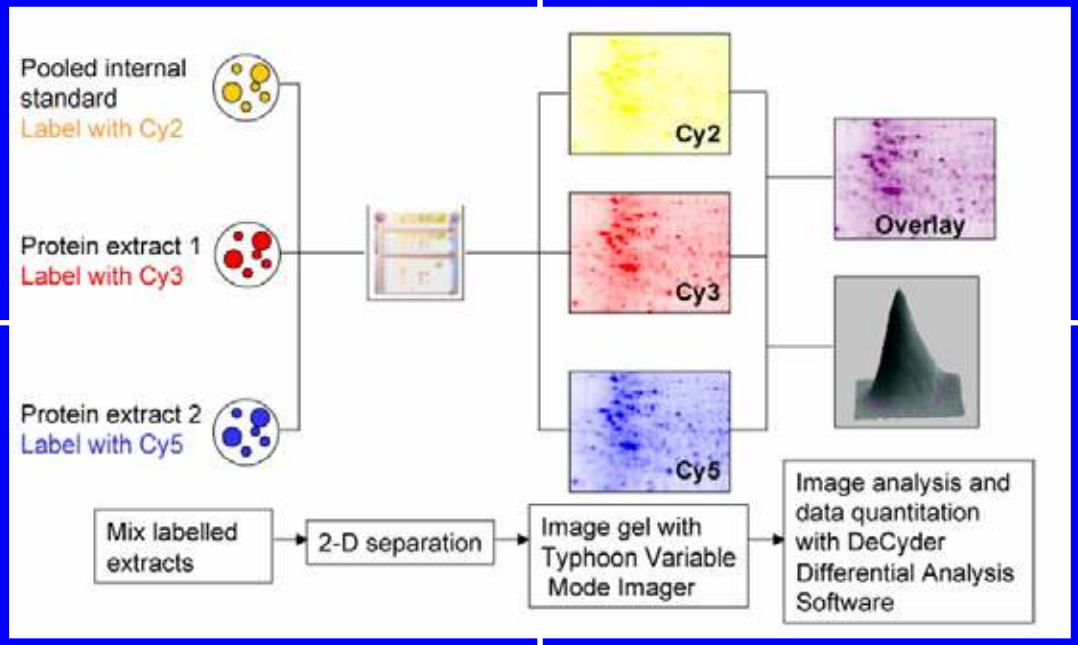


*** FAI CLICK SULLE CROCETTE PER COLLEGARTI A SWISSPROT ***

Two Dimensional Difference In Gel Electrophoresis (2D- DI GE)

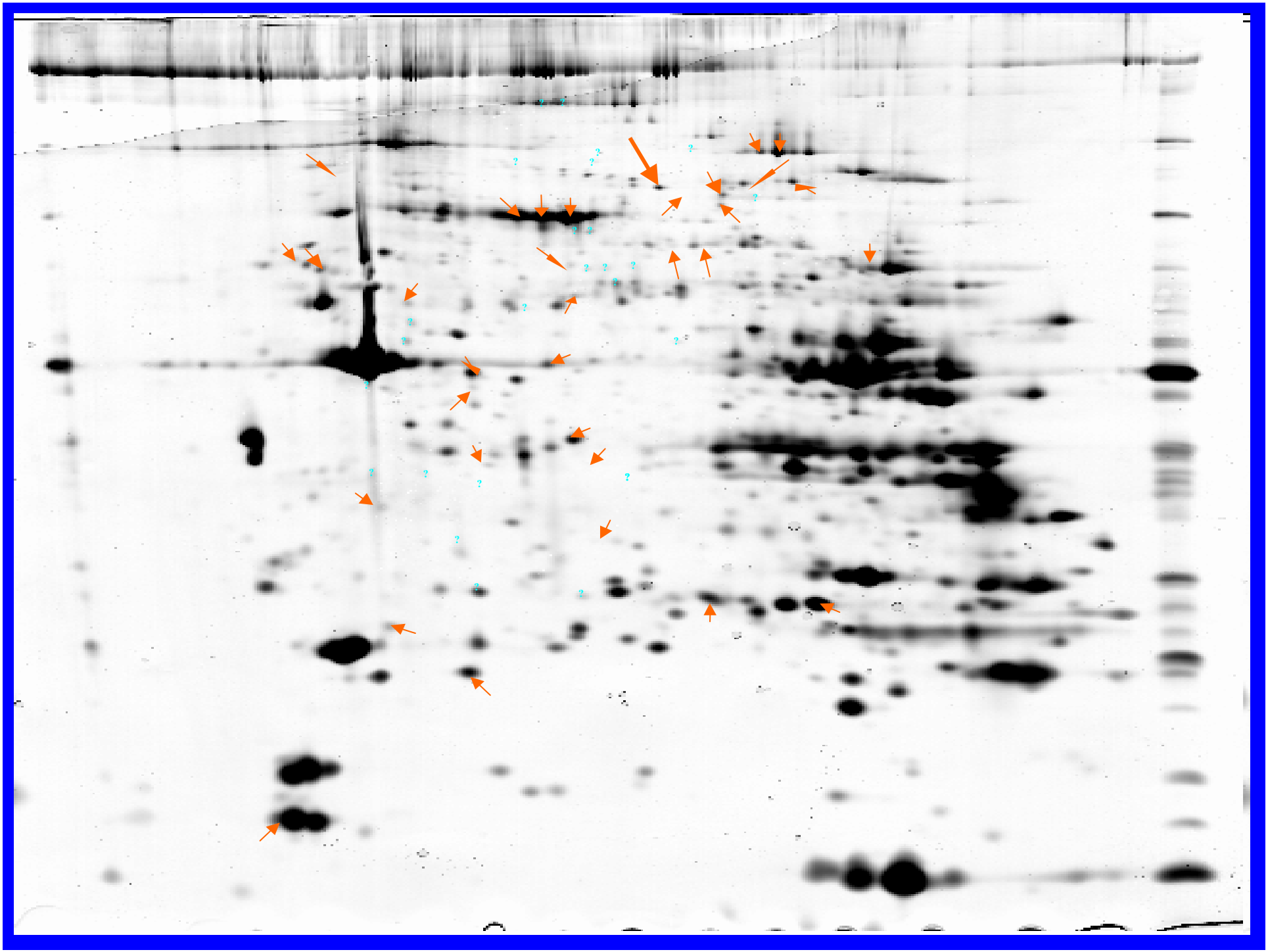
The samples are *minimal labelled*

The sensitivity is 125 pg per spot



2D- Dige increases qualitative and quantitative accuracy of 2- DE results

A pooled internal standard is included in all gels



Does the functional changes induced by different conditions such as aging and bed rest reflect the same variability at the muscle proteomic level?

Does the functional impairment induced by dystrophies with different genetic origin reflect the same changes in muscle proteome?

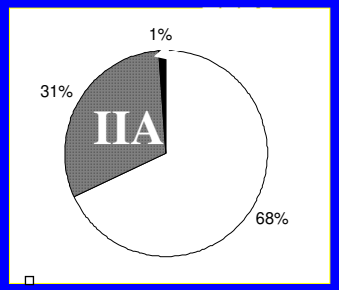
Which are, if any, the specific markers?

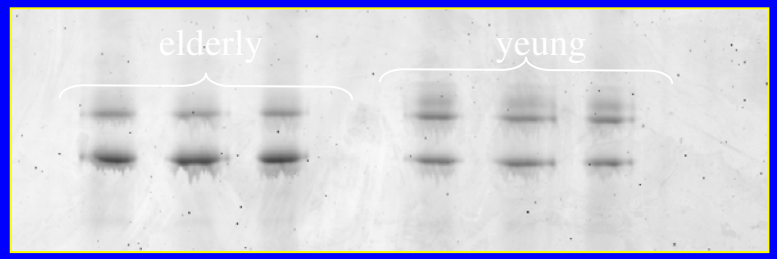
SDS and 2D-Dige for sarcopenia and muscle impairment assessment

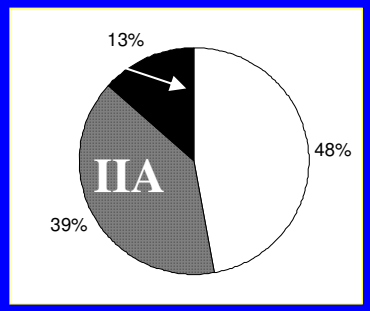
- **Aging**
  - → 6 subjects moderately active , 70-75 yrs old
  - → 6 subjects not specifically trained, 18-25 yrs old
- **Bed rest**
  - → 4 subjects (25-35 yrs old) before and after 55 days bed rest
- **FSHD (unknown genetic origin)**
  - → 9 patients
  - → 9 normal subjects sex and aged matched
- **Dysferlin deficit (defect in sarcolemmal repair)**
  - → 6 patients
  - → 6 normal subjects sex and aged matched

MHC and Fiber Typing

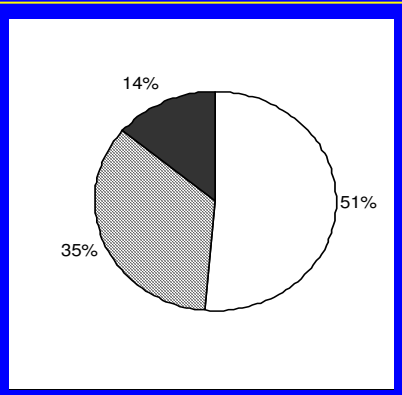
AGING



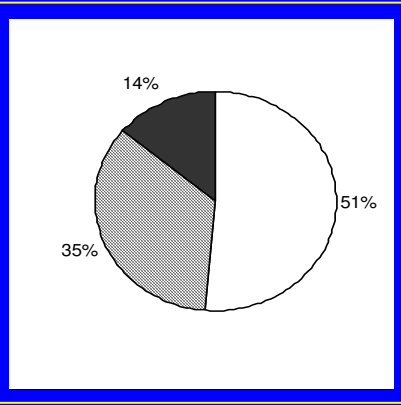




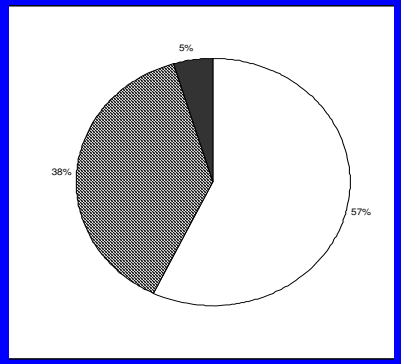
CONTROL



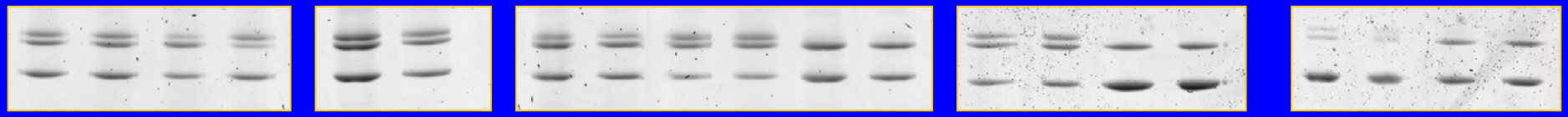
BEDREST



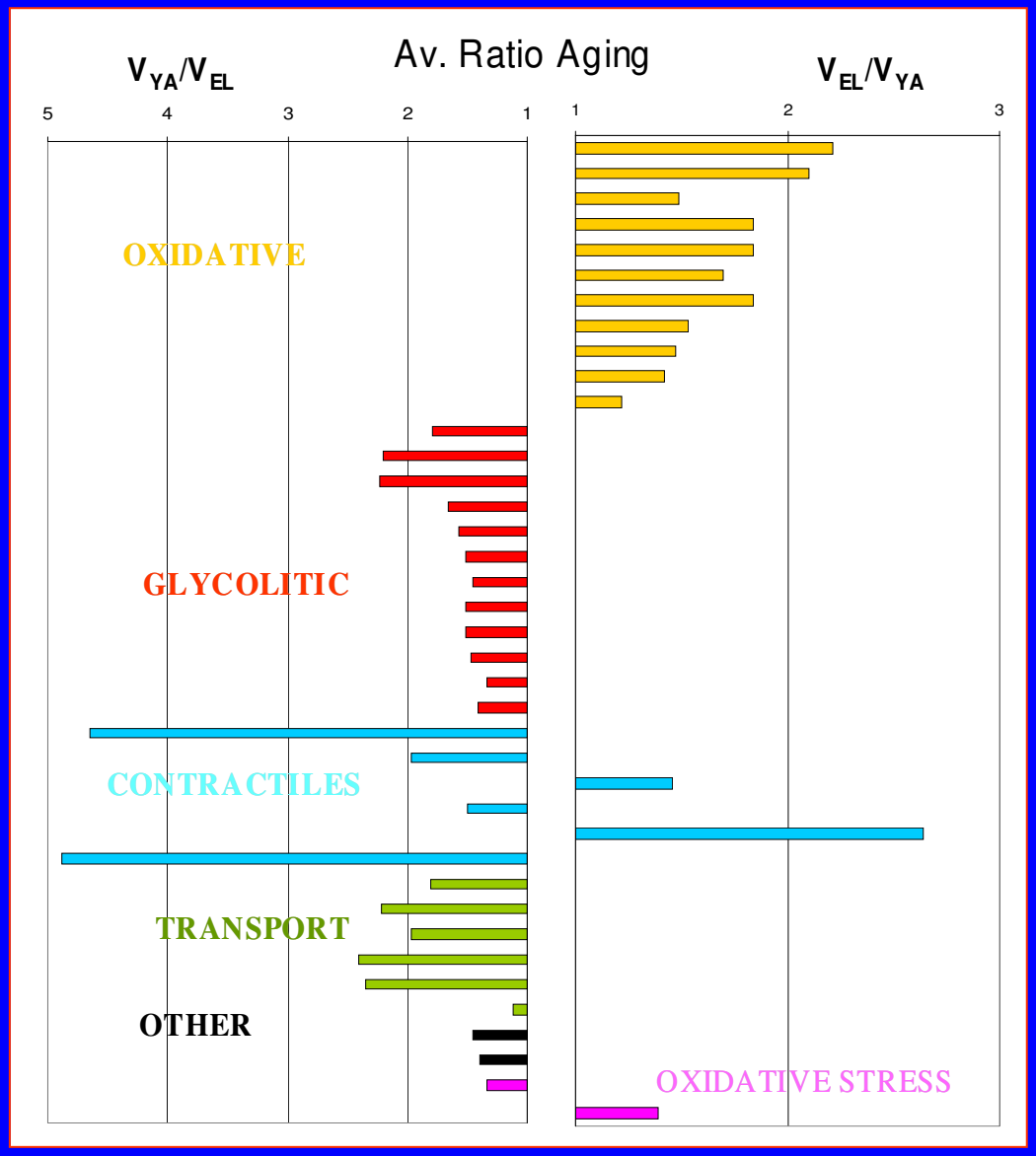
DYSFERLINOPATHY

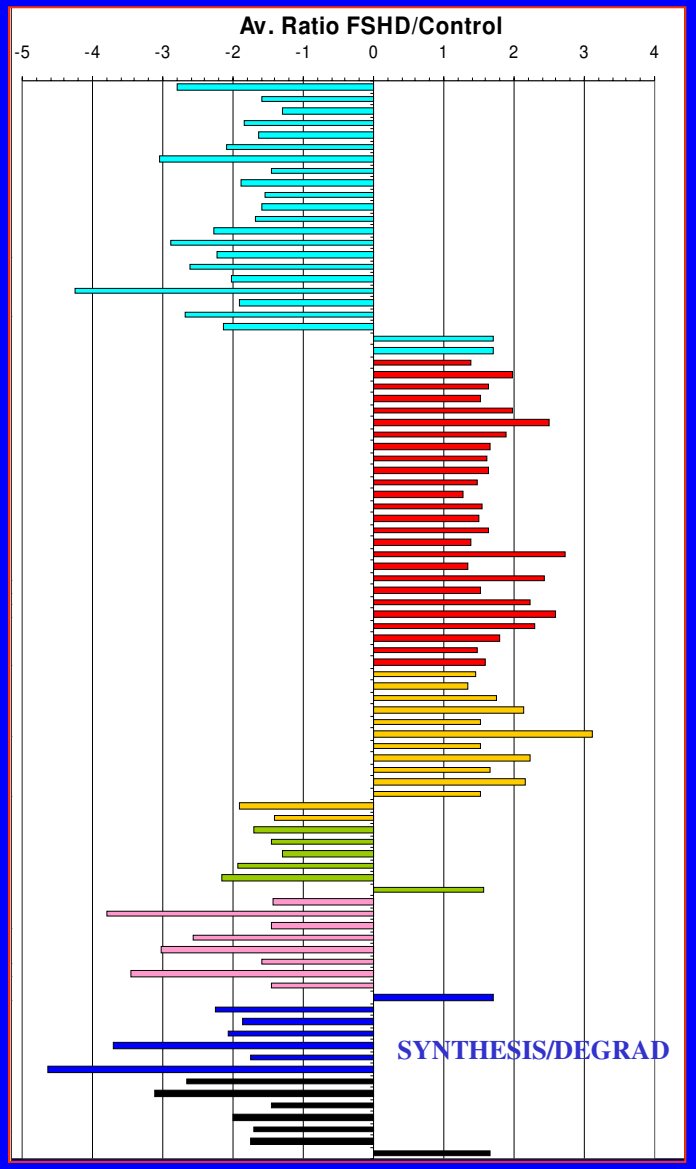


FSHD

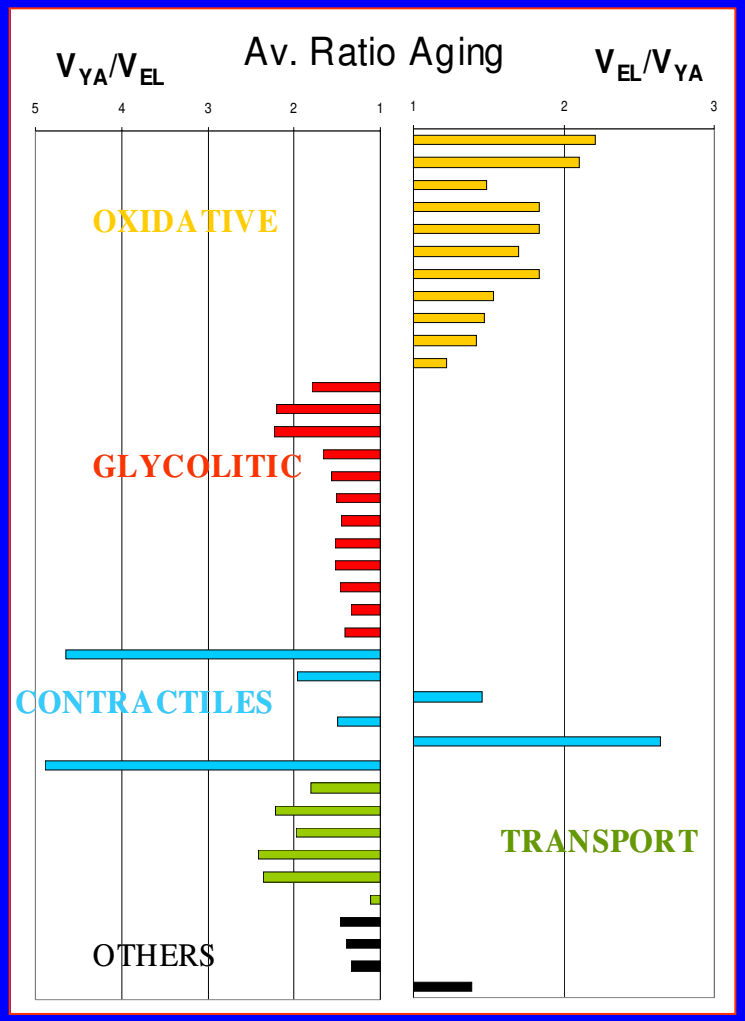


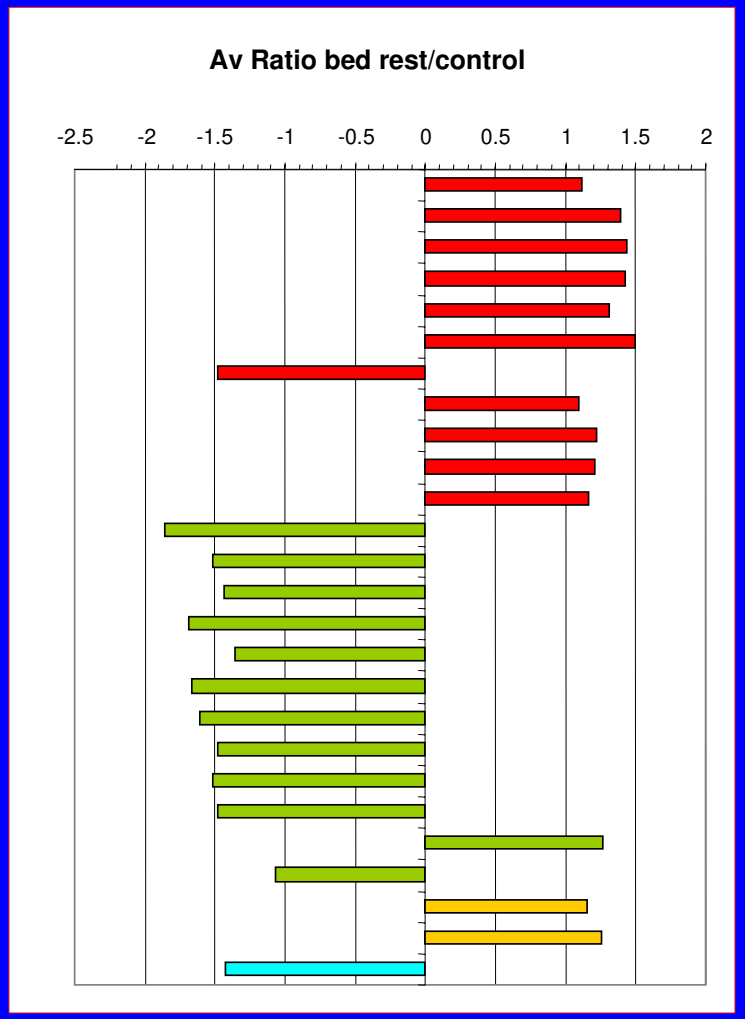
Physiological sarcopenia *vs FSHD*



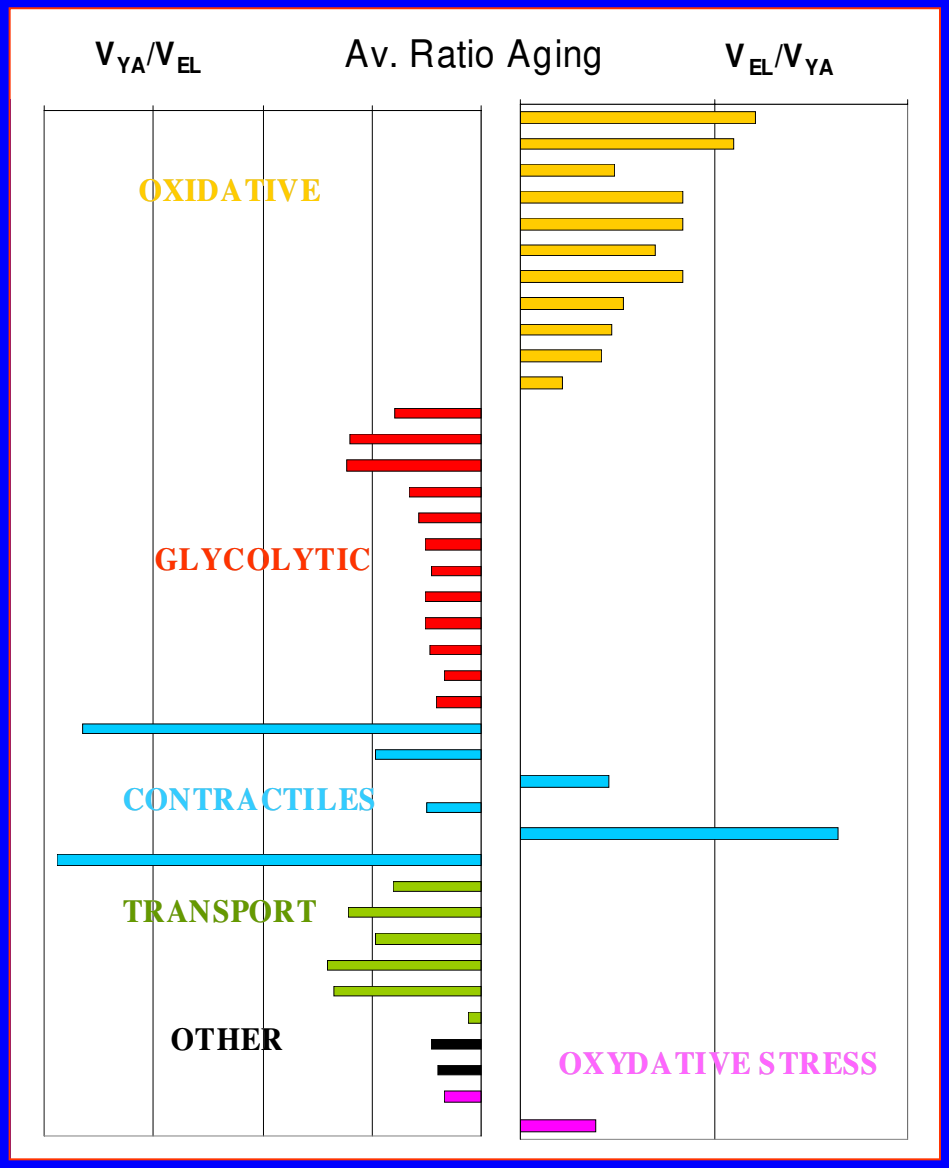


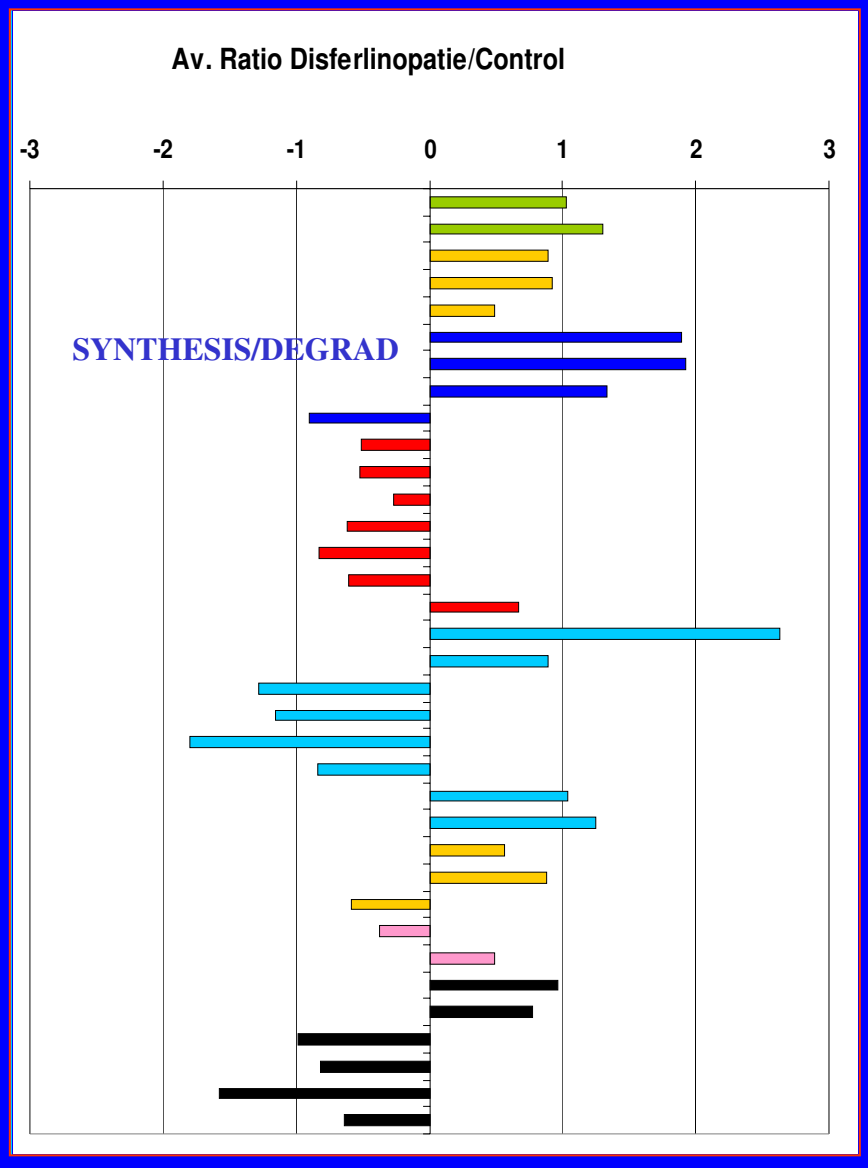
Loss of muscle mass induced by aging and bed rest



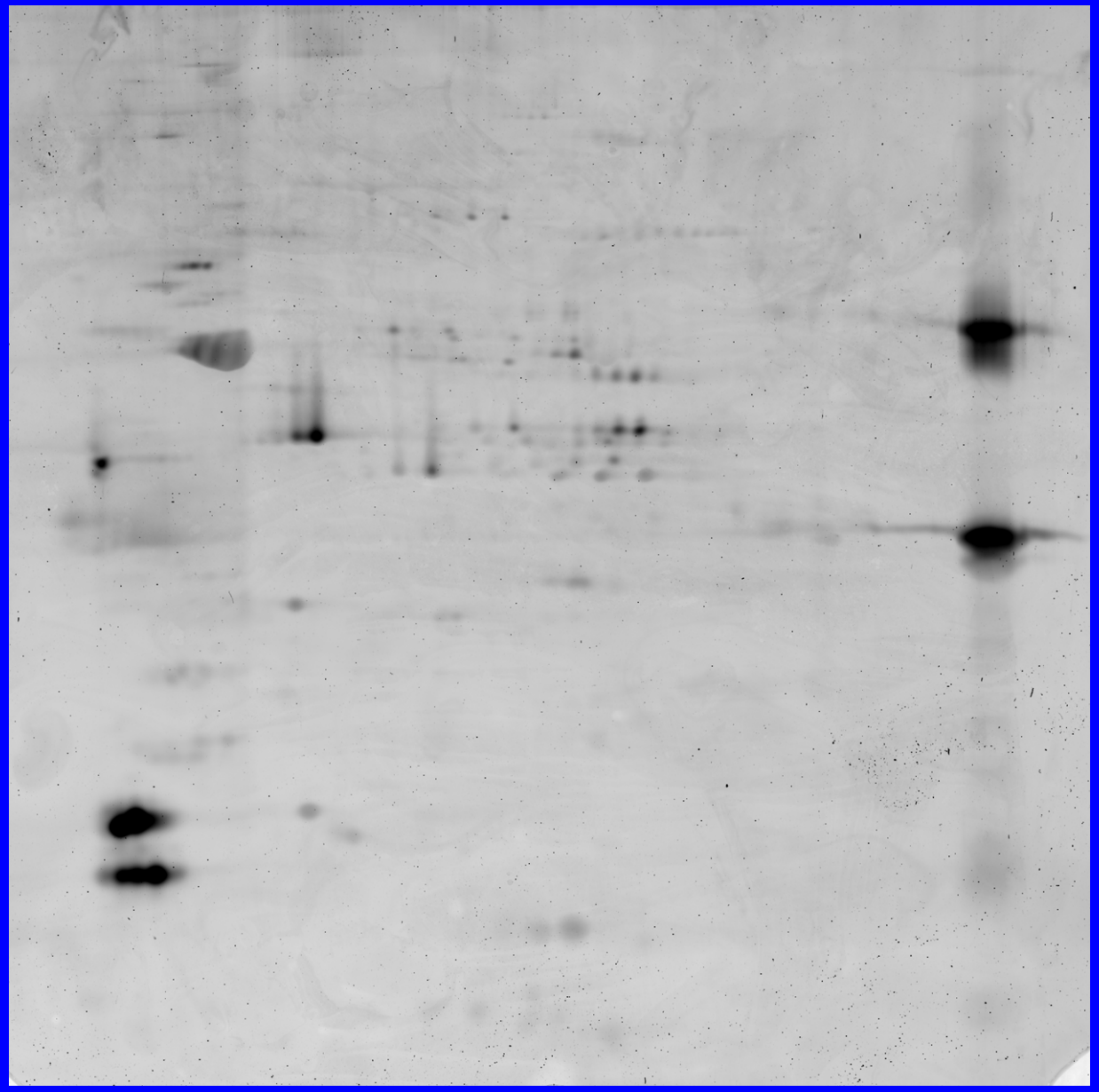


Physiological sarcopenia *vs* muscle impairment induced by dysferlin deficency

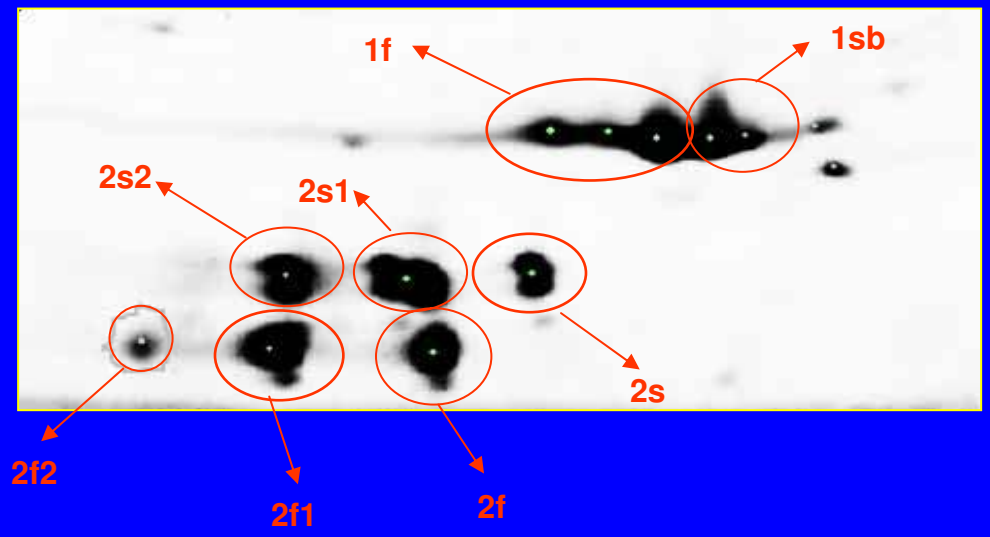




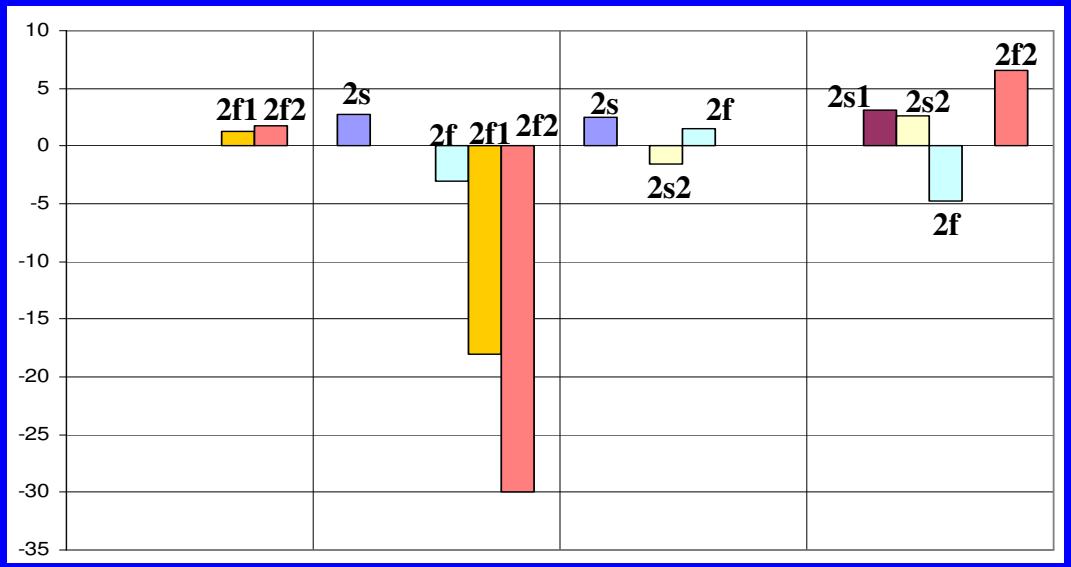
Muscle Phospho-proteome



Myosin Light Chains



Bed Rest Aging Dysferlinophaty FSHD



Conclusions

- 2D-DIGE approach enables the simultaneous assessment of contractile proteins ,their isoforms, a large number of metabolic and signalling markers. The overall evaluation allows to characterize muscle tissue and it represents an essential tool in muscle research.
- The **phosphorylation** signal of regulatory MLC's combined with MHC evalution reveal a function compatible with the modulation of the contraction velocity and could be a marker of muscle function

Aknowledgements

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