The human muscle proteome in aging

Cecilia Gelfi
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
Fiber classification:

* type 1 slow, oxidative
* type 2A fast, oxidative
* type 2X fast, glycolitic
* type 1-2A, mixed fiber
* type 2A-2X, mixed fiber

Human muscle structure
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.

**Functional parameters under debate**

![Bar chart showing distribution of Vo values](image-url)
MHC Distribution

**Pool EL**
- MHC 1: 31%
- MHC 2A: 68%
- MHC 2X: 1%

**Pool YA**
- MHC 1: 39%
- MHC 2A: 48%
- MHC 2X: 13%
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-DIGE)

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

CONTROL 27 Kb 21-26 Kb 16-19 Kb 10 Kb
Physiological sarcopenia vs FSHD

Av. Ratio Aging

- V_{YA}/V_{EL}
- V_{EL}/V_{YA}

- OXIDATIVE
- GLYCOLITIC
- CONTRACTILES
- TRANSPORT
- OTHER

OXIDATIVE STRESS

Av. Ratio FSHD/Control
Loss of muscle mass induced by aging and bed rest
Physiological sarcopenia vs muscle impairment induced by dysferlin deficiency
Muscle Phospho-proteome
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 evaluation reveal a function compatible with the modulation of the contraction velocity and could be a marker of muscle function
Aknowledgements

Proteomic Unit

- Marilena Ripamonti
- Agnese Viganò
- Sara De Palma
- Daniele Capitanio
- Manuela Moriggi

- Robin Wait
  Imperial College London
- Paolo Cerretelli
  University of Milano
- Joern Rittweger
  Manchester University
- Roberto Bottinelli
  University of Pavia
- Enzo Ricci
  Catholic University, Rome
- Lucia Morandi
  Carlo Besta Neurological Institute, Milano

Financial supports:

Telethon, FIRB, CARIPLO, ASI