

Creatine supplementation during knee immobilization attenuates changes in muscle transcriptome

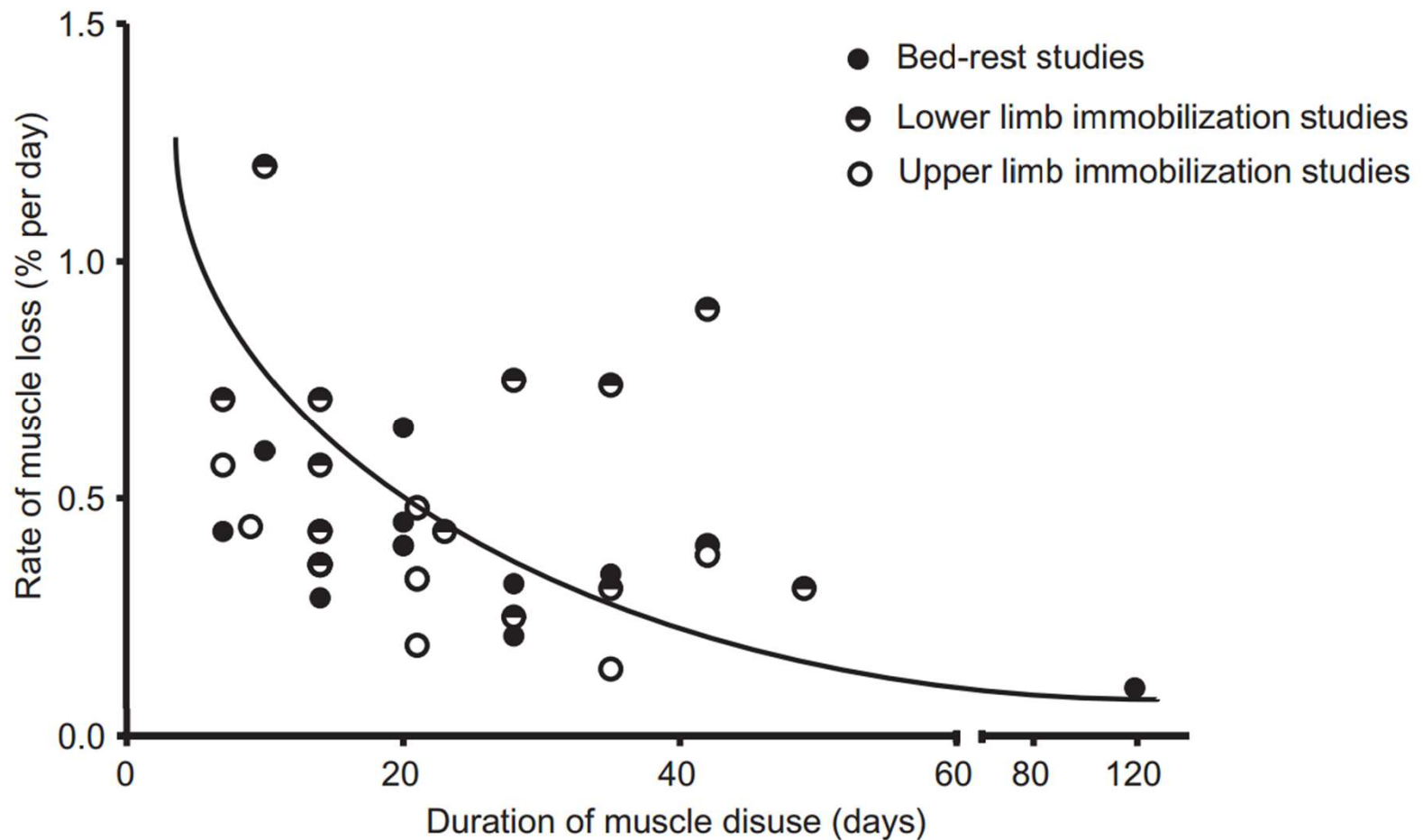
NUGOWeek 2016

Copenhagen

September 7, 2016

Roland Hangelbroek

Physical inactivity dramatically decreases muscle mass



Wall and van Loon, 2013

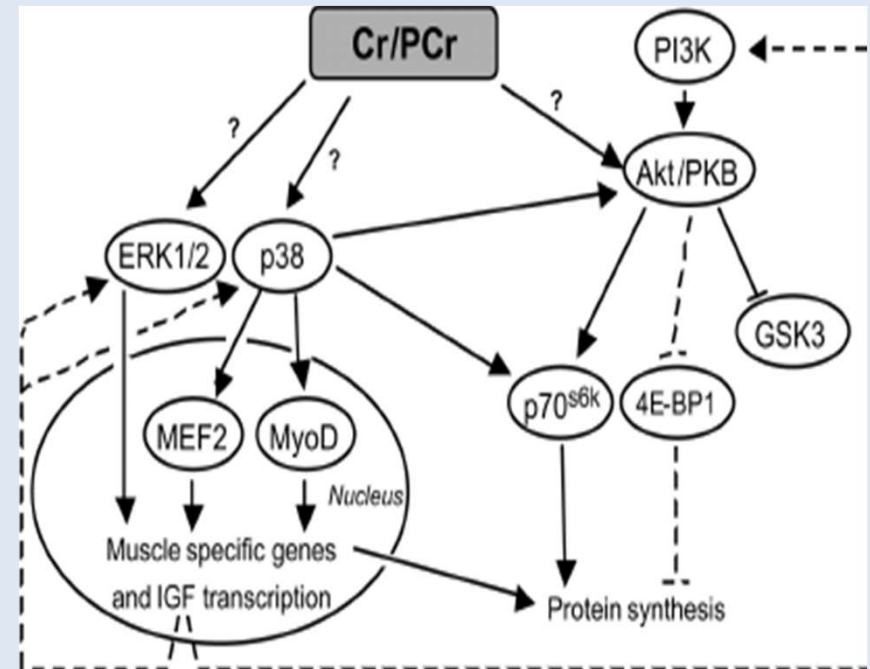
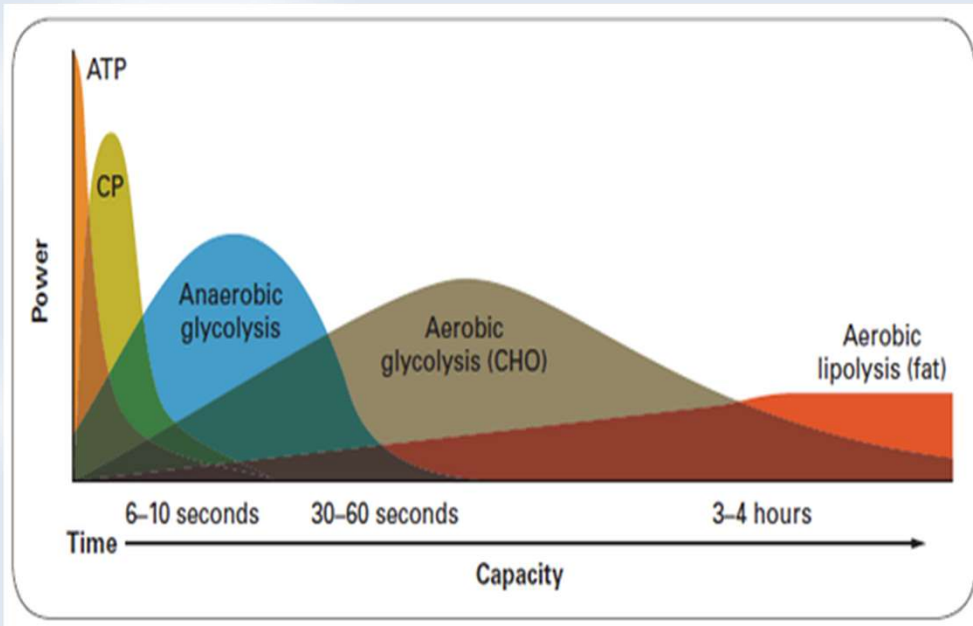
Physical inactivity dramatically decreases muscle mass

3



Image source: <https://kneeobliteration.wordpress.com/tag/acl-reconstruction/>

Creatine as ergogenic aid

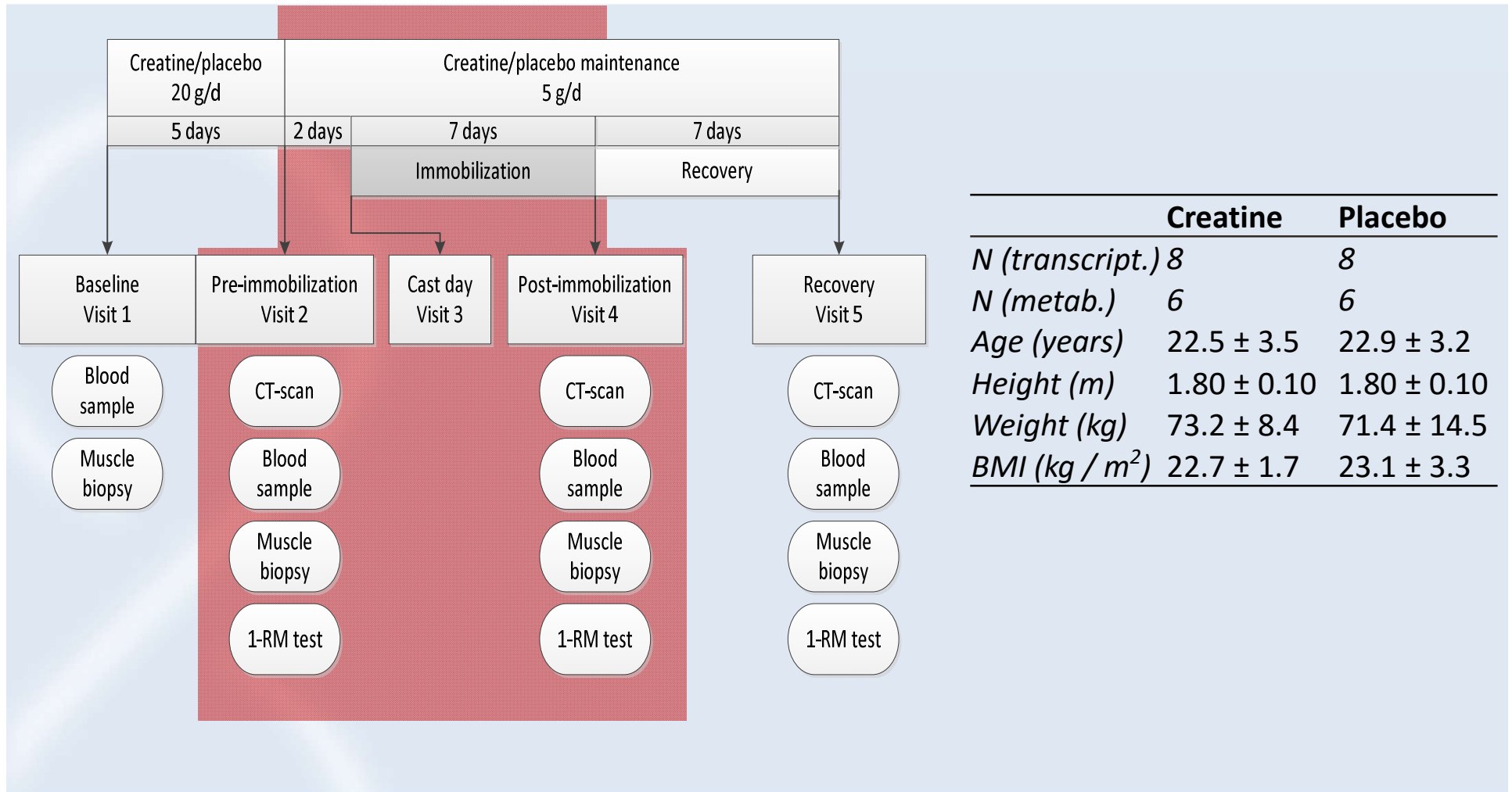


<http://mscsportscience.weebly.com/energy-systems.html>

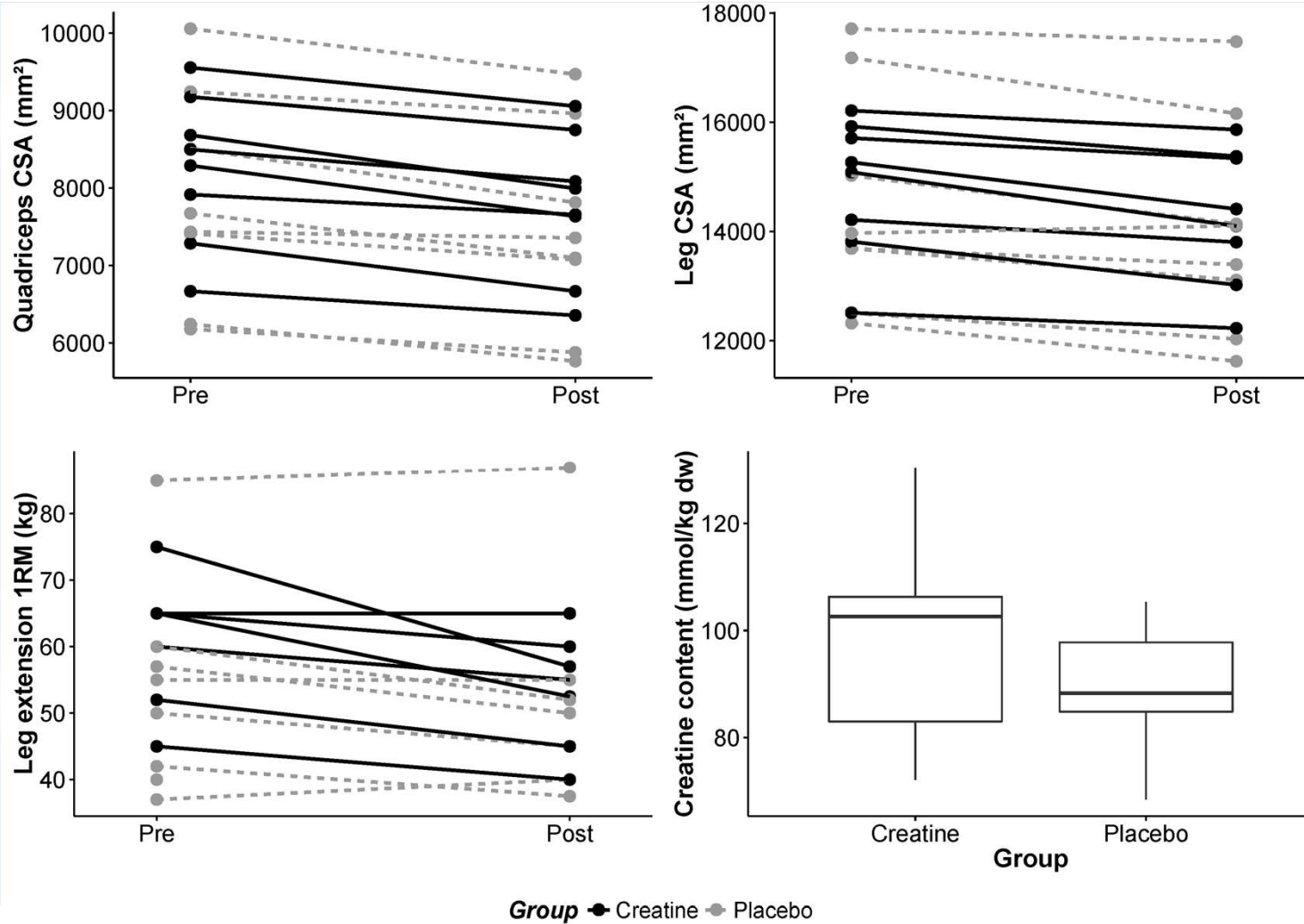
Deldicque *et al.* 2007

DOI: 10.1152/ajpcell.00162.2007

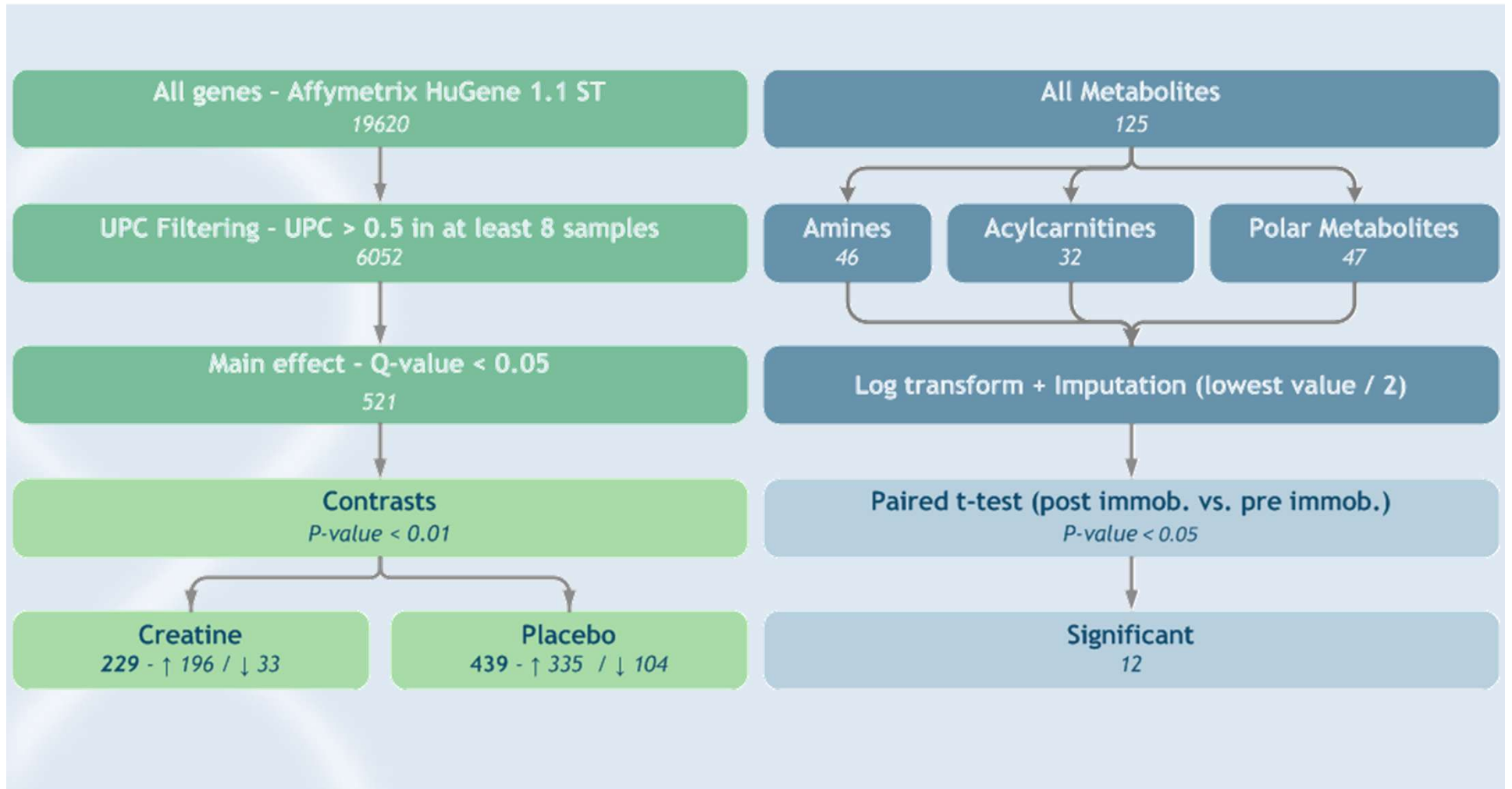
Full Study Design



Immobilization – Physiological Effects

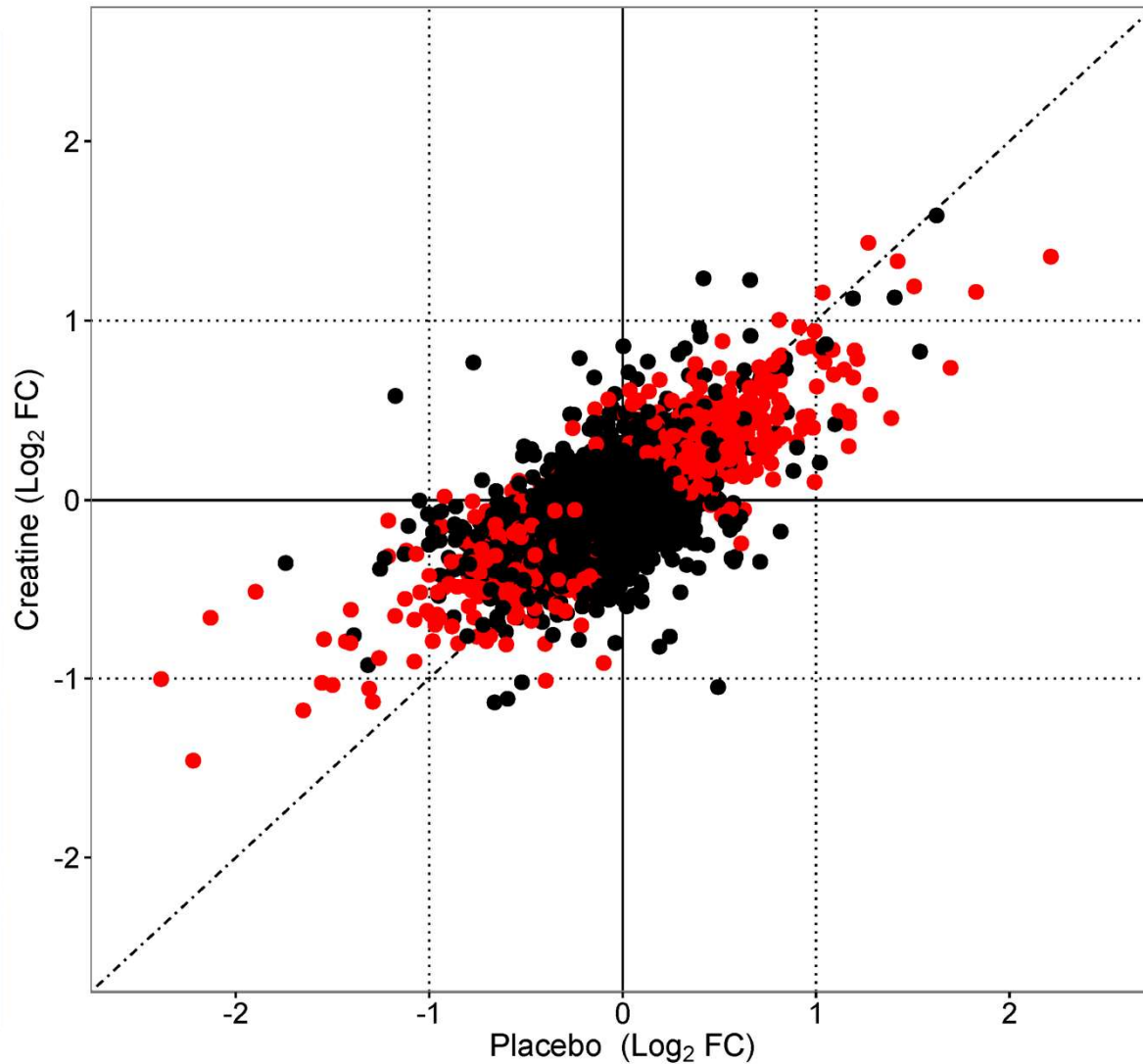


-Omics Workflows



Gene expression changes – Creatine vs. Placebo

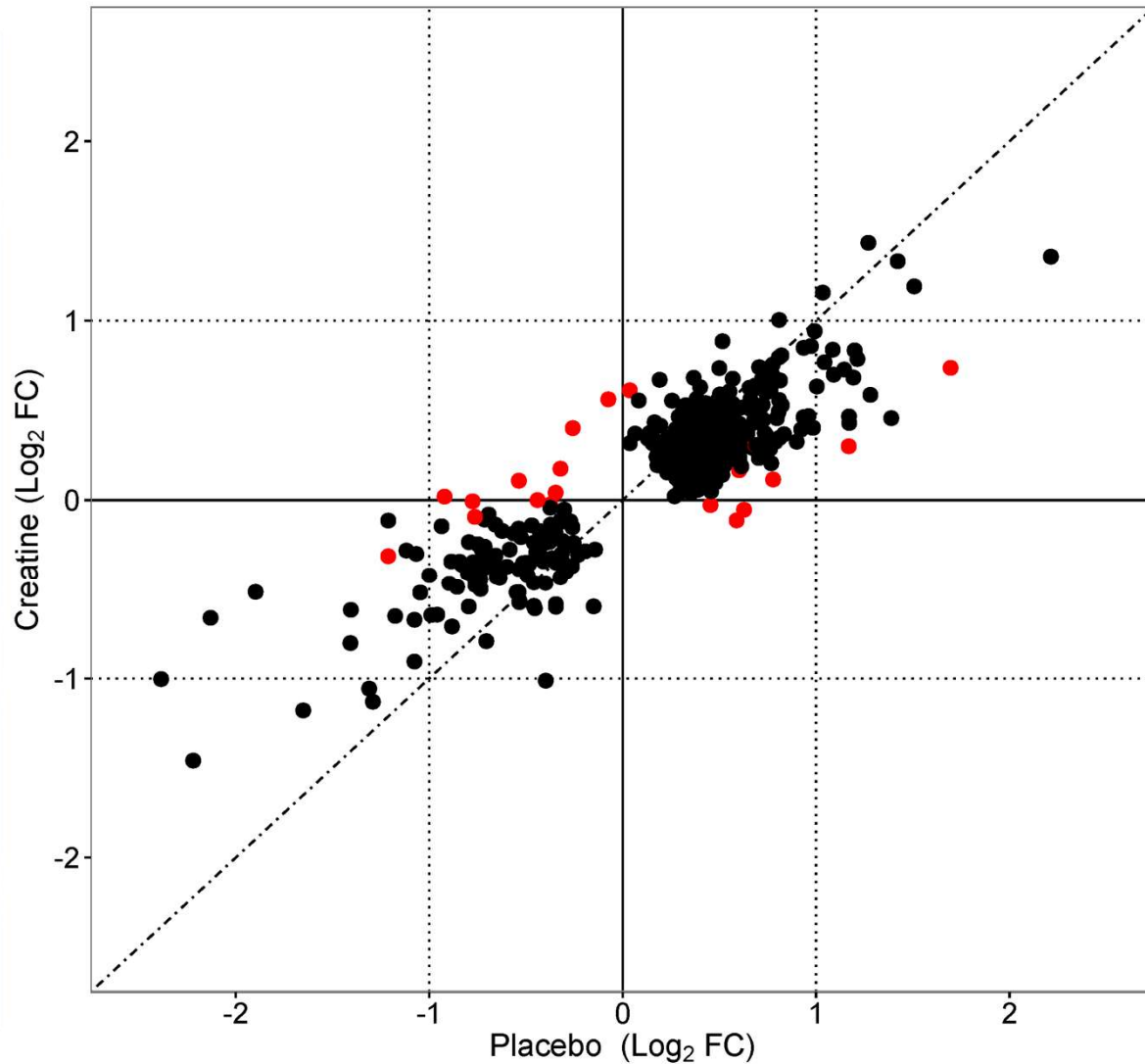
8



● Not Significant ● Significant (F-test q-value < 0.05)

8

Gene expression changes – Creatine vs. Placebo



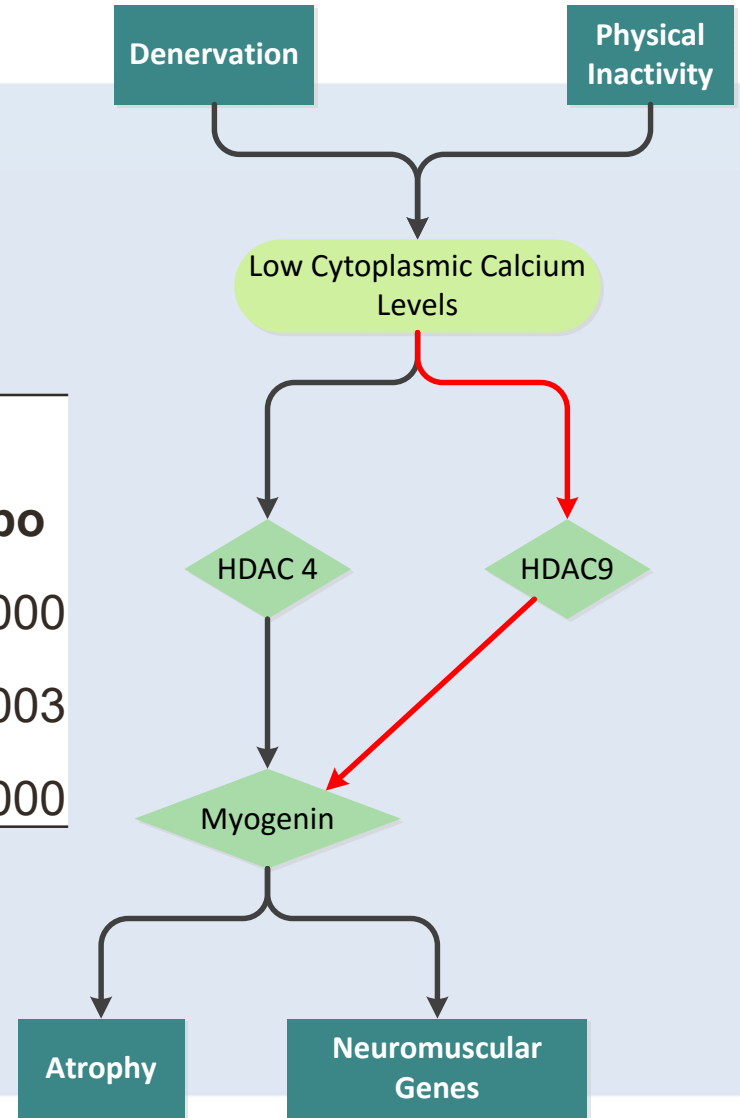
● Not Significant ● Significant Creatine Interaction (p<0.01)

Main Effects of Knee Immobilization

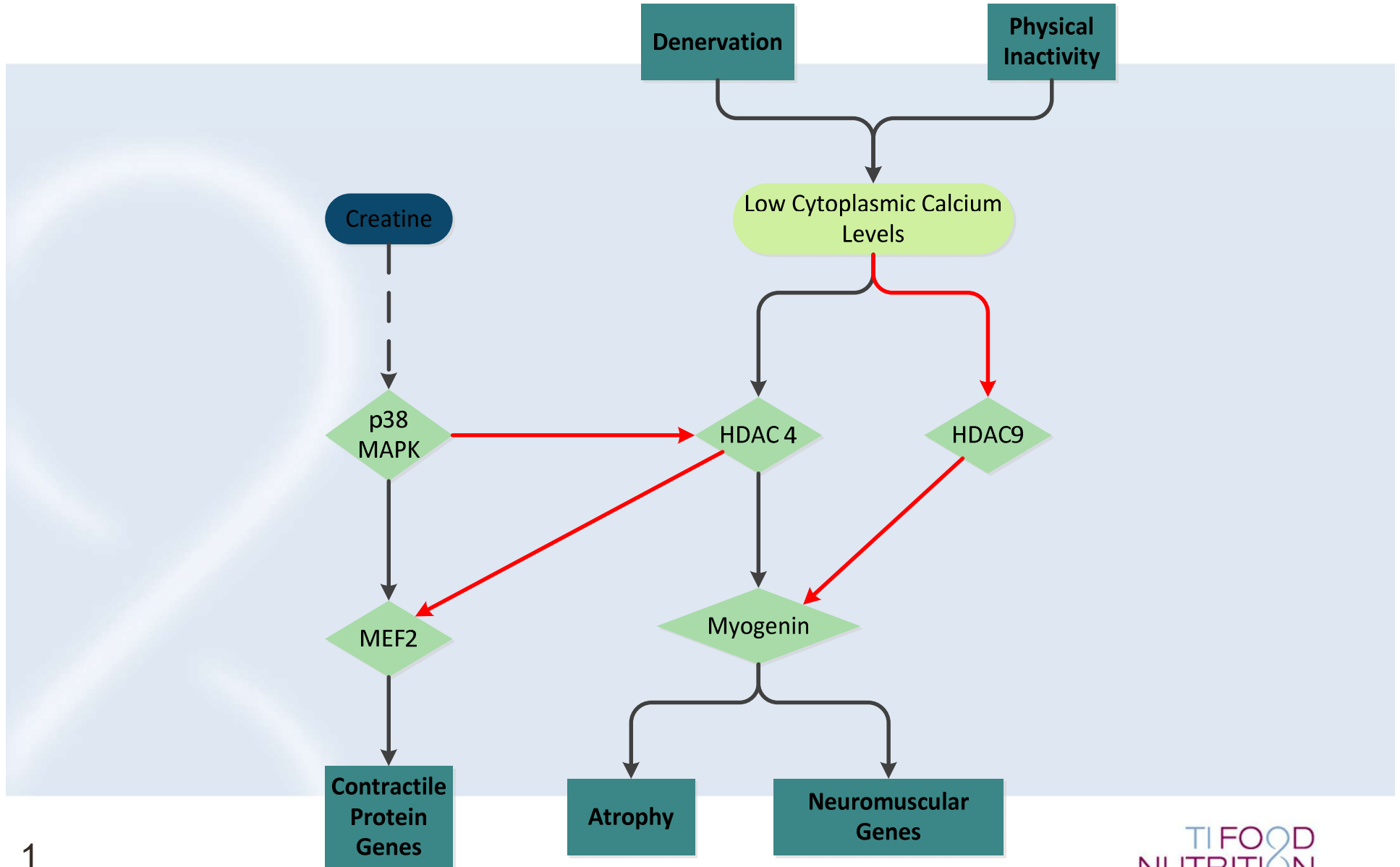
- Top genes related to:
 - Tissue remodelling (Collagen, cytoskeleton reorganization)
 - Neuromuscular (HDAC4, HDAC9, GDNF, CHRN1, ACH1)
 - Calcium signalling and osmotic stress (CALM1, NFAT5)
 - Muscle & muscle pathology (MYHs, MYLs, SOD1, HTT, ATXN1)
- Pathways:
 - Mitochondrial genes (↓)
 - Glucose metabolism (↓)
 - Ubiquitin Mediated Proteolysis (↑)
- Regulators:
 - FOXO1 / FOXO3
 - NR4A1
 - MEF2

HDAC4 / Myogenin Axis

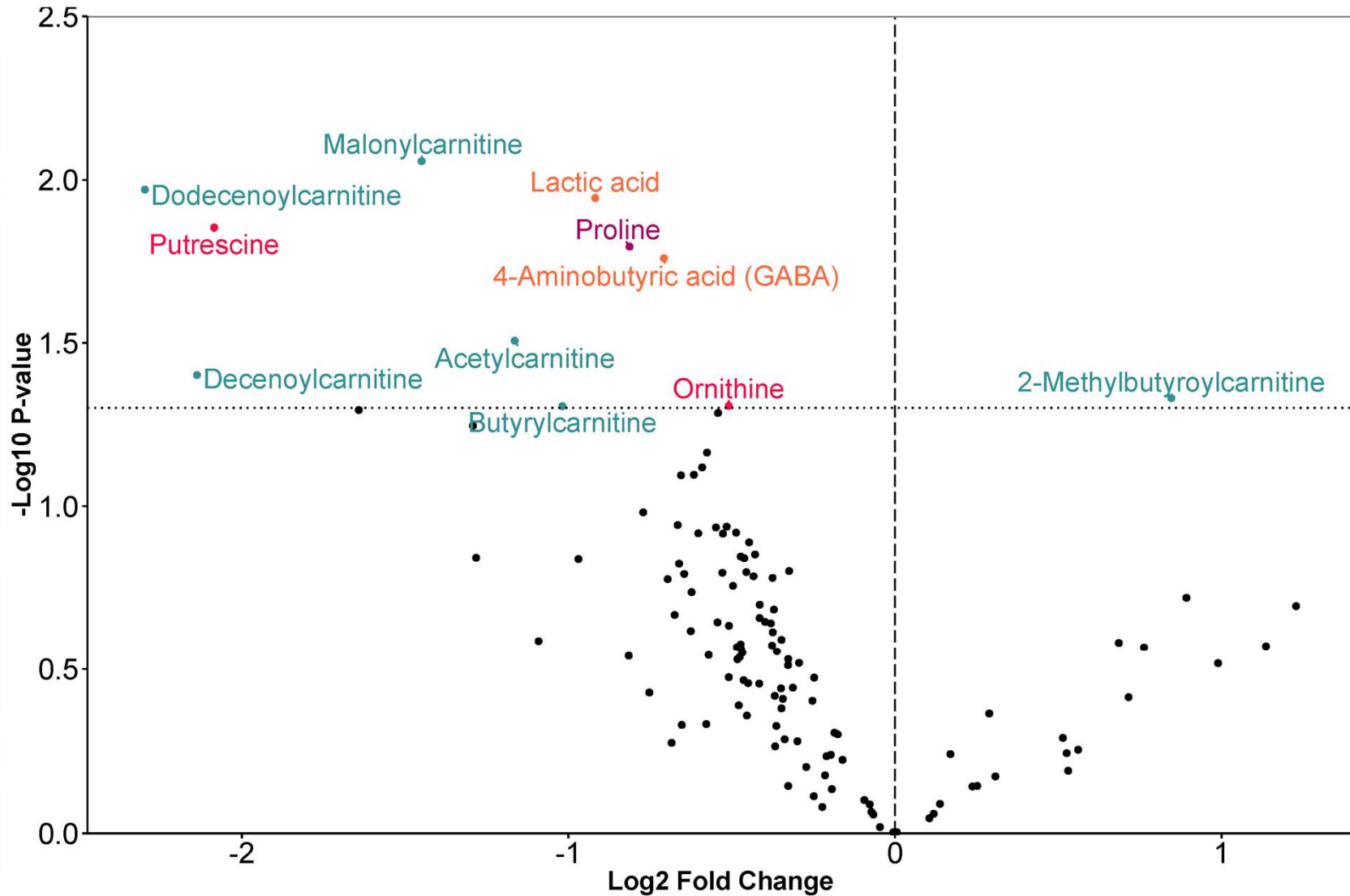
	<u>FC</u>		<u>P-value</u>	
	Creatine	Placebo	Creatine	Placebo
<i>HDAC4</i>	1.67	3.24	0.005	0.000
<i>MYOG</i>	1.07	1.99	0.734	0.003
<i>HDAC9</i>	0.79	0.54	0.099	0.000



Creatine interaction with HDAC4



Metabolome results



Polyamine metabolism

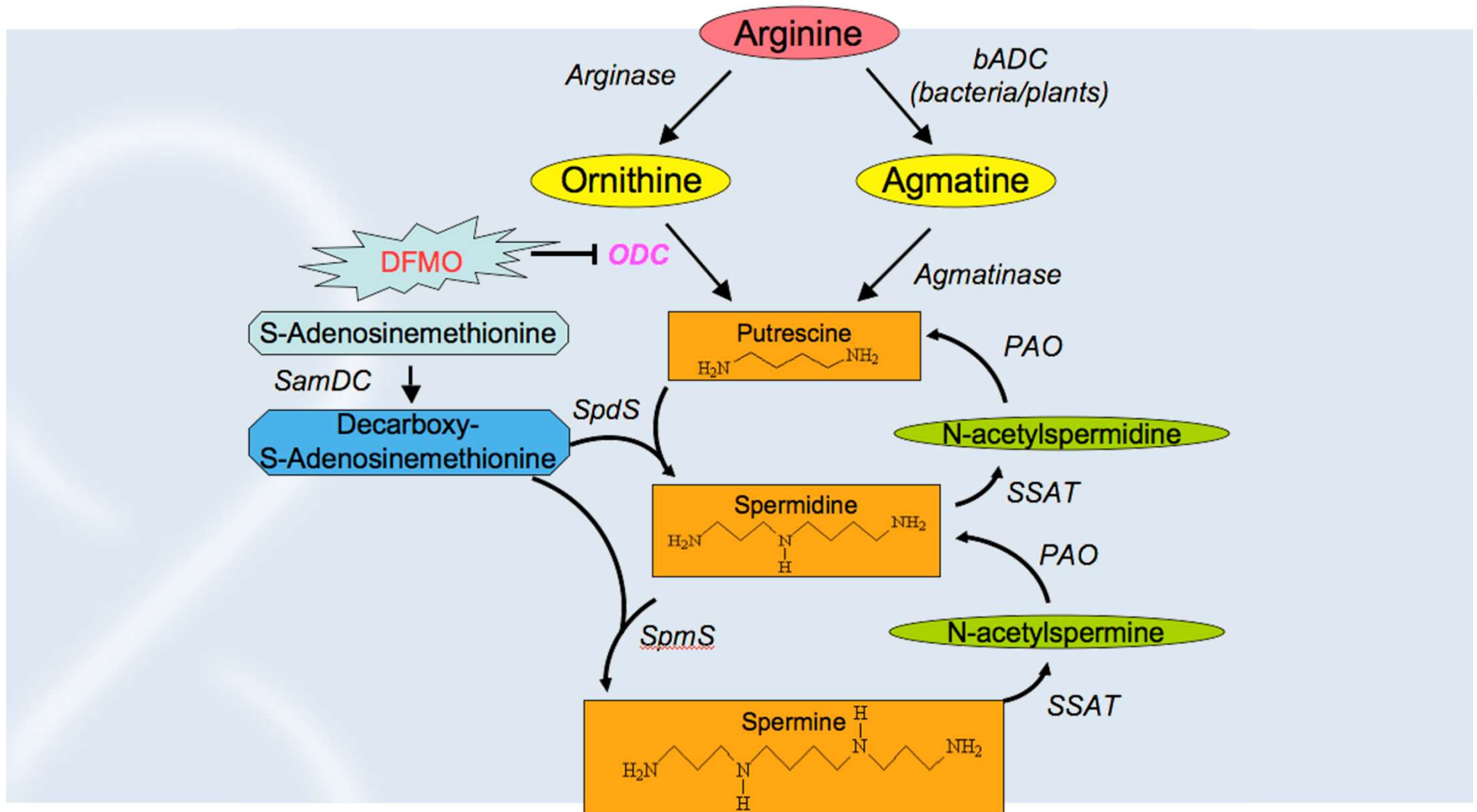


Image source:

<http://www.weizmann.ac.il/molgen/Kahana/polyamines>

Conclusions

- Immobilization induces proteolysis related gene expression and attenuates glucose metabolism and mitochondrial function gene expression
- Creatine appears to have an attenuating effect on changes in gene transcription due to knee immobilization
- HDAC4/Myogenin axis is involved in muscle atrophy during knee immobilization
- Metabolomic analysis reveals decreased levels of fatty acid derived acyl carnitines and increased levels of a amino acid derived acyl carnitine (2-methylbutyrocarnitine)
- Polyamine metabolism appears to be affected by knee immobilization

Acknowledgements



- Human Nutrition
 - Evelien Backx
 - Mark Boekschoten
 - Lisette de Groot
 - Sander Kersten
- Biophysics
 - John van Duynhoven



- Luc van Loon
- Tim Snijders
- Lex Verdijk



Universiteit Leiden

- Thomas Hankemeier

Thanks for your
attention

Questions?