

Evaluating muscle function in mice lacking myostatin by functional Nuclear Magnetic Resonance *in vivo*: preliminary results

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Deletion of the myostatin gene (*mstn*^{-/-}) results in spectacular increase in muscle mass, and opened the path to therapeutic approaches. Yet improvement in strength does not necessarily match the observed increase in mass. If function is to be preserved in hypertrophic muscle, adequate oxygen supply and substrate utilization should also be maintained. Multi-parametric functional (mpf) NMR can explore these aspects *in vivo* and non-invasively. In this work, we simultaneously assessed muscle perfusion, capillary oxygenation level (BOLD), energetic phosphate metabolism and isometric force in response to electrical stimulation in *mstn*^{-/-} mice.

Mstn^{-/-} (n=6) and wild-type (n=10) FVB mice were repeatedly subjected to a “exercise(2min)- recovery(10min)” protocol inside a 4 Tesla NMR imager-spectrometer, using custom-built coils and ergometer. Perfusion/BOLD and phosphocreatine (PCr) were monitored with a time resolution of 10s and 2.5s. Acquisitions were triggered to the electro-stimulation to allow perfusion measurement even during exercise. Phosphorus data were summed across exercises to compensate for the intrinsically low signal without degrading time resolution.

A metabolic steady state was reached after the 2nd exercise for force, perfusion, and BOLD. *Mstn*^{-/-} force was not different from WT when normalized for the 36% increase in muscle cross sectional area measured by NMR imaging. Maximal perfusion at exercise was the same in both groups, but hyperemic profile was prolonged in *mstn*^{-/-}, and PCr recovery significantly delayed ($P<.015$).

Adapting the mpf-NMR approach to mice makes it possible to non-invasively investigate the interplay of muscle oxygen supply and energetics *in vivo*. These preliminary findings show that although muscle strength matches its mass in *mstn*^{-/-}, time to recovery from exercise is prolonged as compared to WT, in terms of oxygen supply and oxidative phosphorylation, compatible with an overall shift towards more glycolytic metabolism.