Vol. 122, n. 1 (Supplement): 185, 2017

Muscle hypertrophy and vascularization induction using human recombinant proteins

Flavio Lorenzo Ronzoni^{1,2}, Gabriele Ceccarelli^{1,2}, Laura Benedetti^{1,2}, Riccardo Bellazzi^{2,4}, Maria Gabriella Cusella De Angelis^{1,2} and Maurilio Sampaolesi^{1,2,3}

¹Human Anatomy Unit, Dept. Public Health, Experimental and Forensic Medicine, University of Pavia, Italy

² Center for Health Technologies (C.H.T.), University of Pavia, Italy

³Stem Cell Biology and Embryology Unit, Dept. Development and Regeneration, KU Leuven, Belgium

⁴Dept. of Electrical, Computer and Biomedical Engineering, University of Pavia, Italy

Met-Activating Genetically Improved Chimeric Factor-1 (Magic-F1) is an engineered protein that contains two human Met-binding domains. Previous experiments in both homozygous and hemizygous transgenic mice demonstrated that the skeletal muscle specific expression of Magic-F1 can induce a constitutive muscular hypertrophy, increasing the vessel number in fast twitch fibers, also improving running performance and accelerating muscle regeneration after injury [1]. We also found that Magic-F1 could be responsible of muscular hypertrophy inteacting with Pax3 signal pathway in skeletal muscle precursor cells [2]. In order to evaluate the therapeutic potential of Magic-F1, we tested its effect on multipotent and pluripotent stem cells [3]. Murine mesoangioblasts (adult vessel-associated stem cells) expressing Magic-F1 were able to differentiate spontaneously forming myotubes. In addition, in Magic-F1 inducible murine embryonic stem cells subjected to myogenic differentiation, the presence of recombinant protein resulted in improved myogenic commitment. Finally, the microarray analysis of Magic-F1+/+ satellite cells evidenced transcriptomic changes in genes involved in the control of muscle growth, development and vascularisation [4]. Taken together our results candidate Magic-F1 as a potent myogenic inducer, able to affect positively the vascular network, increasing vessel number in fast twitch fibers and modulating the gene expression profile in myogenic progenitors.

References

- [1] Cassano M et al. (2008). Magic-factor 1, a partial agonist of Met, induces muscle hypertrophy by protecting myogenic progenitors from apoptosis. PLoS One. 2008 3(9): e3223.
- [2] Ronzoni F et al. (2011). Localization of Magic-F1 transgene, involved in muscular hypertrophy, during early myogenesis. J Biomed Biotechnol. 2011; 2011: 492075.
- [3] Perini I et al. (2015). Myogenic induction of adult and pluripotent stem cells using recombinant proteins. Biochem Biophys Res Commun. 2015 464(3): 755-61
- [4] Ronzoni F et al. (2017). Met-Activating Genetically Improved Chimeric Factor-1 Promotes Angiogenesis and Hypertrophy in Adult Myogenesis. Curr Pharm Biotechnol. 2017 Feb 1 [Epub ahead of print]

Keywords

Embryonic stem cells, Magic-F1, mesoangioblast, myogenic differentiation, recombinant protein.