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Cardiac development and remodelling in Magic-F1 transgenic mice

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MAGIC-F1 (Met Activating Genetically Improved Chimeric Factor 1) is a human recombinant protein, derived from dimerization of the receptor-binding domain of hepatocyte growth factor (HGF). Previous experiments demonstrated that skeletal muscle specific expression of Magic-F1 can induce constitutive muscular hypertrophy, improve running performance and accelerate muscle regeneration after injury in hemizigous transgenic mice [1]. Furthermore, the microarray analysis of Magic-F1+/+ satellite cells showed transcriptomic changes in genes involved in the control of muscle growth, development and vascularisation [2].

In this study we demonstrate that Magic-F1 mice show an alteration of the heart morphology. Morphometric analysis and three-dimensional reconstruction of the hearth revealed that MAGIC-F1 paracrine effect is able to induce a robust remodelling of the left ventricle chamber in transgenic mice. Interestingly, we found in Magic-F1 hearts an alteration of Phd2 and HIF1 protein levels. These two oxygen sensors are found dysregulated in cardiac ischaemic conditions, where generalised hypoxia causes functional impairments in cardiomyocytes and structural tissue damage [3-4]. These preliminary results support the involvement of oxygen sensors in Magic-F1-induced cardiac hypertrophy and dilation. In addition, Magic-F1+/+ mice can be used as non-pressure overload model to further investigate the role of oxygen-sensors in ischaemic heart disease. To better understand the biological effects of MAGIC-F1 on the morphology and function of cardiac muscle, more detailed studies are required. It could be also interesting to have a longer follow-up of the homozygous animals, to investigate the progression of the cardiac remodelling upon a double dose of MAGIC-F1.

References

[1] Cassano et al. (2008). Magic-factor 1, a partial agonist of Met, induces muscle hypertrophy by protecting myogenic progenitors from apoptosis. PLoS One 3(9): e3223.
[2] Ronzoni et al. (2017). Met-Activating Genetically Improved Chimeric Factor-1 Promotes Angiogenesis and Hypertrophy in Adult Myogenesis. Curr Pharm Biotechnol. 18(4):309-317.
[3] Di Conza et al. (2017). The mTOR and PP2A Pathways Regulate PHD2 Phosphorylation to Fine-Tune HIF1α Levels and Colorectal Cancer Cell Survival under Hypoxia. Cell Rep. 18(7):1699-1712.
[4] Piccoli et al (2016). A chemical approach to myocardial protection and regeneration. Eur Heart J Suppl. 18(Suppl E):E1-E7.

Key words

Magic-F1, recombinant proteins, cardiac hypertrophy, oxygen sensors, heart remodelling, transgenic mice.

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