

## **Skeletal muscle repair/regeneration after eccentric contraction-induced damage: effects of S1P**

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Skeletal muscle regeneration is severely compromised in case of extended damage. The current challenge is to find factors capable of limiting muscle degeneration and/or activating the inherent regenerative program. Recent studies from our groups and others have shown that the bioactive lipid, sphingosine 1-phosphate (S1P), promotes myoblast differentiation and exerts a trophic action on denervated skeletal muscle fibres. In the present study, we examined the effects of S1P on eccentric contraction (EC)-injured EDL muscle fibers and resident satellite cells. EC caused alterations in plasma membrane resistance, resting membrane potential and Na<sup>+</sup> and Ca<sup>2+</sup> current kinetics together with morphological and biochemical signs of muscle damage and cell death. Treatment with exogenous S1P attenuated the EC-induced damage, protected skeletal muscle cells from apoptosis and affected extracellular matrix remodelling, through the up-regulation of matrix metalloproteinase expression. Interestingly, S1P greatly potentiated satellite cell activation and enhanced their attitude to fuse into multinucleated myotubes. Notably, the activity of sphingosine kinase 1 (SphK1) and the levels of endogenous S1P were significantly higher in the injured fibres and associated satellite cells, stressing the relevance of SphK1/S1P axis in skeletal muscle protection and repair. Together, these findings are in favour for a role of S1P in skeletal muscle healing and regeneration and offer new clues for the identification of novel therapeutic approaches to counteract skeletal muscle damage and disease.