

POSTER PRESENTATION

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TGF β 1 Signalling in human mesenchymal stem cells is regulated by the primary cilium

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Objective

Mesenchymal Stem Cells (MSCs) are mobilized in response to injury to initiate healing and remodelling. TGF β 1 is known to induce MSC migration and homing in various tissues including bone. However, the molecular mechanisms involved are poorly understood. TGF β 1 signalling has recently been linked to the primary cilium in fibroblasts. This cellular microdomain, enriched in transmembrane receptors, could be a specialized centre for TGF β signalling. Therefore, the aim of this study is to investigate the role of the primary cilium in TGF β 1-induced MSC migration.

Methods

TGF β 1 induced MSC migration was investigated using a Boyden chamber approach. The localization of TGF β 1 signalling components within MSCs was investigated through immunocytochemistry. Deletion of the primary cilia was performed with siRNA targeting Ift88.

Results

Firstly, the constitutively active TGF β RII is expressed in human MSCs and localizes preferentially to primary cilia in up to 80% of ciliated cells. TGF β RI, recruited upon ligand binding to TGF β RII is also localized to the primary cilia (14% of ciliated cells), and this specific localization increases after TGF β 1 stimulation (33% of ciliated cells). This result suggests a recruitment of the receptor into the ciliary microdomain. Moreover, the downstream signalling phosphorylated Smad2 and Smad4 localized to primary cilia. Furthermore, TGF β 1 induces human and mouse MSCs chemotaxis and interestingly, after deletion of the primary cilia, the migration capacity is decreased.

Conclusions

These results reveal that TGF β 1 signalling cascade occurs within the microdomain of the primary cilium and more importantly the primary cilium is involved in TGF β 1-induced MSC migration.

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