Characterization of the roles of HIF-P4H-2, HIF1α and HIF2α in ECM signalling

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The interplay between hypoxia-inducible factor (HIF) signaling and extracellular matrix (ECM) is critical in various physiological and pathological contexts. Here, we investigate the impact of HIF prolyl 4-hydroxylase 2 (HIF-P4H-2) inhibition and HIF activation on ECM regulation and fibrosis using mouse embryonic fibroblasts (MEFs). We utilized MEFs from wild-type (WT) and *Hif-p4h-2* hypomorphic mice along with pharmacological inhibition of HIF-P4H using Roxadustat to explore the long-term effects of HIF-P4H-2 inhibition and hypoxia on ECM.

We observed distinct gene expression patterns in response to *Hif-p4h-2* downregulation compared to other HIF stimuli, emphasizing the unique role of HIF-P4H-2 in ECM regulation. Our study involved exposure of WT MEFs to varying oxygen levels (1% and 5% O_2) and Roxadustat treatment, followed by comprehensive analysis of gene expression profiles using RNA sequencing. Through comparative analyses of gene expression profiles across experimental conditions, we identified significant alterations in ECM-related gene expression patterns. Furthermore, specific knockdown experiments targeting *Hif1α* and *Hif2α* will provide insights into the individual contributions of these genes to MEF function. Overall, this study contributes to our understanding of the crosstalk between HIF signaling and ECM regulation.