MITOCHONDRIAL DYSFUNCTION AND OXIDATIVE STRESS IN MYOSITIS: A CENTRAL PATHWAY FROM MOUSE TO MAN

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Inhibition of miR-125b. Gene ontology revealed apoptosis regulation as the main activated pathway. Apoptotic genes included BAK1, BMF, and BBC3, which are part of the BCL2 apoptosis pathway and predicted targets of miR-125b. Consistently, miR-125b overexpression decreased apoptosis (by at least 50%, n=10, p<0.01) at these time points. Cleaved caspase 3 was upregulated in anti-miR-125b transfected cells (median 2.3-fold, Q1: 1.6, 4; n=10, p<0.01) confirmed by Western Blot. Annexin V live assay showed prevailing of apoptosis after miR-125b downregulation.

Conclusions: MiR-125b is downregulated in SSc skin and primary SSc dermal fibroblasts. MiR-125b downregulation increases apoptosis in dermal fibroblasts that might be a compensatory strategy against excessive fibrosis that could be used for therapeutic purposes.

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Conclusion: Inhibition of miR-125b may have therapeutic benefits in SSc and SSc-related cardiomyopathies.

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