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"Pathophysiological Role of Mesenchymal Stem Cells"

By

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ABSTRACT

Mesenchymal stem cells (MSCs) are multipotent adult stem cells with tremendous clinical application. In the presence of inflammation, these cells can be licensed as immune suppressor cells. MSCs can home to areas of inflammation and release soluble factors to affect the local and systemic microenvironments, yielding reduced inflammation and increased tissue repair. MSCs' homing capacity and ability to cross allogeneic barriers is also under investigation for drug delivery. However, injected MSCs are not identified long-term *in vivo*, leading to questions regarding their fate after licensing, including effects of the microenvironment. NFkB has emerged as a regulator of multipotency, although its activation and signaling in this process are poorly understood. This thesis tested the hypothesis that NFkB maintains multipotency of MSCs, through a cell autonomous method, and by an inflammatory milieu. The results identified an NFkB pathway in inflammatory-mediated multipotency of MSCs. This thesis further showed how the information could be interrogated in clinical pathologies, such as solid and hematological malignancies, and preeclampsia. Overall, the studies identify new putative mechanisms for effective application of MSCs in medicine.