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A NOVEL S100A8/A9 INDUCED FINGERPRINT OF MESENCHYMAL STEM CELLS IS ASSOCIATED WITH ENHANCED WOUND HEALING

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We here investigated a unique capacity of mesenchymal stem cells (MSCs) to re-establish tissue homeostasis using their premonitory potential to sense danger associated molecular pattern (DAMP) and to mount an adaptive response in the interest of tissue repair. Injection of MSCs pretreated with heterodimeric DAMP protein S100A8/A9 into murine full-thickness wounds, led to a significant acceleration of healing even exceeding that of wounds with non-treated MSCs. This correlates with a fundamental reprogramming of the transcriptome in S100A8/A9 treated MSCs as deduced from in-depth validation via global RNAseq, RT-PCR, and immunostaining. We uncovered a network of genes/proteins involved in proteolysis, enhancing macrophage phagocytosis and controlling inflammation, all contributing to profound clean-up of the wound site as well as genes encoding specific extracellular matrix proteins of scar-reduced embryonic tissue repair. This novel MSC transcriptome not only underscores the concept that MSCs are endowed with the unique property of perfectly controlling multiple cells but also holds substantial promise that MSC-based therapies could be extrapolated using refine inductors for fast wound closure.

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