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Cell injury-induced release of FGF2: An overlooked factor in MSC implantation

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Beneficial effects of intracerebral implantation of mesenchymal stromal cells (MSC) and their derivatives are believed to be mediated mostly by factors produced by these cells. However, mesenchymal cell engraftment does not occur, and the majority of cells disappear within a week of implantation. Here, we provide *in vitro* evidence that dying implanted cells can affect surrounding tissues by releasing their intracellular components. We found that FGF2 and FGF1, but not VEGF and MCP1, levels were high in extracts of mechanically damaged (freeze/thaw) cells despite being low in conditioned media (CM). Extracts induced concentration-dependent proliferation of rat cortical neural progenitor cells (NPC) and human umbilical vein endothelial cells (HUVEC); these proliferative responses were specifically blocked by FGF2-neutralizing antibody. In the neuropoiesis assay with rat cortical cells, both MSC extracts and killed cells induced expression of nestin, but not astrocyte differentiation. However, suspensions of killed cells strongly potentiated the astrogenic effects of live MSC. In implantation-relevant MSC injury models (peripheral blood cell-mediated cytotoxicity and high cell density plating), MSC death coincided with the release of intracellular FGF2. The data showed that MSC contain a major depot of active FGF2 that is released upon cell injury and is capable of acutely stimulating neuropoiesis and angiogenesis. We therefore, propose that both dying and surviving implanted MSC contribute to the tissue regeneration.

Biography

Irina Aizman has completed her PhD from Tel Aviv University and since then worked as a Research Scientist in California at Fibrogen and SanBio. Currently, she is an Associate Director of Research at SanBio.

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