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Isolation and expansion of selected potent placental cells for indirect mitigation of acute radiation syndrome, induction of bone marrow regeneration and protection of tissues in various inflammatory conditions

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We developed a technique for direct isolation of human placenta stromal cells from tissues of fetal origin (fPSC) by a unique process which allows the direct migration of the desired cells from tissue fragments to culture dishes. These selected placental stromal cell population was found to be highly potent indirect enhancers the regeneration of failing bone marrow and mitigation of Acute Radiation Syndrome (ARS) following total body irradiation. The study was based on our previous record with similar cells of mixed maternal and fetal origin produced by a corporate in bioreactors to fit for clinical applications. The advantage of IM treatment by fPSC was that these stromal cells were found to be more immunocompetent and could reside longer in the injected muscle with no apparent adverse effects that were described following IV delivery of MSC of different origins, where most of the injected cells were trapped in the lungs. The cell treatments induced rapid indirect therapeutic effects. In studies on mitigation of radiation effects these cells enabled to the fast repopulation of the bone marrow lineages with subsequent regeneration of the peripheral blood cells. This saved the animals from the lethal effects of ARS with dramatic significant raise in ~8Gy irradiated mice from less than a third to almost 100%, with fast recovery of the bone marrow and peripheral blood cells. Cytokines analyses showed that the injected xenogeneic cells respond to the stress of the heavily irradiated mice by secretion of a wide range of related pro-regenerative cytokines. The IM based fPSC treatments have also been investigated as cell therapy for treating bone marrow failure due to different other causes. Other indications tested for optional PSC treatment include regeneration of the salivary glands after heavy dose head and neck irradiation, regeneration of tissues affected by autoimmune diseases. These included Inflammatory Bowel Disease (IBD) and autoimmune inflammatory processes in the brain, such as multiple sclerosis. Further detailed studies are performed to better understand the indirect mechanism of action of the PSC by stress induced activation of relevant family of genes in these cells.

Biography

Raphael Gorodetsky is the head of the Laboratory of Biotechnology and Radiobiology at the Sharett Institute of Oncology, Hadassah - Hebrew University Medical Center in Jerusalem, where he is employed as a faculty member since 1989 (affiliated to the Hebrew University Medical School in Jerusalem). He received his M.Sc. and PH.D from the Hebrew University in 1985 and had his Postdoc at UCLA Medical Center (1985-1988). Among other subjects he was involved in cancer research and radiobiology studies, as well as in projects in regenerative medicine. His earlier studies were associated with trace elements physiology in health and disease. Later directions of his research focused mainly on the invention of fibrin based biomaterials used for tissue regeneration and cell therapies and on different aspects of cancer research and radiation biology. Among the new ventures he co-founded was Hapto Biotech in 2000, where he served as the chief scientist (later merged with Ortec to form Forticel International, NY). In this area he designed fibrin based matrices for tissue regeneration, specifically of bone and cartilage. In recent years he was deeply involved in the development of placental stromal cell based treatment for regenerative and tumour control purposes, including the mitigation of radiation effects. These findings were applied clinically by Pluristem Therapeutics. In parallel he is involved in the development of new anticancer immunotherapies. Besides authoring more than 100 peer reviewed scientific publications and chapters, he edited and authored the book "Stem cells and Tissue Repair" in 2010 (by the Royal Society of Chemistry RSC, Cambridge, UK). He served as secretary of Israel Stem Cells Society (2014-2017) and has been a member in a number of related national and international societies.

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