Ali Farrokhi, J Infect Dis Ther 2016, 4:7(Suppl)
http://dx.doi.org/10.4172/2332-0877.C1.018

Application of a Indoleamine 2, 3-dioxygenase (IDO) expressing allogenic dermal fibroblast populated within an acellular skin substitute as a biological wound coverage

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Acute and chronic wounds contribute to increased morbidity and mortality in affected people and impose significant financial burdens on healthcare systems. Despite of advantages of skin grafts, problems such as complications at the donor site, contracture, loss of elasticity, sensory impairment and undesirable cosmetic results including hypo- or hyper-pigmentation resulted in emerge of tissue- engineered alternatives. Among these, acellular dermal matrix (ADM) as an extracellular matrix-based biomaterial has significant mechanical strength with retained biological activity. Further, repopulating dermal fibroblasts into ADM before transplantation may help the graft to restore its function by synthesizing essential extracellular matrix components, growth factors and cytokines, which are important for wound healing. To prepare ready-to-use skin substitute harboring live fibroblasts, it is not feasible to use autologous dermal fibroblasts and using allogeneic fibroblasts can cause immunologic rejection. Although systemic immunosuppressive drugs are widely used for prevention of allorejection, their side effects are of main concern. Here, we hypothesized that application of indoleamine 2, 3-dioxygenase (IDO) expressing allogenic dermal fibroblast populated within an ADM is sufficient to create an immune-privileged area, within the wound, to protect from rejection while providing a rich source of nutrients and growth factors by fibroblasts, in addition to ADM which is serving as wound coverage. To test this hypothesis, adms were prepared using a new detergent–free method, recellularized with IDO-expressing or control fibroblasts, and were transplanted on splinted full thickness murine skin wounds. Investigating the wound healing process in these mice revealed that ADM significantly enhanced the wound healing process within three weeks. Application of IDO-expressing fibroblasts reduced infiltration of CD4+IL-17+TH-17 and CD4+IFN-G+TH-1 immune cells to the grafts. Further, local expression of IDO resulted in decreased allo- response and enhanced immune-tolerance toward allogenic fibroblasts.

The finding of this study shows a correlation between local expression of IDO by fibroblasts and improved wound healing in an experimental model of allogeneic skin substitute grafting. Further studies are on the way to investigate whether application of this pre-made non- rejectable biological skin substitute is a viable option for treatment of chronic wounds.

Biography

In September 2012, I started my PhD in Experimental Medicine Program under supervision of Dr. Aziz Ghahary. I attended the University of Ahwaz, Iran for my BSc. in Genetic and the University of Tehran, Iran for my MSc. in Cellular and Molecular Biology. My current research interest is the studying application of Acellular Dermal Matrix in skin wound healing. Because of my previous experience in the research area of stem cell, also I am interested in stem cell biology.

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