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Prospects of Low Immune Response Transplants Based on Acellular Organ Scaffolds

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Abstract : Transplantation is an effective treatment option for patients suffering from different end-stage diseases. However, it is plagued by a constant shortage of donor organs and the subsequent need of a lifelong immunosuppressive therapy for the patient. Currently some researchers look towards using of pig organs to replace human organs for transplantation since the matrix derived from porcine organs is a convenient substitute for the human matrix. As an initial step to create a new ex vivo tissue engineered model, optimized protocols have been created to obtain organ-specific acellular matrices and evaluated their potential as tissue engineered scaffolds for culture of normal cells and tumor cell lines. These protocols include decellularization by perfusion in a bioreactor system and immersion-agitation on an orbital shaker with use of various detergents (SDS, Triton X-100) and freezing. Complete decellularization – in terms of residual DNA amount – is an important predictor of probability of immune rejection of materials of natural origin. However, the signs of cellular material may still remain within the matrix even after harsh decellularization protocols. In this regard, the matrices obtained from tissues of low-immunogenic pigs with α3Galactosyl-tranferase gene knock out (GalT-KO) may be a promising alternative to native animal sources. The research included a study of induced effect of frozen and fresh fragments of GalT-KO skin on healing of full-thickness plane wounds in 80 rats. Commercially available wound dressings (Ksenoderm, Hyamatrix and Alloderm) as well as allogenic skin were used as a positive control and untreated wounds were analyzed as a negative control. The results were evaluated on the 4th day after grafting, which corresponds to the time of start of normal wound epithelization. It has been shown that a non-specific immune response in models treated with GalT-Ko pig skin was milder than in all the control groups. Research has been performed to measure technical skin characteristics: stiffness and elasticity properties, corneometry, tevametry, and cutometry. These metrics enabled the evaluation of hydratation level, corneous layer husking level, as well as skin elasticity and micro- and macro-landscape. These preliminary data may contribute to development of personalized transplantable organs from GalT-Ko pigs with significantly limited potential of immune rejection. By applying growth factors to a decellularized skin sample it is possible to achieve various regenerative effects based on the particular situation. In this particular research BMP2 and Heparin-binding EGF-like growth factor have been used. Ideally, a bioengineered organ must be biocompatible, non-immunogenic and support cell growth. Porcine organs are attractive for xenotransplantation if severe immunologic concerns can be bypassed. The results indicate that genetically modified pig tissues with knock-outed α3Galactosyl-tranferase gene may be used for production of low-immunogenic matrix suitable for transplantation.

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