

Application of a New Vascular Graft in Replacing Diseased Blood Vessels: The Amniotic Membrane and its Stem Cells

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As we age, the risk of developing vascular disease increases which requires replacement of the damaged vessel for which several different treatment approaches exist. Even though autologous graft is still the mainstay of therapy, alternative methods such as allografts or prosthetic grafts are used for the patients who do not have suitable vessel that can be used for grafting. There are several problems with using these alternative methods such as high immunogenicity of allogenic grafts [1] and the low capacity of prosthetic grafts to remodel and fit in the human tissue as well as risks of infection, stenosis and thrombosis [2]. These shortcomings have led to a continuous research in the field aimed at seeking alternatives.

Among the new therapeutic methods that have recently been evaluated, the Amniotic Membrane has reported to show unique capacities that can make it a perfect candidate for vascular grafting. This biologic membrane has several specifics that we aim to summarize in this report.

The human placenta has been used for centuries in regenerative medicine and wound healing procedures and recently it is proven that the Amniotic Membrane might be the key contributor of the medical benefits the placenta has [3]. The Amniotic Membrane (AM) is part of the human placenta located closest to the fetus and has special characteristics that make this membrane suitable for use in vascular tissue engineering. The AM consists of a single layer of Amniotic Epithelial Stem Cells (AESC) on a thick basement membrane, and Amniotic Mesenchymal Stem Cells (AMSCs) in an avascular stroma [4] Collagen types III, IV, and V and noncollagenous glycoproteins, including nidogen, laminin, and fibronectin shape the thick basement membrane of the AM. Presence of these factors in the basement membrane of the AM, turns this membrane into a scaffold that can allow seeding and growth of many types of cells, such as epithelial progenitor and endothelial cells that are critical for stopping intrinsic thrombogenicity and creating a successful vascular graft [5]. The importance is in the AM native ability to allow seeding of endothelial cells which can halt thrombogenicity. This is a phenomenon that we cannot see in prosthetic graft implantation [2]. Compared to synthetic materials that need adhesive coating to allow attachment of endothelial cells to the graft lumen, the AM has no need to be coated with an adhesive and can natively support cell adhesion.

Attached to the thick basement membrane, the Amniotic Membrane has two different types of pluripotent stem cells that have shown to contribute to unique properties of this membrane. The AESC have pro-apoptotic and anti-angiogenic capacities that can be applicable in controlling cancer, making the AM a non-tumorigenic tissue and therefore safe for grafting as a vascular substitute [6-8]. The Amniotic Membrane has immunoregulatory, pro-apoptotic and anti-angiogenic [6,7] as well as anti-fibrosis, anti-microbial, and low immunogenicity properties [9] and provides an anatomically, physiologically and immunologically privileged space for the growing fetus. The anti microbial capacities of the AM is due to the AESCs ability to produce beta-defensins, the major group of antimicrobial peptides expressed at mucosal surfaces by epithelial cells [10]. Furthermore secretory leukocyte proteinase inhibitor and elafin are produced by the AM to protect it from infection and inflammation [11].

The anti-inflammatory properties of the AM can help in overcoming one of the main pathologic features of graft rejection which is the Inflammatory changes following activation and infiltration of monocytes [12]. In a study done by Peirovi et al, the AM was used as graft in the external jugular vein of sheep and no sign of inflammation was reported [13]. The anti-inflammatory properties of the AM can be attributable to the markedly suppression of highly potent pro-inflammatory cytokines (interleukin-1 alpha and interleukin-1 beta) by the AM stromal matrix as well as production of natural inhibitors of matrix metalloproteases (MMPs) by the AM [14]. MMPs are expressed by infiltrating polymorphonuclear cells and macrophages and have inflammatory effects even in cancers [15].

In summary, the AM is an immune-privileged tissue with very low risk of rejection and is a potent source of natural antimicrobial and anti-inflammatory agents that can help in limiting infection and other major side effects after grafting. Considering the AM capacity in native vascular graft endothelialization to limit thrombogenicity, and the fact that it is a biologic tissue readily available at a lower cost than prosthetic grafts, we can conclude that the AM can be a superior alternative to synthetic grafts for treating vascular diseases.

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