Mammalian Immune Response to Xenogeneic Biologic Scaffolds Composed of Extracellular Matrix

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Biologic scaffolds composed of xenogeneic extracellular matrix (ECM) have been used to promote constructive remodeling of tissues and organs in numerous body systems including the musculoskeletal system[1, 2], integumentary system, the gastrointestinal tract[3], cardiovascular system[4-6], and the lower urinary tract, among others. The host tissue response to these scaffold materials differs depending in large part upon the method used to process the material. However, there has been relatively little evaluation of the cellular and humoral immune response to these materials. Our laboratory has conducted a series of studies to investigate the host response to implanted in the ECM scaffolds, including determination of: 1) the galactosyl 1,3 galactose ("gal epitope") in decellularized porcine derived ECM, 2) the effect of xenogeneic ECM scaffold upon T helper cell function, 3) the effect of xenogeneic ECM upon Th-1 versus Th-2 response to xenogeneic ECM scaffolds, 4) the effect of xenogeneic ECM scaffolds upon systemic protective immunity to potential pathogens, and most recently, 5) the effect of xenogeneic ECM scaffolds upon the macrophage profile that characterizes a local tissue response. Our test systems have included a mixture of well characterized transgenic mouse models, dog models, and the evaluation of the serologic (humoral) response of humans implanted with commercially available ECM products.

Results have shown that processed porcine derived ECM scaffolds retain the GAL-epitope in very low concentrations and that these scaffolds do not bind complement fixing antibodies as part of the host response[7]. T helper cells are induced to enter an apoptotic pathway upon exposure to ECM scaffolds and the T helper profile is exclusively a Th-2 response regardless of the number of host exposures to the xenogeneic material[8]. Furthermore, in spite of the induction of a Th-2 immune response, systemic immunity against classic antigens such as inactivated influenza virus are not adversely affected. Finally, the local tissue macrophage response to nonchemically cross-linked ECM scaffolds is characterized by an M2 response (accommodation) versus the classic M1 (inflammatory) response to foreign antigens.

Biologic scaffolds composed of mammalian ECM are clinically well tolerated by mammalian recipients. Scaffold degradation as a result of the absence of chemical cross-linking seems to be an important component of this tolerance response. More comprehensive immunologic evaluation of the host response to biologic scaffolds is needed.

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