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SYMPOSIUM

Biocompatibility and Immune Acceptance of Adult Porcine Islets Transplanted Intraperitoneally in Diabetic NOD Mice in Calcium Alginate Poly-L-lysine Microcapsules versus Barium Alginate Microcapsules without Poly-L-lysine

Susan A. Safley, Ph.D.,[1] Hong Cui, M.D., Ph.D.,[1] Sean Cauffiel,[1]
Carol Tucker-Burden, B.S.,[2] and Collin J. Weber M.D.[1]

Abstract

Background:

If alginate microcapsules are to be used clinically for therapeutic cell transplants, capsule formulations must be designed to enhance optimal biocompatibility and immune acceptance.

Methods:

Microcapsules were generated using highly purified, endotoxin-free, ultra-low viscosity, high mannuronic acid alginate. The capsules differed with respect to gelling cation (50 m*M* barium or 100 m*M* calcium), alginate concentration (2.0% or 3.3%), alginate density (homogeneous or inhomogeneous), and the presence or absence poly-L-lysine (PLL) coating. Four types of empty capsules were implanted intraperitoneally (i.p.) in normal NOD mice, and their biocompatibility was evaluated after various time periods *in vivo*. Encapsulated adult porcine islets (APIs) were transplanted i.p. in diabetic NOD mice, and immune acceptance was evaluated by graft survival times, host cell adherence to capsule surfaces, and flow cytometric analysis of peritoneal host cells.

Results:

All empty alginate capsules were biocompatible *in vivo*, but barium-gelled alginate capsules without PLL were clearly the most biocompatible, since 99% of these empty capsules had no host cell adherence up to 9 months *in vivo*. In diabetic NOD mice, APIs functioned significantly longer in barium-alginate capsules without PLL than in calcium-alginate capsules with PLL and had strikingly less host cell adherence, although large numbers of host cells (predominantly macrophages and eosinophils) infiltrated the peritoneal cavities of recipients with APIs in both types of capsules. Addition of PLL coatings to barium-alginate capsules dramatically decreased graft survival.

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Author Affiliations: [1]Department of Surgery, Emory University, Atlanta, Georgia; and [2]Department of Pathology, Winship Cancer Institute, Emory University, Atlanta, Georgia

Abbreviations: (ANOVA) analysis of variance, (anti-LFA-1 mAb) anti-lymphocyte function-associated antigen-1 monoclonal antibody, (API) adult porcine islet, ($BaCl_2$) barium chloride (BG) blood glucose, ($CaCl_2$) calcium chloride, (CTLA4-Ig) cytotoxic T-lymphocyte antigen 4-immuno-globulin, (IEQ) islet equivalents, (i.p.) intraperitoneally, (NOD) non-obese diabetic, (PLL) poly-L-lysine,

Keywords: alginate, barium, porcine islets, microencapsulation, NOD mice, xenografts

Corresponding Author: Susan A. Safley, Ph.D., Department of Surgery, 101 Woodruff Circle, Room 5105, Emory University, Atlanta, GA 30322; email address ssafley@emory.edu

Abstract cont.

Conclusions:

Inhomogeneous barium-gelled alginate capsules without PLL are the optimal candidates for clinical trials, based on their enhanced biocompatibility and immune acceptance *in vivo*.

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