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Killer B cells and their exosomes in immune tolerance

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The active induction of immune tolerance by specialized molecules and cells is critical in protection against autoimmune diseases and is a therapeutic target in solid organ transplantation. Killer B lymphocytes are a small subset of immune cells that express the death-inducing ligand, FasL, and that mediate cell death of antigen-specific CD4+ T cells. FasL+ B cells were shown to be necessary for a donor-specific transfusion (DST) response which promoted the survival of male to female skin grafts in mice. DST has also been reported to be effective at inducing immune tolerance in clinical trials of MHC-mismatched heart and kidney transplants. Our laboratory has focused on the biology of killer B cells with emphasis on the expression of FasL and their interactions with T cells. FasL+ B cells are present in spleens of unimmunized mice and have markers similar to other immune suppressive subsets of B cells. FasL+ B cells express high levels of IL-5 receptor and grow in response to IL-5 stimulation in cell culture. Cultured killer B cells induce apoptosis of activated CD4+ T cells by an antigen-specific and FasL-dependent mechanism. Killer B cells produce FasL+ 'lethal' exosomes, subcellular vesicles that also express MHC Class II and are capable of inducing antigen-specific T cell death. Together, these properties of killer B cells make them attractive new targets for establishing immune tolerance in the clinical setting of autoimmune disease treatment and solid organ transplantation.

Biography

Steven K. Lundy, Ph.D. is a Research Assistant Professor in Internal Medicine-Rheumatology at the University of Michigan Medical School in Ann Arbor. Steve grew up in central Wisconsin and northern Michigan and earned his Bachelor's degree in Biochemistry from Oakland University in 1987. He worked as a research technician for ten years at the Mayo Clinic and Wayne State University and then earned his doctorate in Immunology and Microbiology from Wayne State in 2001. His work for the past decade has focused on killer B cells in chronic inflammatory conditions ranging from schistosome worm infection to asthma and autoimmune diseases.

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