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## Anti-pPKC $\theta$ (T538) delivery *via* cell penetrating peptide mimics as a novel treatment of aplastic anemia

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The objective of this study is to deliver anti-pPKC $\theta$  (T538) into T cells (hPBMCs) by using cell penetrating peptide mimics (CPPMs) to neutralize PKC $\theta$  activity both *in vitro* and *in vivo*, with the eventual goal of treating aplastic anemia (AA). AA is an immune-mediated bone marrow failure disease caused by T helper type 1 (Th1) autoimmune responses, which destroy blood cell progenitors. It was previously reported that protein kinase C theta (PKC $\theta$ ), expressed specifically in T cells, plays an important role in T cell signaling by mediating Th1 differentiation. Mice treated with Rottlerin, a pharmacological inhibitor of PKC $\theta$ , were rescued from the disease when PKC $\theta$  phosphorylation was inhibited. Furthermore, humanized antibodies are increasingly gaining attention as therapies. The delivery of antibodies could be achieved via cell penetrating peptides (CPPs), which are able to internalize cargo into cells. Here, we designed, synthesized and characterized CPPMs to increase delivery efficiency of an antibody against phosphorylated PKC $\theta$  (T538), which subsequently interfered with the function of the kinase. We designed an *in vitro* delivery method for the CPPM/anti-pPKC $\theta$  complex then assessed T cell activation and AA disease marker expression. Also, we generated an *in vivo* humanized mouse model of AA and tested the complex for delivery and effect on survival of these mice. Altogether the results reveal that PKC $\theta$  may be an optimal target for bone marrow failure treatment and intracellular antibody delivery may represent a novel approach for AA treatment.

### Biography

Lisa M Minter received her PhD and post-doctoral training at the University of Massachusetts/Amherst, and is now an Assistant Professor in the Dept. of Veterinary & Animal Sciences at UMass/Amherst. She has publications in several high-impact journals including Nature Immunology, Nature Reviews Immunology, Journal of Experimental Medicine, EMBO, and Blood. She has served as an ad hoc reviewer for Blood, Cellular and Molecular Immunology, Future Medicine and the American Journal of Pathology. Her research interests focus on Notch signaling in peripheral T cells and its contribution to the pathology of autoimmune bone marrow failure.

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