

Induction of Endothelial Tightening to Limit Off-Target Deposition of Nanomedicines. SG Tilden, (Ph.D., GS) TJ Anchordoquy, Department of Pharmaceutical Sciences, University of Colorado – Anschutz Medical Campus.

The overall goal of the project is to decrease off-target accumulation and toxicity of intravenously administered chemotherapeutic nanomedicines. Over the past several decades the field of “tumor-targeted” nanomedicines has failed to make significant strides toward increasing tumor drug accumulation. We propose a novel approach to “targeting” nanomedicines by focusing on decreasing off-target accumulation rather than directly increasing tumor delivery. Recent studies in the field of virology have revealed a novel anti-viral phenotype in epithelial cells that limits the spread of viruses. Changes induced by an anti-viral type III interferon (IFN- λ) lead to tightening of endothelial/epithelial junctions that limits the ability of viral particles to diffuse into tissues. We were able to induce this tightening event, in a murine cancer model, by formulating and injecting a viral-like nanoparticle. Our data shows that injecting this viral-like nanoparticle 24 hours before an injection of FITC-labeled dextran significantly limited off-target deposition of the dextran. Additionally, tumor accumulation of the dextran was dramatically increased. In conclusion, we have demonstrated that a viral-like nanoparticle injection can initiate an endothelial tightening event that limits off-target deposition and increases tumor accumulation of a subsequently administered nanoparticle.