Toxic or Helpful? Exploring the Body's Response to Virus-Like Nanoparticles. SG Tilden (Ph.D., GS), TJ Anchordoquy, Department of Pharmaceutical Sciences, University of Colorado – Anschutz Medical Campus.

For decades now, nanomedicines have been touted as the future of cancer therapy. However, the field of tumor-targeted nanomedicine has failed to significantly advance toward becoming the primary choice for cancer intervention. The largest obstacle that has yet to be overcome is off-target accumulation of the nanoparticles. Even with engineered "stealth" formulations most of the dose will be taken up by the liver, spleen, and other major organs. Today, chemotherapeutic nanomedicines are still highly dose-limited due to off-target toxicities. We propose a novel approach to "targeting" nanomedicines by focusing on decreasing off-target accumulation rather than directly increasing tumor delivery. Acknowledging a poorly understood "refractory" response to intravenously injected gene therapy vectors, observed in ours and other studies, we hypothesize that virus-like particles can be utilized to limit the off-target accumulation of nanoparticles. Indeed, our results show a significant reduction of dextran deposition in the liver (~13% reduction) and spleen (~40% reduction) with a concurrent increase in tumor dextran accumulation (~27% increase) when the dextran was administered 24 hours after a virus-like particle injection. These data demonstrate that an anti-viral response initiated by an injection of virus-like particles can reduce major organ accumulation of a subsequently administered particle while simultaneously increasing tumor accumulation.