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Cytokine storm potential of siRNA in human PBMCs and DCs

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The CD28 antibody TGN1412, intended as a treatment for B cell chronic lymphocytic leukemia, caused systemic organ failure in initial human volunteers. This severe side effect was subsequently attributed to induction of a pro-inflammatory cytokine storm. Failure to detect this effect in animal studies underscores the need to supplement animal data with an evaluation of cytokine storm potential in human cells. We used human peripheral mononuclear cells (PBMCs) and monocyte-derived dendritic cells (DCs) to evaluate the cytokine storm potential of several siRNA compounds by measuring a panel of cytokines using Luminex. While some of the compounds elicited cytokines in PBMCs, the compounds failed to elicit cytokines in DCs. This finding demonstrates the value of an *in vitro* assay to evaluate potential immunostimulatory compounds and suggests that a robust evaluation may require examination of multiple cell types.

Biography

Travis Harrison received his graduate training at Virginia Commonwealth University in Immunology in 2001 with an emphasis in immunotoxicology. He has served as PI on multiple commercial and government contracts, and has managed several subcontracts for large government contracts. One of his areas of specialty has been development and GLP validation of immunoassays including nearly 100 assays to support GLP studies.

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