

# PI3K INHIBITORS TO TREAT CYTOKINE RELEASE SYNDROME

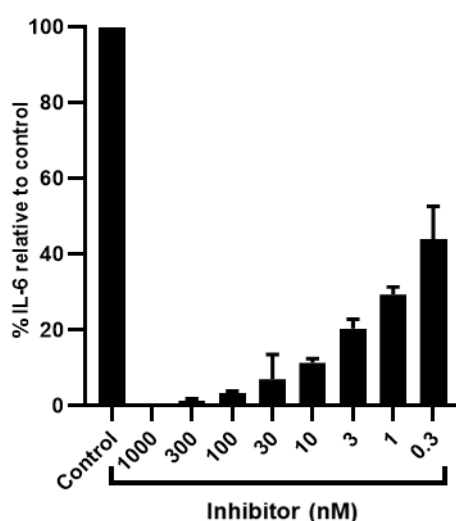
[Amatya, Parmeshwar](#), [Carter, Alun](#), [Cooper, Matthew](#), [DiPersio, John](#)

[Richards, Jennifer](#)

T-019429

## Technology Description

A team of researchers, led by John DiPersio and Matthew Cooper at Washington University in St. Louis, have identified a small molecule kinase inhibitor capable of mitigating cytokine release syndrome following CAR-T cell therapy. PI3K inhibitors can suppress production of IL-6 due to T cell activation without affecting the therapeutic cytotoxicity.



### *PI3K inhibitor suppresses IL-6 secretion by dendritic cells following activation of CAR-T cells*

Cytokine release syndrome, a systemic inflammatory response, represents a significant adverse reaction to CAR-T and other adoptive cell therapies. Researchers have previously identified IL-6 as the most functionally important cytokine elevated during CRS. Since the PI3K signaling pathway regulates secretion of IL-6, PI3K inhibitors (like duvelisib) show promise to mitigate CRS without inhibiting T cell function

## Stage of Research

The inventors showed that a PI3K inhibitor was able to suppress IL-6 secretion *in vitro* by dendritic cells or monocytes, co-cultured with CART19 cells and their targets. The CAR-T cells retained their cytotoxicity at those same concentrations of inhibitor. The same inhibition of IL-6 was seen in an immunocompetent mouse model, in which CRS was induced by *in vivo* administration of a T cell activating antibody.

## Applications

- Treatment for Cytokine Release Syndrome (CRS) following:

- CAR-T cell therapy, and other adoptive cell transfer
- Antibody therapy
- Bispecific T-cell engager (BiTE) therapy

### **Key Advantages**

- Novel application of existing FDA-approved small molecule therapeutics
- Prevents IL-6 secretion, rather than inhibiting IL-6 activity
- Does not inhibit the anti-tumor activity of T cell therapy

**Patents:** Pending

**Related Web Links:** DiPersio [Profile](#) & Cooper [Profile](#)