Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

PI3-k p110 Delta Inhibitor for Treatment of Autoimmunity

Product

PI3K inhibitor

Indication

Treatment of autoimmune disorders

Value Propositions

- Promotes B-cell anergy
- Minimal disruption of adaptive immune function

Market

- $57.6B - Global kinase inhibitors market (6.6% CAGR 2022-2026)

Intellectual Property

- US patent application pending *
- Available for licensing

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Background on CU4617H

Increased risk of development of autoimmunity is conferred by variations in gene sequences leading to altered expression and/or function of their products. Among identified variations is the expression of negative regulators of the phospho-inositide 3-kinase (PI3K) pathway, whose activity is critical for maintenance of B cell anergy; levels of negative regulators PTEN and SHIP-1 are reduced in systemic lupus erythematosus (SLE). While deletion of the SHIP-1 regulator miRNA155 has demonstrated reduced autoantibody responses in mouse models of Lupus, acute deletion of SHIP-1 or PTEN in autoreactive B cells leads to autoimmunity. Methods to correct defects in PI3K pathway regulation while maintaining immune functionality are needed to address these issues.

Technical Innovation

Drs. John Cambier and Elizabeth Franks have demonstrated therapeutic utility of P110δ inhibitors for treatment and prevention of autoimmunity, which act by enforcing anergy of autoreactive B cells. In mice autoimmune by virtue of SHIP-1 knockout in B cells, low dose Idelalisib treatment blocked autoreactive B cell proliferation and differentiation. In addition, **Figure 1**, demonstrates the tested dosage's ability to inhibit the autoantibody responses of both $SHIP^{fl/fl}$ and $PTEN^{fl/wt}$ x $SHIP^{fl/wt}$ B cells, while not affecting autoimmunity caused by knockout of the protein tyrosine phosphatase SHP-1.Importantly, Idelalisib prevents autoimmunity when used at doses $1/30^{th}$ of those currently FDA approved for other clinical applications. Furthermore, this dose does not affect antibody responses to exogenous immunogens. The inventors believe P110δ inhibitors will be particularly useful in treatment of autoimmunity diseases, including SLE and type 1 diabetes, that are caused in part by defects in PI3K pathway regulation.

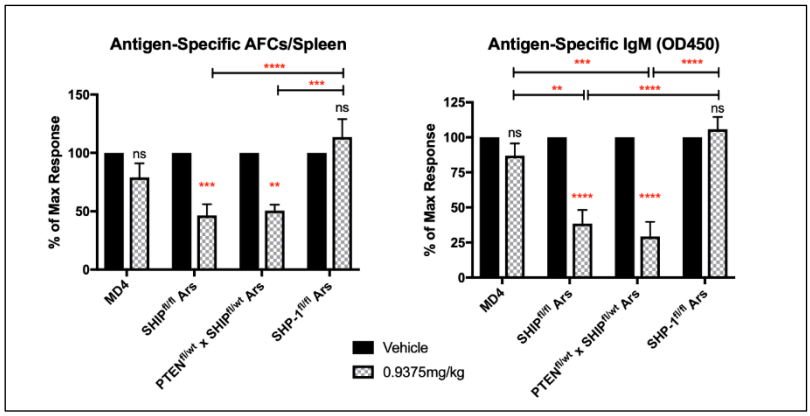

Figure: Depicts post-treatment results in mouse models with 0.9375 mg/kg Idelalisib. B cells with a defect in regulation of the PI3K pathway demonstrated significant reduction in autoantibody responses.

Resources & Documents:

A precision B Cell-Targeted Therapeutic Approach to Autoimmunity Caused by Phosphatidylinositol 3-Kinase Pathway Dysregulation. J Immunol, June 15, 2019, 202 (12) 3381-3393.

***US national stage application pending (6/959,960)** - P110-Delta inhibitors treat and prevent autoimmunity while sparing the ability to mount an immune response to exogenous immunogens*