

Small Molecules that Mimic IFN-Gamma-Mediated Endothelial Cell Activation

Tech ID: 22097 / UC Case 2011-531-0

SUMMARY

Researchers at UCLA, using a novel cell screening method, have identified a family of small molecules that act on endothelial cells to activate an immune response. The invention represents a new repertoire of therapeutics to modulate immune function.

BACKGROUND

The vascular wall is now accepted to play a critical role in activating immune responses. Endothelial cells that comprise the vasculature are active modulators of inflammatory responses. A number of molecular signals have been identified to mediate crosstalk between immune and vascular cells. Specifically, interferon gamma (IFN- γ) is a potent cytokine that mediates anti-microbial and anti-cancer biological functions of immunity and induces over 4000 genes in human endothelial cells. To date, few therapies exploit the interaction between the endothelium and immunity to treat disease. Therefore, great potential exists in identifying small molecules that modulate immunity through endothelial cell interaction. The identification of such compounds would have a particularly promising role in treating cardiovascular disease, chronic inflammatory conditions, and cancer.

INNOVATION

Researchers at UCLA have identified a family of small molecules that mimic IFN- γ in regards to mediating activation of the endothelium and subsequent endothelium-triggered activation of innate immune responses. The small molecules induce far fewer genes than IFN- γ but still result in effective endothelial cell-mediated activation of the innate immune response. Thus, these compounds represent a strategy to selectively induce a minimum set of activating genes to accomplish endothelial cell-triggered immune activation. Clinically, these compounds have utility in treating a wide range of immune-responsive diseases.

APPLICATIONS

- ▶ Treatment of bacterial infections.
- ▶ Treatment of viral infections (e.g. HIV).
- ▶ Treatment of immune-responsive cancers

ADVANTAGES

- ▶ Novel, small molecule modulators of endothelial-triggered immune responses.
- ▶ The compounds induce effective immune responses with minimal gene activation, theoretically reducing damaging effects of excessive IFN- γ stimulation.

STATE OF DEVELOPMENT

Using high-throughput screens, researchers have identified small molecules that demonstrate IFN- γ -mediated endothelial cell activation. The positive small molecule "hits" have been chemically modified and purified to optimize potency.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,197,557	02/05/2019	2011-531

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OTHER INFORMATION

KEYWORDS

Inflammation, small molecule, endothelial, immune activation, cancer, infectious disease

CATEGORIZED AS

- ▶ **Medical**
 - ▶ New Chemical Entities, Drug Leads
 - ▶ Therapeutics

RELATED CASES

2011-531-0

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