Use of AHR Agonists to Prevent or Treat NEC in Premature Infants

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Technology description

UNMET NEED

Necrotizing enterocolitis (NEC) is the leading cause of death from gastrointestinal disease in premature infants. The main risk factors for the development of NEC are prematurity, bacterial colonization and administration of formula feeds, which in the setting of an abnormal microbiome lead to enhanced signaling via toll like receptor 4 (TLR4), ultimately causing rapid progression from mucosal injury, bacterial translocation, systemic sepsis and then death within 24 hours. Inventors discovered that aryl hydrocarbon receptor (AHR) plays a protective role in a mouse model for NEC, and disclosed herein is a panel of AHR agonists identified through a screen against a library of FDA-approved compounds as novel therapeutics for the treatment of NEC.

TECHNICAL DETAILS

Research has demonstrated the involvement of AHR promoting intestinal homeostasis through intraepithelial lymphocytes and lymphoid cells by maintaining a critical line of defense against infiltrating pathogenic microbes. Using their induced-NEC model, inventors elucidated the role of AHR signaling in NEC pathogenesis. Mice with NEC show reduced expression of AHR within the intestine and exhibit severe NEC as manifest by intestinal disruption on histology and severe cytokine induction. Using an AHR-luciferase reporter system inventors screened a library of FDA-approved compounds and identified AHR agonists for use as agents to prevent, treat or reduce the risk of NEC.

Advantages

AHR agonists for the treatment and prevention of NEC in premature infants

Compounds identified through screen of FDA-approved library and anti-NEC activity confirmed in an induced NEC mouse model

Institution

Johns Hopkins University

Inventors

Peng Lu
Assistant Professor
David Hackam
Professor
Chhinder Sodhi
Assistant Professor
Jun Liu
Professor
Pharmacology & Molecular Science SOM

联系我们

叶先生

电 话：021-65679356
手 机：13414935137
邮 箱：yeyingsheng@zf-ym.com