Technology offer IP-038

Repurposed drugs for the treatment of congenital anemias

Repurposed tyrosine kinase inhibitors (TKIs), originally approved for other hematological conditions, act by inhibiting the NLRP1 inflammasome through the ZAKα/P38 MAPK pathway. This inhibition regulates hematopoiesis by restoring the function of hematopoietic stem and progenitor cells. The compounds have shown efficacy in vitro and in vivo in zebrafish models of Diamond-Blackfan anemia, offering an innovative therapeutic strategy to treat congenital anemias.

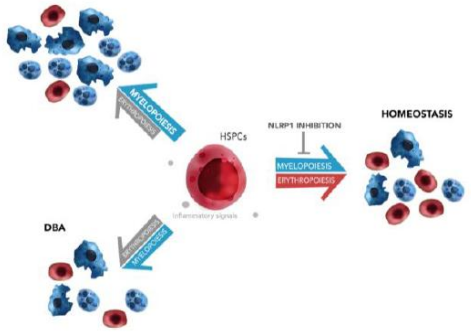

Figure. Activation of NLRP1 by the ZAKα/P38 signaling pathway

State of development

TRL-5 Late preclinic research

Objective of the collaboration

License and/or co-development

Industrial Property

PCT application

Priority date: 25/05/2023

Contact

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Market needs

Anemia, especially in aging populations, poses a growing public health challenge due to its impact on morbidity, quality of life, and healthcare costs. The NLRP1 inflammasome plays a key role in regulating hematopoiesis through the ZAKα/P38 MAPK pathway. Its overactivation impairs erythropoiesis, contributing to the development of congenital anemias such as Diamond-Blackfan anemia (DBA). Current treatments, like bone marrow transplants or blood transfusions, face limitations including donor availability and serious side effects. There is a clear need for safer, more accessible therapies to treat congenital anemias effectively.

Technical solution from IMIB

Researchers have identified the NLRP1 inflammasome as a key regulator of hematopoiesis via the ZAKα/P38 MAPK pathway, enabling its pharmacological inhibition using repurposed tyrosine kinase inhibitors (TKIs). In vitro studies with hematopoietic stem and progenitor cells from DBA patients showed restored erythropoiesis. In vivo validation in zebrafish models confirmed the efficacy of five TKIs in reversing anemia phenotypes, supporting their potential as a therapeutic option for congenital anemias.

Benefits

- High target specificity, achieved through inhibition of the NLRP1 inflammasome via the ZAKα/P38 MAPK pathway, directly restoring impaired hematopoiesis in congenital anemias.
- Drug repurposing of FDA/EMA-approved tyrosine kinase inhibitors (TKIs) enables faster clinical translation and lower regulatory costs.
- Demonstrated efficacy in vitro and in vivo using patient-derived HSPCs and zebrafish models, with reduced risk of adverse effects due to targeted mechanism.
- Cost-effective and more accessible therapeutic alternative to hematopoietic stem cell transplantation, with potential extension to other inflammation-related disorders.