INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Use of Retinoids in Congenital Erythropoietic Porphyria

TECHNOLOGY NUMBER: 2022-276

Technology ID
2022-276

Category
Therapeutics and Vaccines
Life Sciences

Inventor
Bishr Omary
Jordan Shavit

Further information
Megan Griffin
mrost@umich.edu

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OVERVIEW

A novel in vivo model that phenocopies features of congenital erythropoietic porphyria (CEP)

- A zebrafish phenotype which accumulates uroporphyrin and suffers impaired bone development
- Serves as a research model that suggests retinoids as a potential treatment for CEP

MODALITY

Retinoid compounds for oral or topical administration

INDICATION

Congenital erythropoietic porphyria (CEP)

PUBLICATIONS

"Acitretin mitigates uroporphyrin-induced bone defects in congenital erythropoietic porphyria models"

INTELLECTUAL PROPERTY

Patent pending

BACKGROUND

Congenital erythropoietic porphyria (CEP) is the rarest type of porphyria, with a prevalence of less than 1000 in the United States. The condition commonly presents in infancy, though it may

appear at any time of life. Its symptoms include severe skin photosensitivity which may lead to blistering, scarring, and increased hair growth on the face and back of hands. The cumulative manifestations of photosensitivity and skin infections may come to eventually cause the loss of fingers and facial features. Additional signs and symptoms of the disease may include reddish discoloration of the teeth, reddish-colored urine, and anemia. CEP is an autosomal recessive disease that causes a defect in the synthesis of heme in the red blood cells of the bone marrow, leading to a buildup of porphyrin and its precursors. Currently there is no specific treatment for CEP besides bone marrow transplantation, so a need exists for methods by which to more extensively study and treat this disease.

INNOVATION

Researchers have developed a zebrafish model that phenocopies features of congenital erythropoietic porphyria (CEP). Uroporphyrin accumulates in the bones of these zebrafish and lead to impaired bone development, much the same as occurs in humans afflicted with this condition. Additional investigations in vitro have shown that uro-I exposure to an osteoblast-like cell line yields decreased mineralization, aggregated bone matrix proteins, activated endometrial stress, and disrupted autophagy. Using high-throughput drug screening, the researchers identified acitretin, a second-generation retinoid, and showed that it reduces uro-I accumulation and its deleterious effects on bones. Results also suggest that another retinoid, tretinoin, showed similar beneficial effects for clearing porphyrin in zebrafish. These findings provide a new CEP experimental model and identify the use of retinoids as potential, repurposed therapeutic agent for the condition.