A new use and route of administration for a marketed anti-inflammatory compound class for orphan skin indications. Topically formulated drug demonstrated profound benefits in mouse models of the most severe form of congenital ichthyosis, Harlequin ichthyosis, supporting further development for treatment of lipid dysfunction skin diseases.

- Potential to develop first topical formulation for treatment of the orphan disease Harlequin ichthyosis
- New route of administration for a generic drug with long-term clinical use and a strong safety profile
- Topical formulation minimises risk of systemic side effects
- Potential use of new formulation in other lipid dysfunction-related skin indications
- Potential for combination with retinoids

**THE CHALLENGE**

The ichthyoses are a family of over 20 congenital diseases characterized by the development of a thick hyperkeratotic epidermis. Harlequin ichthyosis (HI) is the most severe form of ichthyosis, which leads to neonatal death in ~50% of cases.

For patients who do survive beyond birth, retinoid therapy is the main treatment, as it may promote keratinocyte differentiation and shedding. However, there are a number of undesirable side-effects that limit long-term use, and its effectiveness is debated.

While a modest improvement is observed in survivors, frequent bathing, removal of scales and frequent application of emollient oils is required to manage the disorder.

HI results from mutations in Abca12, a protein that transports lipids required to establish the protective skin barrier needed after birth. Mouse models lacking the gene show that loss of ABCA12 causes defective extracellular lipid trafficking and profound intracellular lipid accumulation within keratinocytes.

**THE TECHNOLOGY**

Monash Researchers have characterised and delineated the molecular pathways impacted by Abca12 mutation in HI and identified upregulation of several pro-inflammatory factors. The team has shown that transgenic expression of the broad spectrum immune suppressor (IL37b) in utero improves defects ordinarily apparent in keratinocyte differentiation. This provides strong evidence linking inflammation to the pathology of HI, and led to the identification of a suitable drug which targets relevant inflammatory pathways.

Topically applying the candidate drug in both ex vivo and conditional in vivo experimental mouse models of HI demonstrated considerable improvement in keratinocyte differentiation lipid and barrier function (Fig.1), lessenng disease severity and improving the skin condition. This supports use of the anti-inflammatory drug as a topical treatment in ichthyosis conditions.

**Intellectual property:** Patent application PCT/AU2016/050185.

**THE OPPORTUNITY**

We seek a partner to develop stable topical formulations of the drug and re-profile for marketing via the 505(b)(2) pathway for orphan skin indications and for related lipid dysfunction skin diseases.

Monash researchers have extensive experience with the biology and experimental models for ichthyosis and other skin diseases associated with lipid dysfunction to test formulations and combinations.

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