MONASH University

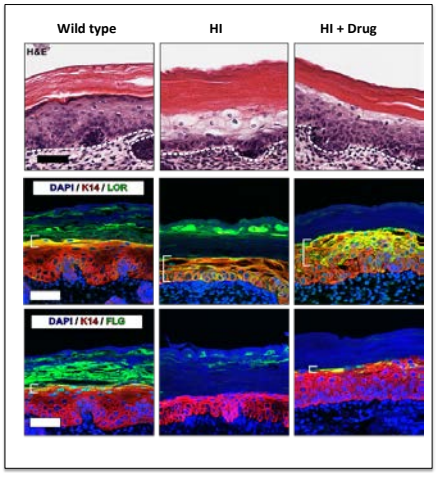
Topical treatment for Harlequin Ichthyosis and other skin disorders

THERAPEUTIC: Anti-inflammatory

Product Type	Small molecule drug candidate / repurposed, reformulated
Indication/ROA	Harlequin ichthyosis (HI, orphan disease) and other ichthyoses, other lipid dysfunction disorders such as psoriasis; topical.
Target/MoA	Lead candidate modulates the ceramide-induced inflammatory responses in ichthyoses, improving keratinocyte differentiation and lipid barrier formation.
Development Stage	Lead candidate selected, efficacy demonstrated
Brief Description & Differentiation	Drug candidate improves the skin barrier dysfunction, inflammation and impaired keratinocyte differentiation that are a feature of lipid dysfunction disorders such as HI, a rare disease without effective treatment. HI is one member of a much larger disease family and a new treatment may have utility in other conditions such as psoriasis. • First-in-class topical anti-inflammatory drug - new ROA for a generic drug having long-term clinical use and a strong safety profile • Potential use of new formulation in other lipid dysfunction related skin indications • Potential for combination with retinoids • Other Anti-inflammatory drugs do not show the same effect
Research Team	Prof Ian Smyth and Dr Denny Cottle
Intellectual Property	PCT/AU2016/050185, a method of treating a skin condition associated with lipid dysfunction, including ichthyosis by administering the anti-inflammatory drug. National Phase in US, JA, EU, CH, IN and AU. KO mouse models, culture-based epidermis assay, conditional mouse models, customised mRNA analysis.
Key Publications	1. Smyth I, Hacking DF, Hilton AA, *et al*. (2008) *PLoS Genet 4(9)*: e1000192. doi:10.1371/journal.pgen.1000192 2. Cottle, DL, *et al* & Smyth IM (2015) *Human molecular Genetics 24(2)* doi:10.1093/hmg/ddu459
Future	Develop commercial formulation, dosing and safety → 505(b)(2) regulatory pathway, orphan designation

➢ Key Data

Efficacy in animal models – drug treatment reduced hydration, normalised differentiation of ichthyosis genes and induced skin thinning with no wounding or side effects.



- Improves keratinocyte differentiation
- Partially normalises Loricrin expression
- Partially restores Filaggrin expression

	drug	asprin	acitretin
Reduced dehydration	√	x	x
Improved differentiation	√√	x	√
Skin thinning	√	x	√
No wounding/side effects	√	x	x