Technology Licensing Opportunity

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A NOVEL PEPTIDE (INDIP) FOR ACNE TREATMENT

Technology:

A topical acne treatment where the active ingredient is an interference peptide designed to reduce production of fatty acids and cholesterol by sebocytes through disinhibition of the INSIG1-SREBP1 signaling pathway.

- **Novel acne therapeutic**
- **Efficacy in acne model**
- **Tolerability *in vivo***
- **Topical dosage formulation**
- **Promising release profile**
- **Strong research team**

Available for Licensing or Collaboration

Principal Inventors:

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Development Stage:

Efficacy done in collaboration with Dr. Christos Zouboulis of the Deasua Medical Center in Germany. Additional experiments on toxicity and PK pursued.

Patent Status:

US Provisional (methods for acne)
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Method of Action: Androgen regulates the synthesis of sebum lipids, underlying acne formation, through the sterol regulatory element – binding protein (SREBP) pathway. **Indip** mimics the ubiquitination targeting sequence of Insig1, a peptide which prevents immature SREBP1 from being released from the ER for proteolytic activation in Golgi and production of active transcription factors responsible for sebocyte lipogenesis. (Fig.1)

Efficacy*:* **Indip** inhibited SREBP1 dependent lipid biogenesis in the immortalized sebocyte (the only standard in vitro model of acne) at 48 hrs post-incubation when compared with control and mutated peptide. (Fig. 2)

The inventors have very clearly demonstrated a beneficial effect for this peptide in acne. Using an *in vitro* model of acne, the inventors demonstrated that this peptide, when administered to cell cultures of SZ95 sebocytes, resulted in a significant reduction in the production of sebaceous (neutral) lipids, both in the presence or in the absence of lipid inducing agents linoleic acid or testosterone. Interestingly, the results were more significant at higher doses, and in a time dependent fashion (ie. inhibition at 48hr > 24hr). The concomitant reduction of polar lipids indicates a parallel reduction of membrane synthesis, i.e. a reduction of the synthetic activity of the cells. This means that the Indip peptide is able to reduce sebaceous differentiation in all conditions tested.

Toxicity: Previous *in vivo* work in stroke/ALS demonstrates tolerability (pub. Nature Medicine 2009; BBRC 2011). **Indip** i.p.injection in wild type mice Indip (3 times/week for 6 months), showed no sign of toxicity suggesting a high level of safety for this peptide and no toxicity was observed with immortalized seboctyes incubated with Indip, as judged based on cell amount.

Formulation: The ultrasonic–solvent evaporation-emulsification technique was used to formulate Indip Solid Liquid Nanoparticles (SLNs). Ten different formulations were designed and tested and one selected based on particle size, polydispersity and zeta potential data. The mean diameter of the chosen SLN in the dispersion was 159 ± 40nm with the polydispersity of 0.3. Zeta potential of the particles in formulation was negative and varied between -3 and -8mV. We also formulated of **Indip** loaded Poly lactic co-glycolide (PLGA) nanoparticles using W/O/W method. The mean particle size of nanoparticles and the polydispersity index were 122±2nm and 0.141±0.08, respectively. The Zeta potential of the particles in formulation was negative and varied between -8 and -10mV. The morphology of PLGA nanoparticles was examined by a scanning electronic microscope operating at 15 kV and showed particles were nano-sized and spherical shaped. (Fig.3)

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Fig. 1

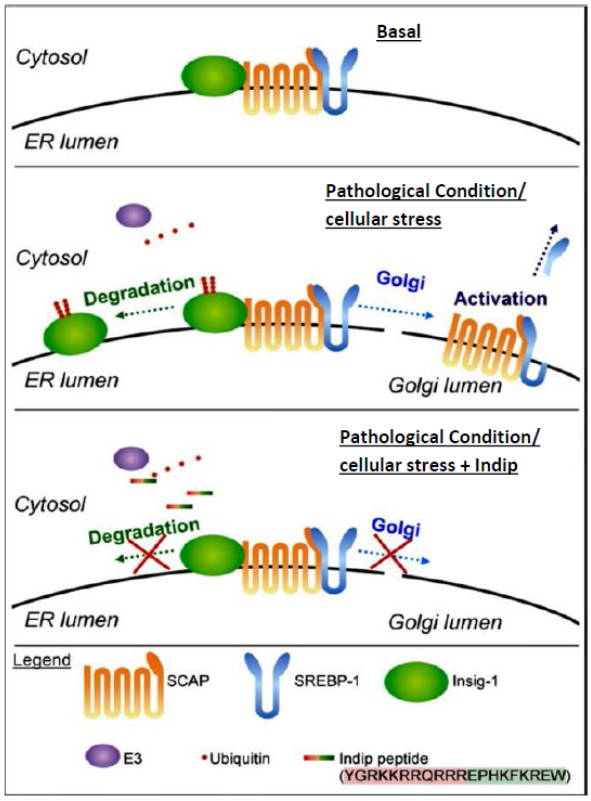

Figure 1. Activation of SREBP1 lipid transcription factor contributes to the pathogenesis of acne and Indip exerts its therapeutic effects by inhibiting SREBP1 activation in skin sebocytes.

Fig. 3

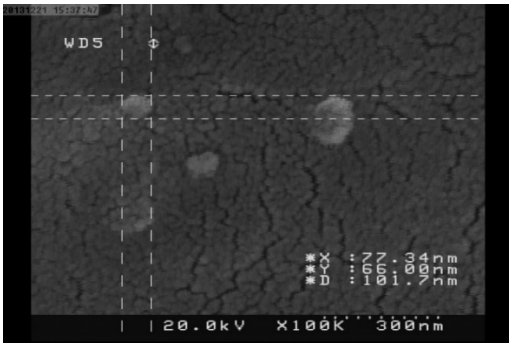

Figure 3- A representative SEM micrograph of the optimized formulation of Indip-loaded PLGA nanoparticles. Nanoparticles are spherical with a smooth morphology.

Fig. 2

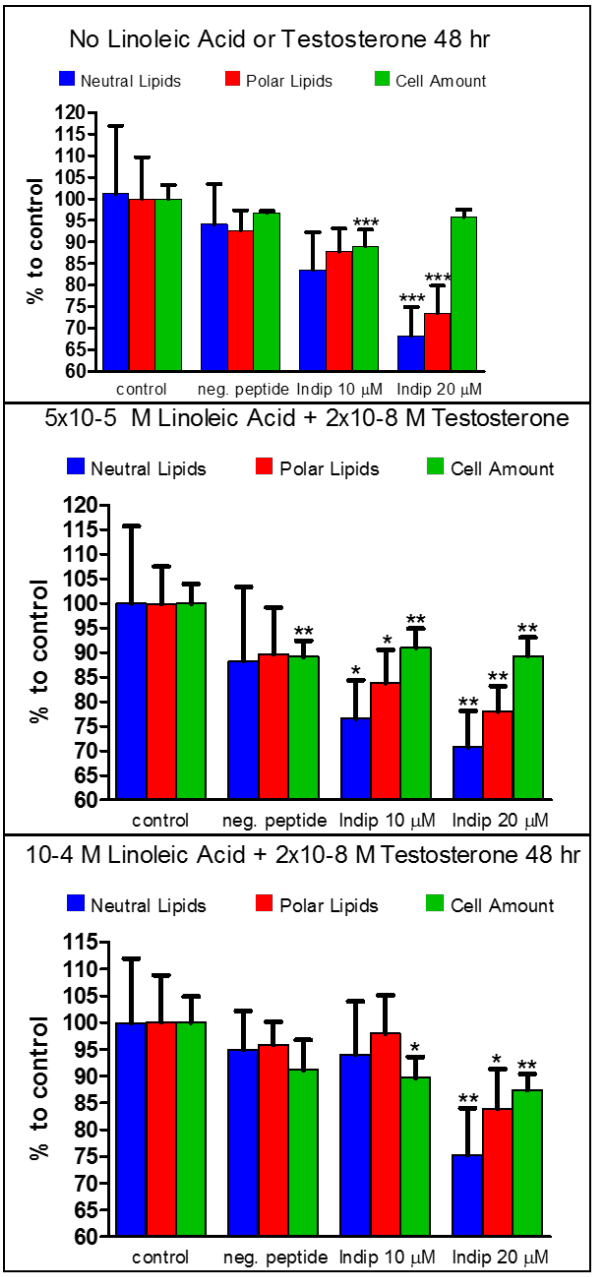

Figure 2- Indip dose dependently reduced biogenesis of both neutral and polar lipids in immortalized sebocytes in the presence and absence of linoleic acid and testosterone following 48 hr incubation.

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