Keratinocytes were irradiated cells. Primary Human Dermal Fibroblasts (HDFs) were seeded in 24-well plates and cultured near the end of each G-protein is a conserved cysteine residue modified with a lipidated Figure 1. IPC Analogs: Structural Mimics of G-Protein C-Terminus. G-proteins participate in eliciting inflammatory responses such as the release of pro-inflammatory mediators and the migration and activation of inflammatory cells. The structure of each G-protein is a conserved cysteine residue modified with a CAAX motif (either G-α, G-β or G-γ subunit). IPC analogs such as SIG1191 are structural mimics of the lipidated C-terminus of the α subunit of all heterotrimeric G-proteins, as well as all small molecular weight GTPases such as Rho, Ras and Rac. Primary Human Dermal Fibroblasts (HDFs) were seeded in 24-well plates and cultured for 24 hours at 37°C and 5% CO₂ before treatments. Cells were cultured in the presence of each compound for 24 hours. Later, compounds were removed and cells were irradiated with 12.5J/cm² UVA. Media supernatants were collected after 24 hours and analyzed by ELISA for IL-6 and TNF-α.

The tumor necrosis factor (TNF) receptor ligand, TNFα, is a key mediator of inflammatory processes. The activation of TNFα receptors leads to the production of inflammatory cytokines such as TNF-α, IL-1β, and IL-6. The IRAK-M pathway is a positive regulator of the NF-κB pathway and independent of the IKK pathway. SIG1191 forms were tested for skin and eye irritation in reconstructed human epidermis 3D models. EpiDerm™ and EpiOcular (MatTek) tissues were acclimated for 1-24 hours and then treated topically with SIG1191 formulations (0.01-1%) and Triton-X100 (0.3% w/v), used as positive control. Tissue viability levels were measured by the MTT reduction assay 48 hours after treatments. The levels of tissue viability after each treatment were compared to vehicle group to estimate the potential for skin or ocular irritation. *p<0.01 by ANOVA test compared with untreated tissues as control (ns = not significant).

Summary/Conclusions:
- SIG1191 demonstrates anti-inflammatory properties in vitro reducing UVA, UVB and TPA induced pro-inflammatory cytokine production in human keratinocytes and fibroblasts.
- SIG1191 potentially targets skin hydration and aging by modulating Aquaporin-3 (AQP3) expression in both monolayer keratinocytes and 3D skin equivalent cultures. The NFκB pathway and independent of PPARγ activation.
- In conclusion, SIG1191 demonstrates to be a novel cosmetic ingredient that can potentially provide skin hydration by increasing Aquaporin-3 and possesses anti-inflammatory properties to help protect the skin.