Discovery of a Small Molecule Inhibitor of the Wnt Pathway (SM04755) as a Potential Topical Treatment for Psoriasis

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Methods

To identify small molecule Wnt signaling inhibitors, a small molecule chemical library was screened in a cellular Wnt pathway-based assay using a β-catenin/TCF reporter. The library was subsequently tested in human keratinocytes following treatment with SM04755 (1 µM) or DMSO for 24 hrs as measured by qRT-PCR. Mean ± SEM, n= 4, p< 0.05, ***p< 0.001, t-test.

Results

SM04755 reduced thickness, inflammation, and proliferation, and improved skin appearance in a mouse IMQ-induced psoriasis model

- SM04755 demonstrated specific and potent inhibition of Wnt signaling
- In an in vivo mouse model of IMQ-induced psoriasis, topical application of SM04755 inhibited inflammation, keratinocyte proliferation, and collagen expression by qPCR.
- SM04755 inhibited cytokine-induced proliferation of primary human keratinocytes in vitro
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References


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