

Inhibition of sAC to Treat Hyperproliferative Dermatological Conditions

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Technology description

Inventions:

Investigators at Cornell who discovered a novel mammalian gene and protein 10 years ago, have discovered that the protein - soluble adenylyl cyclase (sAC) plays a role in hyperproliferative skin disorders. Blocking this protein prevents keratinocyte proliferation. We have in vitro data and in vivo data (IL22 induced psoriasis mouse model) to support that claim. We also have immunostained human skin biopsies from patients with various hyperproliferative skin disorders, showing that the protein is over-expressed in these disorders.

Topical therapies for these disorders include corticosteroids, keratolytics, anthralin, coal tar, Vitamin D analogs, and retinoids. Each class of compounds has substantial drawbacks:

For steroids (corticosteroids), typically a high potency steroid is required and is applied daily. While the exact mechanism of action of topical steroids in psoriasis is largely unknown, steroids are thought to be anti-inflammatory, immunosuppressive, and antiproliferative.

Keratolytics, such as salicylic acid, work by removing scale from the psoriatic lesion. This class of medication does not affect the underlying cause of the psoriasis so the disease will remain, but the psoriasis will be less scaly. By reducing scale, other medications are able to penetrate the plaques of psoriasis more easily allowing for greater efficacy.

Anthralin and Coal tar both appear to have anti-proliferative and anti-inflammatory properties although the exact mechanism of either is not known. They both suffer from being very messy and smelly. Anthralin turns skin and fabric purple while tar stains everything black. For these reasons, patient compliance is very low.

Vitamin D analogs were first employed when physicians noticed that patients with psoriasis and altered serum calcium levels had a resolution of their psoriasis when calcium levels were normalized. Later data found that the bioactive form of Vitamin D, 1,25-dihydroxycholecalciferol, has been shown to inhibit keratinocyte proliferation and promote differentiation. This topical medication is commonly used in conjunction with topical steroids. Theoretical risks of overuse include hypercalcemia.

Retinoids mediate cell differentiation and proliferation. Retinoids, specifically tazarotene, is applied topically on a daily basis and has been demonstrated to have efficacy in psoriasis. Retinoids are contraindicated in pregnancy and can be irritating to the skin.

Institution

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