



Compounds stimulating or inhibiting melanin formation

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Background: Melanin is the natural substance that gives color (pigment) to hair, skin, and the iris. Melanin helps in resisting sunburn, decreases the risk of skin cancer (protection against photocarcinogenesis), decreases the solar degeneration of skin (protection against photoaging), acts as a physical barrier or a filter against ultraviolet radiation and gives skin a cosmetic elegance. Increasing skin pigmentation would be desirable both to increase melanin protection from UV radiation without exposing the skin to UV light, to correct hypopigmentation disorders including postinflammatory hypopigmentation and vitiligo, and for cosmetic purposes to achieve a safe tan or to darken hair color. Currently, molecules capable of increasing skin pigmentation without ultraviolet light stimulation are not available for human use. Conversely, currently available compounds to decrease skin pigmentation are poorly active and typically target a single step in pigmentation, typically by inhibition of the enzyme tyrosinase.

Description: Drs. Seth Orlow and Young-Tae Chang using a unique combinatorial library and the techniques of "chemical genetics" have identified a series of non-toxic small molecules with "druggable" characteristics that are potent promoters of pigmentation in cultured human and mouse melanocytes and melanoma cells at very low (<5 μM) concentrations. They have furthermore identified a novel subcellular target protein for the first group of these compounds. These compounds act synergistically with other small molecules known to stimulate pigmentation in a variety of systems, such as melanotropin and agents that alter cellular cyclic AMP levels such as phosphodiesterase inhibitors. Moreover, treatment of cells, including normal human melanocytes, that typically show little or no response to agents that elevate cyclic AMP with a combination of the proprietary molecules and the cyclic AMP altering molecule generates a robust pigmentary response in a variety of systems. Besides the identification of pigment enhancing compounds, initial screens have identified potent proprietary inhibitors of pigmentation. Studies are also underway to identify the mechanism of action of these compounds and their cellular target proteins.

Applications: The pigment-enhancing compounds could be used to increase pigmentation in the skin, hair and eyes for medical and/or cosmetic purposes without the need for UV exposure ("safe tan"). Compounds with the ability to inhibit pigmentation could be used to treat disorders such as melasma, chloasma, and post-inflammatory hyperpigmentation. The market for pigment-enhancing compounds is unknown, since no effective compounds exist, but is believed to exceed \$1 Billion. The worldwide market for pigment-inhibiting compounds is estimated at >\$3 Billion.

Patent: Patents have been submitted covering the methods of screening, the individual compounds, and the subcellular target proteins and methods of identifying them.

For further information please contact

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