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Phosphorylase kinase inhibition in skin disease

Phosphorylase kinase (Ph-K) is a unique enzyme in which the spatial arrangements of the specificity determinants can be manipulated to allow the enzyme to recognize substrates of different specificities. Thus, PhK is capable of transferring high energy phosphate bonds from ATP to serine/threonine and tyrosine moieties required for the activation of the transcription regulator, nuclear factor-kappa B (NF-kB). In this way, PhK plays a critical role in activation of multiple NF-kB-dependent signaling pathways induced by acute and chronic injury. Phosphorylase kinase is released within 5 minutes following injury, and is responsible for activating inflammatory pathways in psoriatic hyperproliferation. The enzyme is also involved in injury-activated TGF-β (transforming growth factor-β)-mediated scarring following burns and surgical wounds. In photo-damaged skin, PhK plays a key role in promoting photo-carcinogenesis through activation of NF-kB proliferative pathways, while inducing inhibition of apoptosis in photo-damaged cells, thus promoting survival of precancerous cells and allowing for subsequent tumor transformation.

Curcumin, the active ingredient in the spice, tumeric, is a selective and non-competitive PhK-inhibitor. By inhibition of PhK, topical curcumin targets multiple-PhK-dependent signaling pathways, with salutary effects on multiple skin diseases. Curcumin gel plays a key role in the resolution of psoriasis, in the rapid healing of burns and prevention of post-injury scarring in acne, burns and surgical wounds. Curcumin gel is also beneficial in the repair of photo-damaged skin, with improvement in pigmentary changes, solar elastoses, thinning of the skin and telangiectasia, as well as actinic keratoses and dysplastic nevi. In this presentation, we detail signaling pathways targeted by curcumin in the resolution or repair of the above diseases, and present clinical evidence of the efficacy of topical curcumin in multiple skin conditions induced by acute and chronic injury.

Biography

Dr Madalene Heng is currently Clinical Professor of Medicine/Dermatology UCLA School of Medicine. She was chief of Dermatology at the UCLA/San Fernando Valley Internal Medicine Program for 25 years. Dr Heng is a pioneer in the study of phosphorylase kinase activity in skin diseases such as psoriasis, with more than 130 scientific publications including 77 articles in peer-reviewed journals. Dr. Heng is a reviewer of multiple journals, including the Journal of the American Academy of Dermatology, International Journal of Dermatology, British Journal of Dermatology and Cell Biology and Toxicology, among others. Currently, she is a practicing dermatologist at the Centers of Family Health, Oxnard, California.