Synopsis of Original Research Paper

Control of ultraviolet light-mediated Ret tyrosine kinase activation

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The cellular proto-oncogene *c-RET* encodes a receptor-tyrosine kinase. The catalytic activities of Ret kinases as the products of oncogene *RET* with multiple endocrine neoplasia type 2A (Ret-MEN2A) or 2B (Ret-MEN2B) mutations and the hybrid gene from c-RET and RFP (Rfp-Ret) were higher than those of c-Ret. Here we demonstrate that ultraviolet light (UV) irradiation induced activation of c-Ret and superactivation of genetically activated Ret-MEN2A, Ret-MEN2B and Rfp-Ret. The UV-induced activation and superactivation of Ret was closely associated with the redox reaction-mediated dimerization or polymerization of the Ret proteins. UV also induced intracellular dimerization and activation of the extracellular domain-deleted mutant Ret (Ret-PTC-1). Overexpression of Cu/Zn superoxide dismutase in cells due to gene transfection prevented the promotion of UV-mediated dimerization and the superactivation of Ret-MEN2A kinase. These results suggest that the UV-induced intracellular oxidative condition mediates dimerization and the activation of Ret kinases.