

Endogenous Optogenetic Approach to Activate TGF-beta for Anti-Tumor Responses

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Abstract

The roles of TGF- β pathway in a wide range of pathophysiological contexts have led to elaboration of its central role in human health and wellness. TGF- β has been shown to promote tissue healing but also has a key role in promoting tissue fibrosis and scarring. It plays a dual role in cancer, acting as a tumor suppressor in early stages by inducing cell cycle arrest and apoptosis, but switching to a tumor promoter in advanced stages. TGF- β signaling has been shown to drive metastasis, immune evasion, and angiogenesis while fostering an immunosuppressive environment. The complexity of this signaling pathway has been commonly investigated *in vitro* with exogenous recombinant proteins and transgenic approaches that have yielded complex, often contradictory, phenotypes.

Our work has focused on the key role of TGF- β in tissue healing and stem cell differentiation. We first observed the ability of light activated tissue healing involving increased expression of TGF β . Given its abundant latent complex in early wound environments from platelet aggregation, we noted the ability of low-dose light activation to activate latent TGF- β complex via a methionine at position 253 in the latency-associated peptide. Transgenic loss of function studies has unequivocally established the photoactivation mechanism *in vitro* and *in vivo*. The ability to photoactivate endogenous latent TGF- β 1 with spatiotemporal precision has opened unprecedented avenues to explore the role of exogenous and endogenous TGF- β in tissue healing and tumor contexts that will be outlined in this talk.