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Small molecule drugs with TGFbeta signaling activity

The TGF-beta signaling pathway is a key regulator of many biological processes and is involved in the pathogenesis of major diseases. Regulating this pathway could have broad application to treating neurodegenerative diseases, stroke, tumors, wound healing etc. Stanford researchers used a Smad based reporter cell line from a TGF-b1 knockout mouse to search for small chemical molecules that activate Smad signaling. Three lead structures that show signaling activity in cell culture and in a Smad reporter mouse in vivo were identified. The small chemical compounds discovered here have TGF-beta agonist activity and involve novel chemical structures. The compounds are active in vivo in the CNS and activate Smad-dependent genes, independent of the TGF-beta receptor. These compounds could therefore potentially be used to treat tumors that downmodulated TGF receptors, and they could activate TGF signaling in wound healing, stroke, or neurodegeneration.

Applications

- These TGF-beta agonists may be used for the treatment of neurodegenerative diseases including but not limited to AD, Parkinson's, Huntington's, amyotrophic lateral sclerosis, tauopathies, and prion diseases, as well as stroke.

Advantages

- There are currently no effective treatments available for AD and several other related diseases. A drug that reduces and targets both abnormal protein accumulation and neurodegeneration would be an ideal treatment.

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