

MIM-D3, A Small Molecule NGF Mimetic for Dry Eye Treatment

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Dry eye, also known as keratoconjunctivitis sicca (KCS), is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. Symptoms can be caused by defects in the aqueous, lipid and/or mucin layers of tear film. Current therapies for dry eye are palliative with a focus on the replacement of tears to reduce symptoms. While these palliative therapies have benefits over the short term, they have limited utility in long-term control therapy for dry eye.

Recent reports have proposed novel dry eye therapies to induce mucin expression or secretion by the ocular surface epithelia. Conjunctival mucin gene expression and secretion along with a correlated goblet cell density may be decreased in several ocular disorders associated with dry eye. Goblet cells may be stimulated to secrete mucins by direct or indirect innervation of the conjunctiva by sensory, sympathetic and parasympathetic nerves and growth factors.

We have developed small molecule mimetics of neurotrophins. Among those molecules is MIM-D3, a proteolytically stable, cyclic peptidomimetic compound, which mimics a beta-turn region of NGF. We have investigated the use of MIM-D3 as a pharmacological agent to stimulate mucin secretion *in vitro* and *in vivo*. Furthermore, MIM-D3 was investigated as a therapeutic agent to treat dry eye experimentally induced in rats compared to NGF by varying the dosing concentration, dosing frequency and effect of duration following a no dosing period.