**TITLE:** Reduction of Corneal Scarring using RNA-Targeted Therapies

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**RESEARCH PROJECT DESCRIPTION** (brief overview of background, hypothesis, methods, role of medical student, funding and relevant publications)

Corneal scarring is a potential vision threatening complication following trauma, infection, or elective refractive surgeries such as laser-assisted in situ keratomileusis (LASIK). Current clinical therapies to reduce corneal scarring use non-specific anti-proliferative drugs like mitomycin-C that have substantial risk of serious side effects. My lab is developing novel gene-targeted antiscarring therapies that are based on the hypothesis that selective knockdown of the two growth factor systems that stimulate corneal scarring, transforming growth factor beta (TGF-β) and connective tissue growth factor (CTGF), will reduce pathological scarring without causing severe side effects. We are utilizing antisense oligonucleotides, ribozymes and siRNAs that target the mRNAs of the growth factors and their receptors. The agents are delivered to corneal cells using iontophoresis of protected oligonucleotides or by adenoassociated virus vectors. Medical students will participate in cell culture experiments assessing the effectiveness of the RNA based drugs in reducing levels of target mRNAs and proteins using Q-RT-PCR and ELISAs. Effective agents will be tested in rabbit models of corneal scarring. Funding for the project is provided by the National Eye Institute.

M. Sisco, Z.B. Kryger, K.D. O’Shaughnessy, P.S. Kim, G.S. Schultz, X.Z. Ding, N.K. Roy, N.M. Dean, T.A. Mustoe. Antisense inhibition of connective tissue growth factor (CTGF/CCN2) mRNA limits hypertrophic scarring without affecting wound healing in vivo. Wound Rep Reg, 16:661-673, 2008.

Blalock TD, Duncan MR, Varela JC, Goldstein MH, Tuli SS, Grotendorst GR, Schultz GS. Connective tissue growth factor expression and action in human corneal fibroblast cultures and rat corneas after photorefractive keratectomy. Invest Ophthalmol Vis Sci 2003;44:1879-1887.