Erectile dysfunction (ED) affects ~ 50% of men aged 40 to 70 and has a high impact on men’s health and quality of life. Current treatments are ineffective in the difficult to treat prostatectomy (16-82%) and diabetic (56-59%) patients due to injury to the cavernous nerve (CN), which provides innervation to the penis. With denervation the critical smooth muscle (SM) undergoes apoptosis and the penis becomes fibrotic, with increased collagen and a change in subtypes, thus altering the architecture of the corpora cavernosa. Thus in order to develop new therapies that target these difficult to treat patients, an integrated approach is needed in which penile apoptosis is suppressed at the same time as CN regeneration is enhanced.

The sonic hedgehog (SHH) pathway is critical for the response of the penis to denervation. CN injury decreases SHH in the penis, which causes SM apoptosis and ED. CN injury also decreases SHH in the CN (70%), which causes demyelination and axonal degeneration of CN fibers. We are developing two novel and innovative peptide amphiphile (PA) nanofiber hydrogels for delivery of SHH protein to the CN and to the penis to promote regeneration and prevent penile apoptosis. Our preliminary results show accelerated CN regeneration, ~60% improved erectile function (6 weeks) and suppressed penile apoptosis in response to SHH PA treatment of the CN. When a second type of PA for SHH was injected into the penis of CN injured rats, apoptosis was suppressed 25%. These innovative studies are highly promising that optimization of PA methodology, SHH concentration and delivery, will even further enhance regeneration of CN and penile morphology and function. These studies develop novel ED prevention and treatment strategies that impact an unmet clinical need and our model closely resembles the human ED condition and thus has great utility for clinical translation and impact.