The purpose of this project presupposed the anti-inflammatory effects of the HMF-CoA reductase inhibitor, simvastatin, and the potential benefit it could have on ameliorating the bladder dysfunction that is common after spinal cord injury. Studies published prior to this project have established that the deleterious effects on the bladder are mediated through the inflammatory process. Our work began with an investigation into the effectiveness of simvastatin on a classic model of bladder inflammation using cyclophosphamide as the inciting agent. This was done because spinal cord injury models have notoriously high variability and starting with a simple and very reproducible model allowed us to establish simvastatin’s ability to treat bladder inflammation. Our results demonstrated that, indeed, simvastatin did have a beneficial role in diminishing inflammation and improving bladder dysfunction in the cyclophosphamide-induced model. These results were published in the journal *Urology* in January of 2013\(^1\).

Of course, the goal of this grant was to investigate this agent on spinal cord injury and so we proceeded with our study using a contusion model of spinal cord injury in the rat. Briefly, rats were subjected to a spinal cord contusion and then we measured their urinary function with cystometry and harvested tissue for analysis of inflammatory changes. Our groups consisted of 1) a sham group 2) an injury group that received vehicle by gavage, and 3) an injury group that received simvastatin. Results demonstrated high variability and we were not able to conclusively prove that simvastatin had a positive effect on either inflammation or voiding physiology. Our collaboration with the laboratory of Dr. Inderjit Singh led us to the idea of using S-Nitrosoglutathione (GSNO), an endogenous nitrosylating agent that has pleiotropic effects and anti-inflammatory properties. Repeating the experiments described above with GSNO, we were able to measure a significant beneficial response in terms of decreased inflammation and bladder dysfunction. These findings were recently published in the high impact journal, *Neurourology and Urodynamics*, in May of 2014\(^2\). The potential of this agent will be investigated further in a larger animal study and eventually human clinical trials.

While the results of our work have led to a potentially new and useful therapy for spinal cord injured patients, this work that was supported by the SCIRF has had a positive effect of possibly even greater significance in the future. Based on the quality of our data in the above mentioned manuscripts, we were contacted by Dr. Thomas Kessler from Zurich, Switzerland. Dr. Kessler is the chief urologist at the Spinal Cord Injury Center at the Balgrist University Hospital, one of Europe’s premier centers for treatment and research on spinal cord injury. We have developed a strong collaboration and our first manuscript describing a novel technique which we will use for studying bladder dysfunction in spinal cord injury models was submitted to the journal European Urology last month. They have sent one of their scientists to Charleston twice now to work directly with us and, in turn, our staff scientist, Dr. Monty Hughes, spent several weeks in Zurich this past summer completing this recently submitted study.

In summary, this grant award has yielded a promising avenue for treating patients with spinal cord injury derived bladder dysfunction and additionally generated an important relationship between our group in South Carolina and one of the most productive and widely reputed neuro-urology groups in Europe.
