Flubendazole improves recovery following spinal cord injury in rats

James Geddes, PhD[1] • Vimala Bondada[2] • Madison Sands[2] • Christina Pistilli[2] • Kavi Dayaram[2] • Chen-Guang Yu, MD, PhD[2]

5b

[1]SCoBIRC , University of Kentucky • [2]SCoBIRC, University of Kentucky

Neurodegeneration following spinal cord injury (SCI) is due, in part, to inflammation and immune responses. Activation of B lymphocytes and production of autoantibodies contributes to neurodegeneration subsequent to traumatic SCI in humans and in animal models. Flubendazole is a benzimidazole anthelmintic used to attack parasitic worm infections, and approved for human use. It binds to nematode tubulin and impairs microtubule-dependent mechanisms. However, Flubendazole can also interact with mammalian tubulin and impair proliferation of rapidly dividing cells such as B lymphocytes. The aim of this research was to determine whether post-SCI treatment with Flubendazole decreases neurodegeneration and improves functional outcomes when administered post-SCI in a rat model. Flubendazole was administered via intraperitoneal injection, 10 mg/kg/day to Sprague-Dawley rats for 2 weeks, beginning 3 hrs post-SCI (180 kdyn at T10), n=10. This resulted in improved locomotor function (BBB scores) 7 weeks after contusion SCI compared to vehicle-treated controls, n=9. Flubendazole treatment also improved total tissue sparing, white matter sparing, and gray matter sparing at 7 weeks after contusive SCI. Flubendazole reduced the splenic population of CD45RA-positive B cells and suppressed IgG immunoreactivity at the lesion site 4 weeks post -injury. In conclusion, our results suggest that Flubendazole targets the pathogenic B cell pathway and improves functional recovery after SCI.

The authors thank Daisy Ramos for her assistance with behavioral testing. This work was funded by a NIH Clinical and Translational Science Award (CTSA) grant UL1TR000117 (CGY), Kentucky Spinal Cord and Head Injury Research Trust (KSCHIRT) grant #11-9A (to CGY)), and Craig H. Neilsen Foundation award (JG).