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The herpes simplex virus type 2 gene ICP10PK prevents motor neuron degeneration and extends life in the SOD1G93A transgenic rat model of Amyotrophic lateral sclerosis through modulation of glia-neuron crosstalk

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ALS is a devastating neurodegenerative disease affecting half a million people worldwide. Development of effective therapies is complicated by the interaction of multiple cell types and molecular mechanisms. The HSV-2 gene ICP10PK is neuroprotective through activation of Ras signaling pathways and modulation of neuron-glia crosstalk. We used the replication compromised ICP10PK vector (Δ RR) in the rat SOD1G93A model in which motor neurons (MN) death is caused by glia-produced toxic factors. Animals were given intramuscular injections of Δ RR (1×10^7 pfu) in the left and right calf muscles twice a week beginning on day 85 of life (presymptomatic stage) and assessed for motor function and disease symptoms until the loss of righting reflex or 20% weight loss (endpoint). Δ RR treated animals maintained motor control measured by rotarod testing 45 days longer and their lifespan was increased on average 41.5 days longer than the controls, as determined by Kaplan Meier survival curves. Study of lumbar spinal cords collected when the control group reached endpoint indicated that ICP10PK was expressed in $52.7 \pm 4.3\%$ of the MNs from Δ RR-treated animals and this was associated with preservation of $96 \pm 1.2\%$ of the MN, as compared to $11.6 \pm 5.4\%$ in PBS treated animals that were ICP10PK negative. Neuroprotection was associated with neuron-glia crosstalk, as evidenced by: (i) significant reductions numbers activated (ED+) microglia, (ii) reduced astrogliosis (GFAP staining), (iii) no expression of the inflammatory cytokine TNF- α , and (iv) significantly increased numbers of VEGF+ MNs. The data underscore the strong therapeutic promise of ICP10PK.

Biography

Dr. Laing received her Ph.D from the University of Maryland, Baltimore where she is currently a postdoctoral fellow. She has published 12 papers. Dr. Aurelian received her Ph.D from Johns Hopkins University. She is the director of Virology and Immunology Laboratories in the Department of Pharmacology and Experimental Therapeutics at the University of Maryland, Baltimore. She has published more than 250 papers over a career than spans 40+ years.