Brain Disord Ther 2016, 5:3(Suppl)
http://dx.doi.org/10.4172/2168-975X.C1.009

KI induced effects extend beyond kidneys and affect many systems including the brain where it has been associated with encephalopathy

Ali Ayman Mowafy
Mansoura University, Egypt

Ischemic Acute Kidney Injury (AKI) has many consequences that affect the development of chronic kidney disease following ischemia; kidney's tissues are exposed to a reperfusion phase, where damage is caused by inflammatory mediators released following resolution of the ischemia. Accentuation of innate immunity during ischemia reperfusion injury (IRI) seems to be affected by toll like receptors, especially TLR-2 and TLR4. It has been demonstrated that AKI induced effects extend beyond kidneys and affect many systems including the brain where it has been associated with encephalopathy. Animal experiments have shown that AKI leads to inflammation within the hippocampal region which was confirmed by Liu et al., who observed an increased number of activated microglia in the hippocampus of rats with AKI, which may account for a state of uremic encephalopathy. In a previous study at Medical Experimental Research Center (MERC), Salama et al., found that TLR-4 was up regulated in AKI group compared to the sham group as evident by increase the density of TLR-4 in the hippocampus and striatum in parallel to increase in microglia in the same regions as previously reported by Liu et al. The finding confirms the triggering effect of TLR-4 on AKI induced neuro-inflammation that possibly leads to AKI induced encephalopathy. Our new hypothesis states that TLR-4 receptor blocker may have a role in preventing AKI effects on the brain.an experimental trial conducted by our research team.

alimowafy2010@gmail.com

Oncolytic HSV-1 therapy for breast cancer meningeal metastases

Darshini Kuruppu
Massachusettes General Hospital, USA

Meningeal metastasis is a fatal complication of breast cancer that affects 5-8% of patients when cancer cells seed in the meninges. Their subsequent growth results in severe neurological complications involving the cranial nerves, cerebrum and spinal cord, limiting life expectancy to less than 4 months. Currently, there is no cure. Aggressive multimodal therapies such as radiation, intra-cerebrospinal fluid (CSF) and systemic chemotherapy are ineffective. Chemotherapy is often cleared rapidly from the CSF preventing access to cancer cells, while therapeutic doses are highly toxic. This highlights the urgent need for new therapy. Oncolytic Herpes Simplex Virus type 1 (HSV-1) was investigated in this regard. Oncolytic viral therapy is the destruction of cancer cells by replicating virus. It is based on the model of multiple cycles of lytic virus replication in cancer cells until the cancer is destroyed. This investigation was conducted in a murine model of meningeal metastases which has been fully characterized by in vivo molecular imaging, histology and external neurological symptoms and shown to mimic human disease pathology. Based on out results, oncolytic HSV-1 inhibits tumor growth primarily in the base of the brain and spinal cord. The onset of neurological symptoms (bradykinesia, ataxia, anorexia, and paralysis) that accompany a heavy tumor burden in the base of the brain were delayed. Replicating virus is identified in tumors. Treatment at the early phase of tumor growth had a higher response rate compared to that at the late phase of tumor growth. Our investigations show that treatment of meningeal metastases with oncolytic HSV-1 at the early growth phase can inhibit life threatening disease progression. As such oncolytic HSV-1 holds promise as a potential therapy for breast cancer meningeal metastases that can be translated to the clinic.

DKURUPPU@mgh.harvard.edu