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Babak Kateb

Neuroscientist, Canada

Traumatic Brain Injury

Traumatic brain injury (TBI) is an enormous public health problem, with 1.7 million new cases of TBI recorded annually by the Centers for Disease Control. However, TBI has proven to be an extremely challenging condition to treat. Here, we apply a nanoprodrug strategy in a mouse model of TBI. The novel nanoprodrug contains a derivative of the nonsteroidal anti-inflammatory drug (NSAID) ibuprofen in an emulsion with the antioxidant a-tocopherol. The ibuprofen derivative, Ibu2TEG, contains a tetra ethylene glycol (TEG) spacer consisting of biodegradable ester bonds. The biodegradable ester bonds ensure that the prodrug molecules break down hydrolytically or enzymatically. The drug is labeled with the fluorescent reporter Cy5.5 using nonbiodegradable bonds to 1-octadecanethiol, allowing us to reliably track its accumulation in the brain after TBI. We delivered a moderate injury using a highly reproducible mouse model of closed-skull controlled cortical impact to the parietal region of the cortex, followed by an injection of the nano prodrug at a dose of 0.2 mg per mouse. The blood brain barrier is known to exhibit increased permeability at the site of injury. We tested for accumulation of the fluorescent drug particles at the site of injury using confocal and bioluminescence imaging of whole brains and brain slices 36 hours after administration. We demonstrated that the drug does accumulate preferentially in the region of injured tissue, likely due to an enhanced permeability and retention (EPR) phenomenon. The use of a nanoprodrug approach to deliver therapeutics in TBI represents a promising potential therapeutic modality.

Speaker Biography

Babak Kateb, MD is a neuroscientist with more than 20 years of research experience. His research has been focused on introduction of advance diagnostics and therapeutics into clinical neuroscience in order to rapidly identify and introduce game changing technologies to treat neurological disorders such as brain cancer, Alzheimer's disease, Parkinson's disease, and other brain and spinal disorders. He did his educational training at TUSOM, USC, did his research fellowship at USC-keck School of Medicine, Department of Neurosurgery and also studied VLSI system design at USC Department of Electrical Engineering at the Ming Hsieh Institute.

e: Babak.Kateb@WorldBrainMapping.org

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