OFFICIAL ABSTRACT and CERTIFICATION

Neuronal HMGB1 Facilitates the Inflammatory Response via Increased Release of Proinflammatory Cytokines

Sari Strizik
Half Hollow Hills High School East, Dix Hills NY, United States

Inflammation is an important part of the immune response to harmful stimuli. Upon recognition of these stimuli, the inflammatory response begins, which involves the release of cytokines. Cytokines call immune cells to the site of infection. This inflammatory response may become over exaggerated and spread to parts of the body where inflammation is unnecessary, resulting in organ damage as blood flow can be cut off to the organs leading to fatalities. HMGB1 is a proinflammatory cytokine found in high quantity in inflammatory conditions. In order to better examine the role of HMGB1 released from neuronal cells, and HMGB1-specific knockout was developed using the Cre-Lox breeding technique. Through the utilization of Western Blots, it was determined that HMGB1 was successfully knocked out of neuronal tissue. From there, a group of the knockout mice along with wild type mice were given chronic constriction injuries around their right sciatic nerve in order to stimulate inflammation and the release of HMGB1. There were significantly lower levels of HMGB1 in the knockout model compared to the control. A sham group was also tested to show that the CCI procedure was not the cause of the difference in HMGB1 levels. Additionally, several ELISA' s were performed to show that CXCL1, IL-18, and TNF were also decreased in the knockout mice. Thus, neuronal HMGB1 must play a role in promoting inflammation external to neuronal tissue.

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