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Consequences of neuron-specific NF κ B modulation on the outcome of traumatic brain injury

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The outcome of traumatic brain injury (TBI) greatly depends on the extent of secondary pathologies. This posttraumatic phase is characterized by diverse cellular events including neuroinflammation, apoptosis and necrosis as well as counteracting regeneration and remodeling processes. IKK/NF κ B signaling is a key player in the regulation of inflammation, immune responses, cell survival and neuronal differentiation and is known to get activated in different cell types of the CNS upon TBI. However, the cell-type-specific functions of NF κ B remain unclear. We therefore conducted a systematic approach to analyze whether IKK/NF κ B signaling has either beneficial or detrimental effects on the outcome of TBI depending on the cell type. For this purpose, we used an experimental model of closed head injury in combination with either loss-of-function or gain-of-function mice allowing conditional inhibition or activation of NF κ B in principal forebrain neurons. Outcome parameters consisted of in vivo neurological scoring as well as post mortem investigation of inflammatory, apoptotic and synaptic markers. We provide evidence that repression of IKK/NF κ B signaling in neurons increases the acute posttraumatic mortality rate and worsens the neurological outcome of survivors at various time points post TBI. Interestingly, IKK2 D^{NC}Camk2a mice are more prone for hematoma formation and show increased neuroinflammation, reactive astrogliosis and alterations in gene expression. These findings suggest that neuronal NF κ B inhibition plays a detrimental role for the outcome of TBI. Currently we investigate whether enhancing neuronal NF κ B activation can reduce these harmful effects of secondary TBI pathogenesis. This study is supported by the German Research Foundation (SFB 1149/A03).

Biography

Melanie Tepper has completed her Bachelor studies in Molecular Biotechnology at the University of Heidelberg, Germany. Afterwards she had the chance to study one year at the San Francisco State University, CA, USA as a Fulbright student in Cell and Molecular Biology and finished her Master Studies in Molecular Medicine at Ulm University, Germany. She is currently in her 3rd year as a PhD student from the International Graduate School Ulm in the group of Prof. Dr. Thomas Wirth and Dr. Bernd Baumann.

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