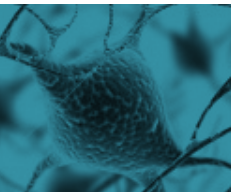

PROJECTS RECOMMENDED FOR FUNDING

TBI Epilepsy \\ Proteolytic remodeling of the extracellular matrix in aberrant synaptic plasticity underlying epilepsy evoked by traumatic brain injury

Austria\ Belgium\ Canada\ Finland\ France\ Germany\ Israel\ Italy\ Luxembourg\ Poland\ Portugal\ Romania\ Spain

Traumatic brain injury (TBI) is major health problem. Yearly cost from TBI in Europe exceeds €100 billion and is steeply rising. There are no therapies to improve the recovery or to prevent the development of life-compromising comorbidities. One of the major long-lasting consequences of TBI is post-traumatic epilepsy (PTE). However, almost nothing is known about the mechanisms that lead to the development of epilepsy (epileptogenesis) after TBI. Recent evidence shows that the extracellular matrix (ECM), which surrounds neurons and glia, plays a major role in remodeling of neuronal connections after injury. In particular, the two enzyme systems – matrix metalloproteinase-9 (MMP) and urokinase-type plasminogen activating system (uPA) – can degrade various components of the ECM, enabling the occurrence of very focal and targeted plastic changes. We plan to test a hypothesis is that MMP-9 and uPA systems play a major role in reshaping the brain connections during development of epilepsy after TBI. We will investigate whether animals with genetically modified MMP-9 or uPA systems have altered susceptibility for post-TBI epileptogenesis. In parallel, we will investigate whether patients who have suffered TBI have mutations in MMP-9 or uPA systems, and whether the levels of these molecules are changed at acute post-injury phase. We will also investigate when, and in which brain areas, MMP-9 and uPA systems are active after TBI, and what are the molecular mechanisms that mediate their effects. The major goal of our research is to reveal novel mechanisms that can be used as treatment targets to be developed to prevent post-traumatic epilepsy.

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