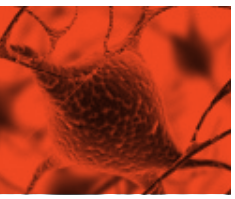

PROJECTS RECOMMENDED FOR FUNDING

CIPRESS \\ CELL STRESS INDUCIBLE PROTEIN EXPRESSION SYSTEM FOR RECOVERY FROM SEIZURES PROJECT DESCRIPTION:

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

The epilepsies are chronic neurological syndromes that severely degrade life quality, due to the unpredictable occurrence of seizures. Most temporal lobe epilepsy (TLE) syndromes have no discernable genetic component, suggesting that epileptogenesis depends on disease-promoting mechanisms of neuronal plasticity. The pathological changes underlying TLE are induced by multiple brain insults, such as traumatic injury, infection, stroke, intracerebral hemorrhage and infantile convulsions. Yet, brain mechanisms involved in this process of epileptogenesis are only partially understood. Neuronal death and glial activation is often an early component. Subsequent changes may affect neuronal pH and Cl- regulation, energy metabolism, and inhibitory actions of the neurotransmitter GABA. Thus, this proposal aims to develop novel approaches to identify the molecular mechanisms underlying not only disease-promoting but also adaptive mechanisms triggered during epileptogenesis. This information will let us test specific strategies to block processes of epileptogenesis. We will use a novel molecular tool (CIPRESS) which permits induction of protein expression in response to cellular stress during epileptogenesis. We will ask which candidate proteins (or combinations) can suppress seizure activity in animal models of epilepsy as well as in organotypic hippocampal slice cultures of human patients with TLE. This approach should both provide insights into molecular, cellular and network mechanisms of epileptogenesis and also permit rigorous tests for the development of a gene therapy based on the molecular processes involved.

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