

**PROTEA \\\ INFLUENCE OF PROTEASES BEFORE, DURING AND AFTER STROKE.**

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

Every day, 1000 Europeans die from a stroke and about twice that number survive but are disabled. Despite tremendous progresses in our understanding of the pathophysiology of stroke, translation into effective acute therapies has largely failed, apart from tissue-type plasminogen activator (tPA)-induced thrombolysis. Nevertheless, strict inclusion criteria for eligibility restrict thrombolytic opportunity to only 2-5% of stroke patients. Thus, it is an emergency to look for new and possibly combined therapies within and beyond the acute phase of stroke to increase the proportion of treated patients. Proteases, especially plasminogen – plasminogen activators and metalloproteinases, critically control several stages in the evolution of stroke lesions. Emerging concepts suggest that these proteases can influence the fate of all cell types of the “neurovascular unit”, through both extra- and intra-cellular mechanisms/signalling(s). These neurovascular perturbations contribute to the risk of thrombosis, blood-brain barrier leakage, excitotoxic neuronal death, oedema, haemorrhage, inflammation and repair processes, over hours or even days, weeks and months after stroke. Protea proposes to characterize the influence of these proteases before, during, and after stroke and to point out novel diagnostic/therapeutic avenues that may result from this knowledge. To achieve these goals, we will perform an extensive pre-clinical and clinical stroke related proteasomic analysis, investigate whether proteases conveyed by microparticles may be messengers of cell activation/damage in the neurovascular unit, validate combined strategies to improve stroke recovery and thus determine the influence of the plasminogen/tPA/metalloproteinases triad at the different stages of stroke.



COORDINATOR | DENIS VIVIEN

## PROJECT PARTNERS:

**Denis Vivien**

INSERM, Caen, France

**Jari Koistinaho**

University of Eastern Finland , Kuopio, Finland

**Joan Montaner**

Vall d'Hebron Institute of Research, Barcelona, Spain

**Jose a. Paramo**

FIMA, Pamplona, Spain