

VIRAL VECTOR-MEDIATED DELIVERY OF NEUROTROPHIC FACTORS: A NEW APPROACH?

Paradiso Beatrice,¹ Marconi Peggy,¹ Zucchini Silvia,¹ Binaschi Anna,¹ Buzzi Andrea,¹ Mazzuferi Manuela,¹ Navarro Mora Graciela,² Rodi Donata,¹ Fabene Paolo F.,² Marzola Andrea,¹ Manservigi Roberto,¹ Simonato Michele¹

¹Neuroscience Center, University of Ferrara and ²Section of Anatomy, University of Verona, Italy

Neurotrophic factors (NTF) are involved in the survival, proliferation and differentiation of neurons from their precursors. Therefore, modulating NTF levels in lesion areas may represent a new approach for the therapy of seizure-induced damage. It is reported here that recombinant herpesvirus-based vectors expressing a combination of two NTFs, FGF-2 and BDNF, increases survival and proliferation of neural progenitors and favors their differentiation into neurons *in vitro*. These vectors were also tested *in vivo*, in a model of status epilepticus-induced neurodegeneration and epileptogenesis. When injected in the hippocampus 3 days after status epilepticus, FGF-2/BDNF expressing vectors partially repaired neuronal damage and prevented the occurrence of spontaneous seizures. Thus, supplementation of FGF-2 and BDNF promotes neuronogenesis and repair of existing neuronal damage, modifying the disease natural history in a model of epilepsy associated with hippocampal damage. Importantly, these findings were obtained under conditions that reproduce those that allow therapeutic intervention in patients.