

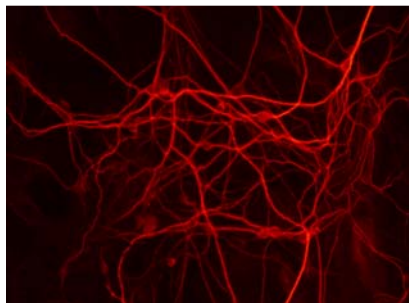
Neurochemical and morphological *in vivo* and *in vitro* models in neurodegenerative diseases

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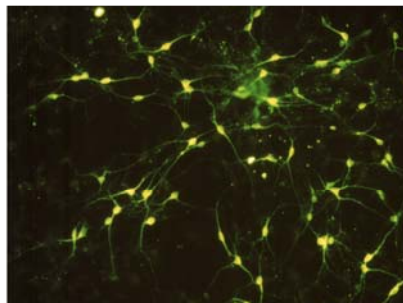
Mesencephalic cell cultures, which contain dopaminergic neurons and express different functional receptor subtypes, provide a suitable model for testing the influence of new compounds on the degree of dopamine (DA) cell damage. The neuronal damage may be evaluated by analysing neurochemical and morphological parameters such as [³H]DA uptake, release and tyrosine hydroxylase (TH) immunocytochemistry.

Cortical cell cultures, mainly containing GABAergic and glutamatergic neurons, and hippocampal cell cultures, especially containing glutamatergic neurons, can be used to study the cell degeneration following neurotoxic insults. The neuronal damage may be evaluated by analysing neurochemical ([³H]GABA and [³H]glutamate uptake and release, biochemical (MTT assay, LDH levels) and morphological (Hoechst 33258 nuclear staining, MAP-2 immunoreactivity) parameters.

Cortical cell cultures



Mesencephalic cell cultures



1. Description of the product

In vitro models of neurodegenerative diseases including model of Parkinson disease and pathologic events such as hypoxia and ischemia have been developed and optimized. These *in vitro* experiments, performed in primary neuronal cultures, cerebral tissue slices and/or synaptosomes, are complementary to the *in vivo* microdialysis experiments and by combining them it is possible to investigate on the efficacy as well as the neurochemical and molecular mechanisms of new drugs against neurodegenerative pathologies.

In vivo microdialysis technique in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats allows to understand the possible relevance of new pharmacological approaches in the treatment of this pathology. The simultaneous evaluation of the release of several neurotransmitters such as dopamine, acetylcholine, glutamate and GABA in the striatum, globus pallidus and/or other close related brain nuclei of the indirect and direct pathways

of the basal ganglia, gives the opportunity to evaluate the efficacy of new therapeutic and genetic strategies in the control of the “motor” pathways both in physiological and pathological conditions.

2. Innovative aspects of the product

Standardized parameters.

3. Main advantages of the offer

These *in vitro* models allow the evaluation of the possible neuroprotective properties of new drugs.

4. Technology keywords

Mesencephalic cell cultures, Cortical cell cultures, Parkinson disease, [³H]GABA, [³H]glutamate.

5. Current stage of development

In vivo and in vitro pilot study of active molecules have been performed.

6. Intellectual property rights

Non patentable as part of laboratory expertise.

Technical and scientific publications

Antonelli T, Tomasini MC, Fournier J, Mazza R, Tanganelli S, Pirondi S, Fuxe K, Luca F. Neurotensin receptor involvement in the rise of extracellular glutamate levels and apoptotic nerve cell death in primary cortical cultures after oxygen and glucose deprivation. *Cereb Cortex*. 2008; 18:1748-57.

Antonelli T, Fuxe K, Tomasini MC, Mazzoni E, Agnati LF, Tanganelli S, Ferraro L. Neurotensin receptor mechanisms and its modulation of glutamate transmission in the brain: relevance for neurodegenerative diseases and their treatment. *Prog Neurobiol*. 2007; 83:92-109. Review.

Antonelli T, Tomasini MC, Finetti S, Giardino L, Calzà L, Fuxe K, Soubriè P, Tanganelli S, Ferraro L. Neurotensin enhances glutamate excitotoxicity in mesencephalic neurons in primary culture. *J Neurosci Res*. 2002; 70:766-73.

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