Press Release

Mechanisms underlying neurodegeneration revealed

Research carried out at the Institute of Molecular Biology and Biotechnology (IMBB; Foundation for Research and Technology, Crete, Greece), part of which is published in the international scientific journal *Nature* today, revealed one of the central biochemical mechanisms responsible for degeneration of nerve cells.

Neurodegenerative disorders such as amyotrophic lateral sclerosis, the diseases Alzheimer's, Batten, Huntington's, Parkinson's and many more, rank among the most debilitating and ultimately fatal human pathological conditions. A common denominator among various neurodegenerative conditions is the progressive or massive loss of nerve cells, which precipitates dramatic reduction of physical and mental capabilities, and frequently leads to inexorable death. Similar phenomena are also observed during stroke following ischemic episodes, in epilepsy, and in severe cases of drug abuse and intoxication.

In all above instances neurons undergo a process termed necrosis or necrotic cell death. Despite the involvement of this type of cell death in numerous devastating pathological conditions, there is a large gap in our understanding of the basic cellular and molecular mechanisms that transpire during necrosis. This lack of basic knowledge is in part responsible for the relatively disappointing progress towards the development of truly effective methodologies to battle neurodegenerative disorders and related conditions. Therefore, deciphering the biochemistry of necrosis is of critical importance, and a significant step in our efforts to achieve the goal of countering neurodegeneration.

By using the simple nematode worm *Caenorhabditis elegans*, two IMBB researchers, Dr. Nektarios Tavernarakis and Dr. Popi Syntichaki have identified two classes of genes that are required for the execution of necrotic cell death. Each of the two groups of genes encodes specific proteolytic enzymes. Under normal conditions, such proteases participate in the regulated degradation of specific cellular proteins, thus mediating their recycling, and also acting as important modulators of cellular and biochemical processes. Based on their results Tavernarakis and Syntichaki propose that these, otherwise benign enzymes, turn rogue under certain pathological conditions and wreck havoc inside the cell by frenziedly and indiscriminately degrading essential cellular proteins, inducing acute cell death.

The characterization of the mechanism underlying necrosis described above is of great significance since specific enzymatic activities are directly implicated in neurodegenerative cell death. By providing novel insight into the biochemical events that transpire during neurodegeneration, these findings should facilitate innovative intervention strategies, aimed at ameliorating or even blocking cell death. For example, it is conceivable that protease inhibitors are likely to have neuroprotective effects. In fact, the IMBB researchers have shown that this is indeed the case for *Caenorhabditis elegans* neurons, *in vivo*.

It should be noted that the award of this year's Nobel prize in Physiology or Medicine to three researchers (Sydney Brenner**,** Robert Horvitz και John Sulston), who pioneered studies in *Caenorhabditis elegans*, underlines the prowess of this animal model in exploring mechanisms of development and cell death.