DESCRIPTION FOR THE GENERAL PUBLIC

Apoptosis is a type of PCD (programmed cell death) found in animals. The release of apoptotic factors from mitochondria initiates apoptosis in the so-called permeability transition. The next stage is characterized by chromatin condensation and self-destruction of DNA by the cell's own nucleolytic DNases. Then the cell breaks into membrane-bound, ultrastructurally well-preserved fragments that are ingested by macrophages, which prevents the induction of inflammation. The classical studies were performed on *C. elegans* proved that apoptosis was programmed, not accidental. Adult worms have a predetermined number of cells: an adult hermaphrodite has 959 cells and the generation of the 959 cells in the hermaphrodite was accomplished by the death of 131 cells.

Apoptosis play important role in medicine. Apoptosis is a key part of the innate tumor-suppression mechanism. On the other hand apoptosis is involved in the pathology of neurodegenerative diseases such as, Alzheimer's and Parkinson's diseases,

According to the 'endosymbiotic' hypothesis, the apoptotic machinery originated in mitochondria. Probably mitochondria originated from bacteria that had been incorporated as endosymbionts ("living together inside") of larger eukaryotic cells. Mitochondria are organelles in which aerobic respiration takes place. Mitochondria are usually a key player in apoptosis. It was suggested that bacterial ancestors of current mitochondria during primitive apoptosis kill their hosts.

During long tine it was widely believed that apoptosis occurs only in animals. However in recent programmed cell death induced by mitochondria was described in a broad range of eukaryotic organisms by different studies (including studies performed in our group).

It is not clear what is the function of apoptotic cell death in unicellular organisms. Our preliminary studies indicate that apoptotic factors are required for a proper function of unicellular model organism baker yeast in aerobic conditions (when there is an access of oxygen).

The main aim of the presented project is testing hypothesis that apoptotic mechanisms has mitochondrial origin and that was involved in ancient adaptation for aerobic conditions. This hypothesis will be tested using baker yeasts. In experiments yeast apoptotic factors will be replaced by their counterparts from other organisms: bacteria, protists, plants and animals. If functions of apoptotic factors are evolutionary conserved transformed yeasts with apoptotic factors from other organisms will be similar to the wild yeasts. This mean they will be well adopted to aerobic conditions and their apoptotic cell death will be similar to the cell death of wild yeasts.

Assuming that apoptotic machinery is involved in adaptation to aerobic conditions evolution in conditions of glucose repression (with high level of glucose) will lead to selection of mutants with suppressed apoptosis machinery. This hypothesis will be tested using experimental evolution. Presented project has important medical implication. It has been shown previously that activity of mitochondrial metabolism correlates with apoptotic activity. Namely it has been shown that inactivation of apoptosis in cancer cells causes frequent respiratory metabolic shifts toward non-mitochondrial glycolysis, known as the ‘Warburg hypothesis of cancer origin’. In contrast, neurons that rely on mitochondrial respiration die due to apoptosis during neurodegenerative diseases. The common origin of apoptosis and mitochondrial respiration may be key factor in our understanding of this phenomenon.