Dissecting of the novel mechanisms in multi-drug resistance associated with vault's proteins and translation initiation factors in cancer diseases

Cells are the basic building blocks that build virtually all living organisms (except for viruses and prions only, which are not able to live without their host - cells). A single cell may be an autonomous organism (e.g. all known to us from the school - *Paramycium*), but it can also be part of such a complex structure as our brain. Regardless of where it is found, whether in the lake or in our body, it is exposed to changes in the surrounding environment. And only those cells that adapt to this environment will be able to survive and "give birth" to offspring. They are therefore subjected to continuous selection, because those who have not been successfully are eliminated from this environment. This is, therefore, the evolution in the purest edition being the resultant of variation and selection.

The cells we call cancerous are from the biological point of view, the same cells as *Paramycium* or the neuron, but the difference is that instead of obeying the larger puzzle called the multicellular organism, they started to live on their own leading to disorder in the whole system causing its destruction, or even death. A human kind struggling with cancer, or more precisely with cancer cells, began to change their environment by introducing drugs there and trying to eliminate them. Therefore, a man applied a strong selection pressure. As a consequence, the cells began to change in response to deadly toxins, i.e. anti-cancer drugs. They changed their metabolism, that is biological processes occurring in their interiors. Some were saved by the additional production of "pumps", i.e. proteins located on the external border of the cell (outer cell membrane) pumping out toxins out of their compartment (elimination of the drug). Others have learned to modify the toxin molecule so that it does not harm them (neutralisation of the drug). Of course, the effect of the drug caused the killing of most cells. Unfortunately, in the environment were the best adapted ("the smartest"), which had time to develop defence mechanisms and acquired the so-called drug resistance. They learned to live in such unfavourable environment and even began to reproduce in it. They are responsible for the recurrence of cancer.

The aim of this research project is to learn the defence mechanisms of cancer cells. We are particularly interested as scientists and potential contractors of this project, to investigate what is happening in cancer cells immediately after administering drugs that kill these cells. However, we will not "watch" cancer cells in the body of patients, because it is practically impossible to do. We will use cells that have been isolated once from a patient's tumor and are maintained in an environment resembling our body's environment (so-called *in vitro*, i.e. in glass). To put it a bit simply, administering the drug to cells living in glass in a special medium results in the same or very similar changes in them as in the cells forming the tumor in the patient (in biology we talk about models reflecting the natural state). Thanks to this approach, we can examine in detail the changes taking place in cells. This is possible because of the rapidly developing field - molecular biology and new techniques, such as confocal microscopy. These techniques allow us to "look at" the processes taking place inside the cells, describe them and draw conclusions from these observations.

Understanding how cancer cells function and what defence mechanisms develop after administration of anticancer drugs may be used in the future to design even more effective drugs.