**Finding a cure for cancer: the holy grail of science**

To find a cure for cancer, the modern-day plague of our society – is synonymous to finding the holy grail of science.

At a recent EuroDYNA conference in Brno, Czech Republic, scientists from around Europe came together to share their research carried out in the field of genetics and cell nucleus architecture. A greater understanding of the body's building blocks might ultimately lead to a better understanding of human diseases.

Understanding DNA damage

Jiri Bartek from the Danish Cancer Society in Copenhagen in Denmark, is one step closer to understanding the route of cancer through his work on cell response to DNA damage. By using a UV laser to damage DNA strands inside tumour cells, the Copenhagen team is able to directly observe the different checkpoints in the cell.

Each time a cell divides its genetic information must be doubled in order for the genes to remain the same. A cell that is about to become tumorous can not make this genome replication and division without errors. To spot errors in the genetic material cells have evolved mechanisms to slow down or block cell division (so called cell-cycle checkpoints), promote DNA repair, or eliminate damaged, hazardous cells by engaging a cellular suicide program. How cells make the choice between life and death in response to DNA damage is critical not only for the fate of each cell, but also for avoiding life-threatening diseases such as cancer.

In cells with an early pre-tumorous change, the entire checkpoint network is activated. The system puts an end to such cells or blocks their division by a process of cellular senescence. On the other hand, defects in the DNA damage response machinery, or a phenomenon of checkpoint adaptation (when the cell arrest is long-term and not irreversible) may allow the cell to escape from the DNA damage-imposed blockade and despite its damaged DNA, it may multiply. This can give birth to a tumour.

Bartek and his team have found that if an inhibitor called Chk1 kinase is added, this ends what is called the G2-phase cell cycle checkpoint, a mechanism that is often still preserved in cancer cells, and this can tip the balance of life-or-death decisions towards cell death. This strategy might be useful to sensitise cancer cells to treatment with DNA-damaging irradiation or chemotherapeutic drugs, by eliminating the sick cells. Although a cure for cancer is still far away, this has great implication for the future of cancer research.

The team is also looking in depth at the pathways of repair in response to DNA damage and they have found that a whole host of proteins rapidly congregate in and around the damage site and begin repair. When the repair proteins fail to fully repair the DNA damage, there is a danger of the DNA lesion to be fixed as a mutation, and eventually this might lead to a cell becoming tumorous.

"If we can understand the function of these preventative proteins, we can learn how cancer develops and then better prevent or treat it, " says Simon Bekker-Jensen from the Danish Cancer Society team."

Understanding the pathways

The understanding of individual disease response pathways is increasing as Pavel Kovarik from the Max F. Perutz Laboratories at the University of Vienna has demonstrated. He is looking at two signalling pathways which are regulated by stress or interferon and related to immune response. Although both pathways can be

activated by independent stimuli, an immune response is only obtained when both pathways are acting on the gene at the same time. This happens when the body is defending itself against pathogens and tumours. By looking at the order, location and contribution of stress and interferon induced changes on chromatin modifications (DNA damage) and nuclear architecture, our understanding of gene expression regulation will improve. This will open up new possibilities to combat disease.

Measuring radiation

There is still a lot to learn about DNA damage response. The conference emphasized that current research is only scratching the surface but EuroDYNA's efforts have brought about exciting new methods such as the ion microbeam developed by Anna Friedl and colleagues from the University of Munich.

"We want to understand what is disturbed by ionizing irradiation, and what are the cellular responses to these disturbances, in order to further understand how ionizing radiation induces cancer or cell death. People currently start to think not only about DNA damage and mutations, but also about epigenetic disturbances, for example alterations in chromatin structure, which may affect gene expression, " said Friedl. "We came up with the idea of using an ion microbeam in 1999 but it has taken us a long time to make our idea happen"

By using several types of ions all with different velocities she can transmit energy levels of different strengths through a substrate and induce very precise double-strand DNA breaks. UV lasers can also be used to target individual cells or even subcellular regions, and they are cheaper and much easier to handle, but the ion beam has the advantage of using real ionizing radiation.

In reality, UV lasers would not be harmful humans but the effect from ionizing radiation (background, medical applications and so on) is inevitable. Friedl.'s work gives the ability to make detailed observations of the effects of ionizing radiation on individual cells, research which might ultimately give us an idea of the effects of radiation treatment on cancer patients

"Another important point is intercellular communication. Can a cell that has experienced radiation damage give signals to undamaged cells and change the behaviour of these cells" Friedl questions?

Friedl.'s work is preliminary but she and her team have found a first gene product (Mdc1) that appears to be required for inhibiting mobility of damaged chromatin. If damaged chromatin were allowed to move around in the cell nucleus, chances would be higher for DNA ends from different breaks to meet, and this might increase the frequency of chromosome aberrations.

To sum up the conference, it was clear that pan-European collaboration was the driving factor making this research possible.

"It is important to note that these kind of projects require a close collaboration of nuclear physicists, cell biologists and radiobiologists", commented Friedl about her project.