A Never Ending Story...

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... \textit{and this is cancer}. Equally for patients and for their doctors.

For patients, because having cancer is still considered a sentence to death. In these very years, too many announcements in the media make known publicly that this or that great personality, despite best medical treatment, finally dies because he/she lost the battle with cancer.

For doctors, because each new year they learn about newer and newer weapons in the fight against cancer: genomics, epigenomics, proteomics, metabolomics, chromatin, theranostics... But they end up being defeated so many times. It still happens in 2017.

Why still? It is said that „cancer is the disease of the genome”, while (1) human genome was deployed in the first year of the millenium, and (2) curiously (or not?), the Nobel Prize has not been attributed to this discovery yet.

Each tumour has its own set of genetic changes. To complicate things, some tumours have different genetic alterations in their different anathomopathological regions. And these alterations may even change during the evolution of the tumour. So, it is hard to imagine how these changes could be used as a therapeutic target. However, some projects – such as the Cancer Genomic Atlas (TGCA) of the National Institutes of Health (USA) – try to put together everything we discover in this field.

But the host has his/her own genetic characteristics, which make him/her establish a special relationship with cancer. First, there are several genetic features that predispose to cancer, but they account for a few cancers. Globally, it is considered that only 10-15\% of all cancers are of hereditary origin (1); the rest are due to environmental or behavioural factors (diet, exercise, lifestyle in general). Interaction between such adverse factors – which are present in a lower or higher amount around the host and the host genetically driven predisposition to such an aggression – is so complex, that it is hard to be strictly defined.

However... The cancer process is initiated by mutations in genes, but later on it is developed by proteins and enzyme-mediated signal transduction (1). This is the task of another huge project of the International Epigenome Consortium...
(IHEC), that develops reference maps of human epigenome for different cellular states. The epigenome is constituted by the chemical compounds which surround the DNA and modify genome activity without changing its basic structure. The complex of macromolecules consisting of DNA + proteins + RNA is called chromatin and constitutes another complex field of research. The main functions of chromatin are to package DNA into a compact stage, reinforced for mitosis, to prevent DNA damage, and to control replication. The Human Epigenomic Atlas tries to identify modifications in this process. For instance, a bad function of the previously described sequences is accomplished when there is a hypo-methylation of the DNA. Another point described in such an atlas is the aspect of RNA sequence and especially the small noncoding RNA (miRNA), which in special conditions may lead, however, to cancer development. Another database developed in this field is NIH Roadmap Epigenomics.

The next „regional” science in the field is called metabolomics; it studies all the metabolites in the cell – which are generally small molecules with an essential contribution to the understanding of a cell functional state. They are studied, for instance, by mass spectrometry or nuclear magnetic resonance spectometry, which deployed to date hundreds of thousands of chemical entities (1).

The last huge field of research in cancer, and not only in cancer, is the specific response to therapy – pharmacogenomics. This means the ability of the tumour and/or the host to respond to a therapy in respect to their gene composition. Because it implies different genetic compositions, this is a very complex issue. In the field of some cancer pharmacogenomics, today we may affirm that a specific cancer therapy does not work. For instance, in breast cancer, the presence of poor metabolizers on the CYP2D6 cytochrome means not to cure with tamoxifen (1). Or in colon cancer, the KRAS mutation announces the lack of response to cetuximab or panitumumab (3). Of course, it would be much better to have an atlas to show which marker announces a 100% response to a specific cancer therapy. But this is still a dream.

To resume, genetics, epigenetics, metabolomic and pharmacogenomics may give important information about the inherited predisposition to a special cancer, to the predisposition of a poor defence against the aggression of environmental factors, to bad habits of lifestyle regarding cancer and to the ability to respond or not to respond to a specific cancer therapy. A dramatic example in the field was Angelina Jolie’s decision to surgically remove her ovaries and breasts because of a poor genetic heritage predisposing to cancer.

The complexity of data presented so far makes the daily life of an oncologist very hard. That’s why a new synthetic science, called theranostics, develops. Using nanotechnology, it brings a single group of information for diagnostic and target therapy.

We may understand why this devastating amount of knowledge finally penetrated in the field of politics. In 2015, president Obama had an important talk dedicated to Precision Medicine (meaning „personalized medicine”) – as the medicine of the future and maybe of the present. He presented the American Government’s decision to provide substantial funds for this field. Attracting funds, research and brilliant minds to cancer personalized medicine is the only way of bringing us today the medicine of tomorrow.

Conflicts of interest: none declared.
Financial support: none declared.

References