

PRESS RELEASE

*SEMME – European School of Molecular Medicine
University of Milan*

*IFOM – FIRC Institute for Molecular Oncology
IEO – European Institute of Oncology*

TURN THOSE GENES BACK ON!

A drug, recently approved by the FDA (USA), shows the ability to reactivate some genes involved in Myelodysplastic Syndrome, and could represent an innovative therapeutic perspective for some kinds of leukaemia. The research was presented today, at the 2nd International IFOM-IEO Campus Meeting on Cancer.

Scientists call it “epigenetic therapy of cancer”. Today it represents one of the most interesting available perspectives to “correct” some genetic anomalies involved in the onset of neoplastic diseases, with the aid of drugs. So promising is it that, a few days ago, the US Food and Drug Administration (the American Agency in charge of controlling foods’ and drugs’ quality and safety) approved the diffusion of a drug that shows the ability to wake up again some genes, whose inactivation triggers the so-called Myelodysplastic Syndrome (MDS). The bone marrow of people affected by this disease is unable to work properly, and the disease can easily progress into the acute myeloid leukaemia (AML). The drug was described by Peter Norris, from the Norris Cancer Center of the University of Southern California (Los Angeles, USA), during the 2nd International IFOM-IEO Campus Meeting on Cancer (Milan, May 5-8).

As scientists well know, tumours are diseases caused by the accumulation of “mistakes” within genes. These mistakes trigger a severe malfunctioning in cellular mechanisms. Some of these errors are real slips in the genetic code of the DNA. If the base sequence ACTG (Adenine, Cytosine, Guanine, and Thymine) of the gene is wrong (if, for example, instead of C there is a G) the protein which is synthesized following the instructions of this gene is different from the normal one, and it is unable to play the role it was meant for. In another example, if the base sequence of a gene is erased, the correspondent protein cannot be produced. But there is another kind of error: when a gene correctly written gets bound by substances that inactivate it. This type of mistake is called “epigenetic silencing” (epi- means over), because it doesn’t imply any changes in the genetic code. What happens is that the gene is turned off. If we assume that the gene is a tumour suppressor, namely a gene whose activity is to protect the cells from tumour degeneration, it is easy to see how the possibility to revert such a mistake sounds interesting for anticancer therapies.

Now, the research that Jones and colleagues performed has proven that a gene can be turned on again by means of a pharmacological therapy. Jones described a drug called Dacogen, which proved effective in clinical trials (based on the results obtained in Jones’s laboratory) when used to treat the Myelodysplastic Syndrome (in the sample of patients treated during phase III of the clinical trials, the scientists observed a 21% response; in the US, the clinical study was directed by Hagop Kantarjian, from the University of Texas). MDS shows up as an ensemble of disorders in the bone marrow and until recently no therapy whatsoever was available. The disease has many different symptoms: anaemia, haemorrhage, infections and a sense of weakness, and it can progress towards acute myeloid leukaemia (AML). “This drug – Jones explained – is able to reactivate a set of genes that in MDS are epigenetically silenced, thus rescuing several functions: control of proliferation, drug sensitiveness, cell adhesion (*a behaviour that can hamper the metastatic process, writer’s note*), the response to interferon and the immune response. All these mechanisms are markedly altered in MDS.”

Moreover, there are novel ongoing clinical studies testing the combined use of this drug in association with classical chemotherapeutics (HDACi or inhibitors of the histone-deacetylases enzymes) for the treatment of MDS, of AML and of chronic myelogenous leukemia (CML).

“It is becoming increasingly clearer – said Jones – that epigenetic silencing of tumour suppressor genes plays a causative role in human carcinogenesis. Since epigenetic changes are potentially reversible, the role of epigenetic therapy in cancer treatment is likely to become more relevant over the next few years.”

The 2nd IFOM-IEO Campus Meeting on Cancer is promoted by the European School of Molecular Medicine (SEMM) and by the University of Milan, in collaboration with IFOM (The FIRC Institute of Molecular Oncology Foundation) and IEO (European Institute of Oncology). The Meeting (May 5th - 8th 2006, IFOM-IEO Campus, Via Adamello 16, Milan, ITALY) hosts eminent cancer researchers from all over the world and offers the possibility of a “full immersion” in the field, with presentations of the latest and most relevant findings in molecular oncology. It represents a unique opportunity for scientists to exchange expertise and ideas, as well as a trigger for translational research and for the development of new diagnostic and therapeutic strategies.

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