Press Release

A Snapshot of the epigenome: en route to personalized cancer therapies

An innovative technology for the rapid and reliable screening of the human epigenome (or rather, the set of functional DNA elements that regulate gene state and activity is being developed by an international team of scientists at the IFOM-IEO Campus in Milan, in collaboration with the J. Craig Venter Institute and Sangamo BioSciences (both in US). The technology provides a new tool for disease diagnosis, and for the development of personalised cancer therapies. The research was published today in the international journal Developmental Cell.

An innovative technology that allows the epigenetic profiling of patients in 3-4 days, using only a small sample of cells, has been developed by an international team of scientists coordinated by Saverio Minucci from **IEO's Department of Experimental Oncology,** based at the **IFOM-IEO Campus** in Milan. The study, published today in the scientific journal Developmental Cell, was performed in collaboration with American scientists in Sam Levy's group at the **J. Craig Venter Institute** in Rockville, and Fyodor Urnov's group at **Sangamo BioSciences** in Richmond. The **University of Milan** (Department of Biomolecular Sciences and Biotechnology) and the **Congenia-Genextra Group** in Milan were also involved in the study.

This study falls within the scope of **epigenetic research**, an important branch of molecular biology that focuses on the mechanisms regulating gene expression and how alteration of these processes can lead to diseases such as cancer.

What do we mean by epigenetic regulation of **gene expression**? Almost all our body's cells share the same set of approximately **30,000 genes,** inherited from the original cell, the zygote, formed at the moment of fertilization. When cells adopt a **specific fate** in the body (becoming, for example, a neuron, a blood cell or a liver cell) only a fraction of these 30,000 genes are active, while the others are **permanently silenced.** The mechanisms responsible for selectively switching on/off genes act at the level of chromatin (the material that makes up chromosomes, containing proteins and DNA), and involve **chemical modifications** that orchestrate **gene expression**, activating some and repressing other genes, **without altering the DNA sequence**.

A recent, but increasingly accepted idea among the international scientific community, is that the majority of cancers are caused by alterations, not only at the **genetic** level (i.e. mutations in the DNA sequence), but also at the **epigenetic** (from the Greek epi- "on top of-" genes) level, thus altering **mechanisms that regulate gene expression**. Epigenetic research is becoming an important field of molecular research that complements genetic research and holds very promising prospects for the development of new therapies; epigenetic alterations, unlike genetic mutations, can be **efficiently reversed** using **pharmacological approaches,** making it more feasible to design **therapeutic interventions** that target epigenetic alterations.

The technology under development at the **IFOM-IEO Campus** in Milan, one of the most prominent centers at the international level for epigenetic research, provides a new tool for screening epigenetic alterations and opens promising horizons for disease diagnosis and the development of therapies targeting these alterations.

"in the near future – explains Saverio Minucci, Director of the *Chromatin Alterations in Tumorigenesis* Programme at **IEO's Department of Experimental Oncology,** based at the **IFOM-IEO Campus** in Milan, and Associate Professor of General Pathology at the Department of Biomolecular Sciences and

Biotechnology at the University of Milan – we will be able to **rapidly and reliably obtain the epigenomic profile** of patients, adding a new dimension to molecular diagnosis of diseases, and to the identification of personalised therapies". The new experimental method employs ***high-throughput*** DNA sequencing technologies to rapidly identify the "active" DNA in a given cell type.

The test is performed using a **very small sample** of human cells. "We use around one **million** cells – explains Gaetano Gargiulo, first author of the paper –, and samples of this size can be easily obtained *from the patients.* With our test we can obtain **highly reliable results (90% accuracy in prediction of the epigenetic state)** with relatively few cells, while similar technologies presently under development give results that are consistently less accurate, and require much larger amounts of sample (that is limiting for diagnostic applications).

At present the test is being conducted on healthy individuals, in order to map the epigenetic profile of normal cells. The next step will be to test cancer patients in order to identify sistematically epigenetic alterations that are involved in cancer.

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