Press release

Anticancer therapies of tomorrow: help from old drugs

Using existing drugs to fight tumours is a prospective emerging from an increasing number of international studies. The latest confirmation of this trend comes from a study conducted at IFOM and IEO in Milan that combines knowledge obtained in the fields of genetic research and pharmacology, opening the way to possible new uses for drugs already on the market. The study, realized in collaboration with the University of Milan, will be published online today in the prestigious journal Nature.

Developing new drugs is a highly complex process that begins with understanding the molecular mechanism that causes a particular pathology to develop. Only then is it possible to develop a molecule capable of influencing that process. Recently, the classic "linear" pathway leading to drug design and synthesis is giving way to research that starts with existing drugs and works "backwards", or in other directions, sometimes revealing that drugs have unexpected functions.

The study, published today in the prestigious journal Nature and conducted by the team of Marco Foiani, director of the *cell cycle control and genome stability* unit at the FIRC Institute of Molecular Oncology and Professor of Molecular Biology at the University of Milan, together with the team of Saverio Minucci, director of the Research Unit on *chromatin alterations during tumorigenesis* at the European Institute of Oncology and Professor of Pathology at the University of Milan, investigated the activity of two drugs, valproic acid and rapamycin. Valproic acid has been used for decades as an anti-epileptic, while rapamycin is used as an immunosuppressor in organ transplantation. The study revealed that these drugs have a versatility that could be valuable in antitumor therapy.
"Our study takes advantage of an interesting strategy that combines the potential of genetic analysis conducted in simple biologic systems with analysis of the mechanism of action of drugs already in the clinic. In this way, we try to take maximum advantage of model systems while shortening the time required for discoveries to reach the patient" claims Marco Foiani. In particular, the study shows how these drugs act simultaneously on processes that are very important for tumour development: response to DNA damage, autophagy (ability of a cell to self-destruct) and protein acetylation (a protein regulation process). Contrary to the previously held notion that these three phenomena are completely independent, this study reveals that they are tightly correlated and act synergistically to prevent cancer cell formation.
"The drugs used", illustrates Saverio Minucci, "represent two examples of what is defined as 'drug repositioning', in other words, the identification of new activities for drugs that are already available and used for treating disease, making their application for other purposes possible".

Clearly, the results from this study must be confirmed in humans to verify that these drugs have the same activities that were discovered in simpler biological systems. “This process, defined in jargon as ‘target validation’, is becoming so critical to the identification of new drugs that we are assembling a team dedicated entirely to this task at our Campus” explains Saverio Minucci. If studies yield positive results, we can envision early clinical trials of the drugs in combination with other drugs or with treatments that interfere with DNA damage response mechanisms.

Based on the results obtained, these combinations should have a potent antitumor effect. However, cancer may not be the only disease to benefit from these treatments. “Connecting the action of valproic acid and rapamycin with the response to DNA damage, could also provide a key to interpreting some fascinating results obtained in recent years by scientists researching diseases associated with aging. It will be extremely interesting to study how the mechanisms identified in this study operate during aging.” concludes Marco Foiani.

The research published today in Nature was made possible by funding from AIRC (Associazione Italiana per la Ricerca sul Cancro), Telethon, the European Community (GENICA) and from the Italian Ministry of Health.