The quest for specific anti-inflammatory treatment

January 8 2009

Anti-inflammatory drugs affect the cells taking part in inflammatory processes, but also those that do not. This is why it is important to develop specific anti-inflammatory drugs which affect healthy cells. With this aim in mind, a team from the University of the Basque Country is working on analogues of the C1P molecule.

Today two types of anti-inflammatory pharmaceutical drugs are available: steroids and those known as NSAID (Non-steroidal anti-inflammatory drugs). This second type are the most used, have fewer side-effects but they have an effect over a wider spectrum, i.e. they are less specific. Thus, there are no specific anti-inflammatory drugs for each cell type.

The team led by Antonio Gómez-Muñoz, from the Department of Biochemistry and Molecular Biology at the Science and Technology Faculty of the University of the Basque Country (UPV/EHU), is investigating alternatives to current anti-inflammatory drugs, creating synthetic analogues of the C1P (ceramide-1-phosphate) molecule. This molecule was discovered in 1990 in a case of human leukaemia After synthesising it in the laboratory, it was observed that it was an important mytogenic agent (provoking cell growth and blocking the natural death of the cells). Moreover, it causes cell inflammation, i.e. when the cells detect the presence of this molecule, they secrete molecules that generate inflammation - prostaglandin and cytokine cells, for example.

But this process does not occur with all types of cells. Although

apparently contradictory, in some cells this same molecule functions in an anti-inflammatory manner. With this in mind, the Basque research team, annulling the inflammatory capacity of the C1P molecule, was able to use it as an anti-inflammatory drug for certain cell types without affecting other cells.

Removing one of the capabilities

To this end, and in collaboration with a research team from the University of Barcelona, they developed synthetic molecules similar in structure to that of C1P. The team is being led by doctors Josefina Casas and Gemma Fabriás, from the *Consejo Superior para la Investigación Científica* (CSIC) and includes Doctor Antonio Delgado from the University of Barcelona. They are the pharmacists and organic chemists who provide the UPV/EHU team with the made-to-measure molecules.

50 analogues of C1P have been tested to date of which three have provided the desired results, i.e. an anti-inflammatory function without causing inflammation in other cells These analogues do not generate prostaglandin, as does C1P and, thereby, do not produce any inflammation.

The three analogues mentioned have been tested with smooth muscle cells, with macrophages and with cancerous lung cells. The best results were obtained with the second and third type of cell. These types have been chosen as having a strong response to pro-inflammatory molecules.

Inflammation and cancer

Inflammatory processes may have various causes, an infection, for example. Chronic inflammatory diseases also exist, such as ulcerous colitis or multiple sclerosis, where, due to a constant state of

inflammation, the cells are destabilised, provoking neoplasic processes, i.e. they generate new tissue of a tumorous nature. And this constant inflammation has great influence on the cells. They are destabilised and may cause an uncontrolled growth of the cells, even blocking their programmed death.

There are very few teams today researching the anti-inflammatory abilities of the C1P molecule - one team in Virginia (USA), the pharmaceutical company Novartis (Austria) and specific research teams such as that of Antonio Gómez-Muñoz, the first to investigate them in 1995. At present, the research is being undertaken at the cell level and shortly they should begin investigating with tissues and organs.

Source: Elhuyar Fundazioa