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Compounds that show potent anti-cancer activity in breast and colon tumour cell lines

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The Universitat Jaume I (UJI), the Spanish Centre for Advanced Scientific Research (CSIC) and the University of Pavia (UP) have patented new compounds with potent anticancer activity in breast and colon tumour cell lines that have low toxicity in healthy cells, which can dramatically decrease side effects during chemotherapy treatment. In addition, new compounds may also inhibit the expression of oncogenes (genes predisposing to cancer) by blocking the generation of telomerase and other proteins related to tumour activity.

According to Universitat Jaume I researcher Miguel Carda Usó, one of the most interesting aspects of the new compounds is the presence of parts of sugar in their chemical structure that "facilitate the entry into the cancer cells, allow reaching the chromosomes and preventing telomerase from conferring immortality to these cells."

As explained by the UJI researcher Eva Falomir, responsible for biological analyses, "these compounds act against telomeres, structures of the chromosomes that are shortened in each cell division. When the shortening is very prolonged, the cell ages and dies. This is natural, but in cancer cells shortening does not occur because an enzyme, telomerase, prevents the shortening of telomeres: tumour cells do not age and become immortal, so it is so difficult to fight them."

This encouraging finding is part of the new therapeutic strategies in oncology aimed at boycotting the mechanisms that serve the tumour cells for their uncontrolled proliferation. The group of researchers from the

CSIC Institute of Parasitology and Biomedicine, the UJI Group of Organic Synthesis and the UP Department of Chemistry have designed a series of small molecules or bonds that downregulate the expression of a variety of genes by joining the G-quadruplex (non-canonical DNA or RNA structures), thus causing inhibitory effects on aberrant cell growth.

As Carda explains, "before, antitumor treatments were very unspecific and caused side effects in other parts of the body not affected by the tumour. Treatments that are more specific are now being sought for each type of cancer, and these new compounds could be applied to personalized therapies that would lessen the side effects of oncological treatments." In this sense, the researcher Eva Falomir highlights as a direct consequence the selectivity of the new compounds towards tumour cells because "healthy cells, with less proportion of transport proteins, incorporate a small amount of anticancer compounds and are less affected."

The compounds designed may be the basis for the development of cancer drugs with high selectivity and low toxicity, because they have demonstrated a high efficiency to kill cancer cells, they have shown a low toxicity in non-tumour cells, and their synthesis is simple: it is achieved only in three reaction stages from accessible starting materials and with remarkable yields.

Another innovative aspect of these molecules is that they are directed to a new line of research of great potential, the G-quadruplex, considered as an emerging therapeutic target in oncology for its key role in DNA replication and translation. The technology is useful for the pharmaceutical industry, specifically for companies engaged in the development, manufacture and marketing of cancer treatments. At present, in vitro efficacy and toxicity studies have been performed with positive results, pending the initiation of clinical trials.

More information: Matilde Arévalo-Ruiz et al. Synthesis, Binding Properties, and Differences in Cell Uptake of G-Quadruplex Ligands Based on Carbohydrate Naphthalene Diimide Conjugates, *Chemistry - A European Journal* (2017). DOI: 10.1002/chem.201604886