NEW COMPOUNDS WITH POTENT ANTICANCER ACTIVITY

DESCRIPTION OF THE INVENTION

The Universitat Jaume I of Castelló (UJI), the Spanish National Research Council (CSIC) and the University of Pavia (UP) have developed and patented new compounds displaying highly potent anticancer activity against breast and colon tumoral cell lines. Moreover, the new potential drugs have shown low toxicity in non-tumoral cell lines, which can dramatically reduce side effects during chemotherapy treatment. Companies in the pharmaceutical sector are sought to transfer the compounds via patent licences or with which to collaborate in clinical trials.

In recent years, telomeres and the enzyme that forms them (telomerase) have attracted growing attention from leading research groups around the world, to such an extent that the scientists who discovered them were awarded the Nobel Prize in Medicine in 2009. Telomeres are nucleoprotein structures located at the ends of chromosomes and their main function is to stabilise and protect chromosomes by preventing them from degrading when replicating in the process of cell division.

Telomerase is deactivated in mature somatic cells, which explains why the telomeres shorten after each cell division and the cell dies when the telomere reaches a critical minimum length. In a large percentage of cancers, however, telomerase is activated, the telomeres of the tumoral cells retain their length and those cells do not die as a result of senescence and become *immortal*.

Understanding the role of telomeres and telomerase in the process of cell division allows the development of pathways to new therapeutic strategies in oncology aimed at hindering the mechanisms used by tumoral cells for their uncontrolled proliferation. One of these pathways, presented here and developed by researchers at the UJI, the CSIC and the UP, is characterised by the binding of ligands to G-quadruplex sequences.

G-quadruplexes (G4) are non-canonical DNA or RNA structures consisting of spontaneous arrangements of four strands of guanine bases stacked upon one another in DNA and RNA. These arrangements are present in telomeres and numerous gene promoters. It has been proved that the binding of ligands to these G4 sequences could, on the one hand, stabilise telomeres and block the mode of action of telomerase, thus making them eligible as anticancer drugs and, on the other hand, directly inhibit specific oncogenes.

This has been the approach taken by CSIC, UJI and UP researchers, who have designed a series of small molecules or ligands which, when binding to G4, lead to the inhibition of the transcriptional machinery and the down-regulation of expression of a variety of genes, with the resulting therapeutically useful inhibitory effects on aberrant cell growth. Such therapeutic effects are particularly strong in breast and colon tumoral cell lines.

Thus, the patented compounds NDI-359 and NDI-504 have proved to be highly efficient in killing cancer cells (IC50 = 0.1-0.4 µM). They have also exhibited a high degree of selectivity towards tumoral cells, since they show low toxicity in non-tumoral cells (HEK-293/MRC5, IC50 = 0.5-2.0 µM, ≈2-5x less toxic).

SECTORS FOR COMMERCIAL APPLICATION

The technology is useful for industry in the pharmaceutical sector and, more specifically, for those companies working on the development, manufacture and marketing of treatments against cancer.

TECHNICAL ADVANTAGES AND COMMERCIAL BENEFITS

The main advantages of the invention are:

- Potent anticancer activity: the compounds NDI-359 and NDI-504 display very potent anticancer activity against breast and colon cancer.
- Low toxicity and high selectivity: the compounds NDI-359 and NDI-504 show low toxicity in non-tumoral cell lines.
- Simple synthesis: the synthesis of the compounds is accomplished in only three reaction steps from readily accessible starting materials and with notable yields.

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The main innovative aspect of these molecules is that they represent a new therapeutic target with great potential. G4 are currently viewed as emerging therapeutic targets in oncology, since they play a key role in DNA replication and translation.

STAGE OF DEVELOPMENT OF THE TECHNOLOGY

The compound synthesis phase has finished. In vitro efficiency tests and toxicity studies have been carried out, and the results have been positive in both cases. Acute toxicity studies are currently being conducted with zebra fish. The next step is to start clinical trials.

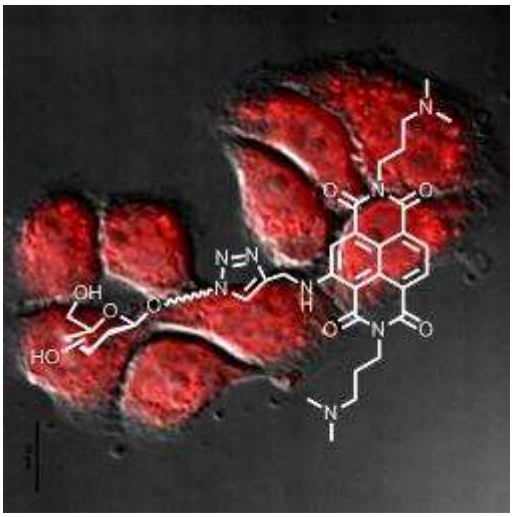
INTELLECTUAL PROPERTY RIGHTS

A Spanish patent has been applied for with the reference P201631265 and filing date 29 September 2016.

COLLABORATION SOUGHT

- Licence agreement for use, manufacture or commercial exploitation.
- Conducting clinical trials.

RELATED IMAGES



CONTACT DETAILS

Hugo Cerdà
Oficina de Cooperación en Investigación y Desarrollo Tecnológico (OCIT)
Universitat Jaume I, Castelló de la Plana (Spain)
Tel: +34 964387487
E-mail: hcerda@uji.es
Website: http://patents.uji.es