Cell differentiation as a novel strategy for the treatment of an aggressive type of skin cancer

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Skin squamous cell carcinoma (SCC) is a subtype of very aggressive skin cancers that usually develops in sunexposed body regions, but can also affect a large number of organs such as the bladder, esophagus, lungs etc. However, little is known about the biology of these cells, which consequently makes difficult the generation of new specific therapies; actually, the standard treatments are based on surgery and subsequent radiotherapy.

Researchers at the Spanish National Cancer Research Centre (CNIO) led by Erwin Wagner, vice-director of Basic Research and director of BBVA Foundation-CNIO Cancer Cell Biology Programme, have discovered a molecular mechanism that favours the disappearance and inhibition of SCC development. The authors propose that these mechanisms could be crucial for the development of targeted therapies that could potentially overcome drug resistance.

The study, which also involves the participation of medical researchers at the Medical University of Vienna, Austria, is published today on the online edition of The Journal of Clinical Investigation.

"The guardian of the genome" p53, decreases cell division in favour of cell differentiation

Using in vitro models, mouse genetic models and human tumors, researchers have uncovered the molecular signals by which the p53 protein, also called "the guardian of the genome", prevents the formation of skin SCC tumors.

"We demonstrate for the first time that p53 promotes differentiation [cell functional specialization] of keratinocytes [the most predominant cell type in the epidermis], thus avoiding their division and providing a protective effect against tumors", states Juan Guinea Viniegra, "Ramón y Cajal" investigator at the CNIO and first author of the work.

The alteration of these pathways decreases cell differentiation and hence produces an increase in cell division. "We found that samples from patients with skin SCC show reduced activity of proteins that promote cell differentiation and an overactivation of inhibitory signals," says Guinea.

An additional contribution of this work is the use of compounds that induce cell differentiation at the expense of cancer cell division. "The next step is to test these molecules in mouse models of skin cancer and assess whether they impair cell division and tumor development", reveals the author.

Treatment of tumors based on differentiation therapies is a new avenue in the development of innovative cancer treatments. These therapies, unlike conventional ones, seek to transform cancer cells into differentiated cells, which remain in the body with few possibilities to divide and likely avoiding the appearance of drug resistance.

More information: Differentiation-induced skin cancer suppression by FOS, p53, and TACE/ADAM17. Juan Guinea-Viniegra, Rainer Zenz, Harald Scheuch, María Jiménez, Latifa Bakiri, Peter Petzelbauer, Erwin F. Wagner. *The Journal of Clinical Investigation* (2012). DOI: :10.1172/JCI63103

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