# BRG1 mutations confer resistance to hormones in lung cancer

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Retinoic acid (vitamin A) and steroids are hormones found in our body that protect against oxidative stress, reduce inflammation and are involved in cellular differentiation processes. One of the characteristics of tumours is that their cells have lost the ability to differentiate; therefore these hormones have useful properties to prevent cancer. Currently, retinoic acid and steroids are being used to treat some types of leukaemia.

A study led by the research group on Genes and Cancer of the Bellvitge Biomedical Research Institute (IDIBELL) has shown that the loss of BRG1 gene implies a lack of response of cells to these hormones, and therefore the tumour may continue growing. Study results have been published in the journal *EMBO Molecular Medicine*.

**BRG1 gene**

The IDIBELL research group on Genes and Cancer led by Montse Sanchez-Cespedes discovered some years ago that the BRG1 gene, a tumour suppressor, is inactivated in non-small cell lung cancer by genetic mutations. "The BRG1 protein is part of a chromatin remodelling complex that regulates the expression of several genes", explains the researcher, "and it is related to the differentiation of lung cells, allowing cells response to certain hormones and environment vitamins like vitamin A or steroids."

When BRG1 is mutated and therefore inactive, tumour cells do not

respond to the presence of these hormones and they continue growing and spreading. For this reason, these types of tumours are refractory to the treatment with these substances.

## Clinic Application

"At the moment", says Montse Sanchez-Cespedes, "we are not able to restore the functionality of a tumour suppressor gene as BRG1 in patients. Therefore, we are still far from a therapeutic application but this discovery enables us to understand better the biology of tumours. What we will try to do in the immediate future is to look for agents that specifically destroy the cells with mutated BRG1, following the strategy of lethal synthetics".

In any case, this finding it can be useful in advancing personalized medicine, because "it explains why lung cancer patients are resistant to these treatments and may serve to rule out therapies with lipid-derived hormones in patients with BRG1 mutations, not just in lung cancer but also in breast and prostate, among others."

**More information:** The tumor supressor and chromatin remodeling factor BRG1 antagonizes Myc Activity and promotes cell diferentiation in human cancer. *EMBO Molecular Medicine*. Doi 10.1002/emmm.201200236

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