

International study approaches new therapeutic strategies for lung cancer

June 4 2020



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The international study "Resistance to targeted therapies as a multifactorial, gradual adaptation to inhibitor specific selective pressures," recently published in the scientific journal *Nature Communications*, has taken a further step in the development of new therapeutic strategies to treat lung cancer.

This study, the result of more than three years of research, was conducted at the Moffitt Cancer Center in Tampa (Florida, USA) and makes progress toward the evolution of resistance to different tumor inhibitors. Scientist Robert Vander Velde is the main author of it.

"Although the use of specific inhibitors targeted against a tumor often induces good clinical results at initial stages, certain cell populations might not be completely eliminated, acquiring resistance to treatments and developing relapse as tumor recurs," explains Diego Lozano, researcher of the Supercomputing and Bioinnovation Center (SCBI) of the University of Malaga (UMA) and one of the authors of this study.

Resistance to tumor inhibitors

Using an in vitro model of isolated ALK positive [cells](#) of a specific type of lung cancer, namely, non-small or non-microcytic cell [lung cancer](#), researchers explored the evolution of resistance to different clinical ALK inhibitors.

"We demonstrated that the acquisition of resistance to [tumor](#) inhibitors not only arises from the pre-existence of cell subpopulations in mutations that enable tumors to survive drugs, or due to emergence of point mutations that confer such resistance, but from a gradual and

predictable adaptation to the selective pressures of the different ALK inhibitors, at the genetic and epigenetic level," says the researcher of the UMA.

Opportunity for more effective therapies

Lozano explains that during the evolution of drug resistance, intermediate [cell populations](#) present collateral sensitivity to other inhibitors, thus providing a temporary opportunity to apply effective therapies.

"The findings of this study could be transferred to other similar scenarios, where tumors also acquire [therapy](#) resistance," clarifies Lozano, who guarantees that by understanding the evolutionary mechanisms and trajectories of drug resistance in [tumor cells](#), evolutionarily-informed therapies could be designed.

More information: Robert Vander Velde et al, Resistance to targeted therapies as a multifactorial, gradual adaptation to inhibitor specific selective pressures, *Nature Communications* (2020). [DOI: 10.1038/s41467-020-16212-w](#)

Provided by University of Malaga

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