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New study finds molecular mechanisms that control Rb2/p130 gene expression in lung cancer

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Despite innumerable studies on lung cancer, many aspects of the disease have yet to be understood, including the role played by the retinoblastoma-related protein Rb2/p130 in the evolution of the disease.

In a new study, researchers from the Sbarro Health Research Organization Center for Biotechnology Research (SHRO), a cancer, cardiovascular and diabetes research center located in the College of Science and Technology at Temple University in Philadelphia, PA, and at the University of Siena in Siena, Italy examined mechanisms that control Rb2/p130 gene expression in lung fibroblasts and characterize the effects of Rb2/p130 deregulation on the proliferative features of lung cancer cells. Most importantly, their findings reveal why the gene is expressed differently in small and nonsmall lung cancer cells.

The study was funded by SHRO and the Human Health Foundation, a nonprofit biomedical research organization in Terni, Italy. It was published in *Molecular Cancer Research*.

The new findings disclose the mechanism controlling Rb2/p130 gene expression in lung cells, and that involve two relatively new proteins, CCCTC-binding factor (CTCF) and BORIS (CTCF-paralogue).

"Our research shows that CTCF and BORIS directly regulate Rb2/p130 gene expression in lung cells," says Marcella Macaluso, Ph.D., one of the

authors of the study. "We observed that in small lung cancer cells Rb2/p130 exhibits low expression levels, while in non- small lung cancer cells it is overexpressed compared to normal lung cells. However, until now, there were insufficient and conflicting data that did not allow us to precisely link the deregulated expression of Rb2/p130 in lung cancer cells with the genetic mutation of this gene. This study finally disclosed the mechanism and the players controlling Rb2/p130 expression, and these findings have the high potential to provide important information for understanding the proliferative and antiproliferative signals triggered by Rb2/p130."

Also, the research shows that Rb2/p130 is engaged in a complex network of interactions with DNA methyltransferases (DNMTs) and other proteins, including CTCF and BORIS, that are involved in the epigenetic control of chromatin organization and transcription. This complex network of proteins seems to regulate cellular senescence – or aging -- that is a potent anti-cancer mechanism.

"Our studies may provide new insights into the molecular pathways that that are active and correlated to Rb2/p130 expression, new biomarkers for an early diagnosis of lung cancer and/or predictive factors to determine the effect on tumor treatments and insights into the development of therapies based upon clinical modulation of Rb2/p130, CTCF and/or BORIS expression," says Dr. Macaluso.

Provided by Sbarro Health Research Organization

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