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New marker of drug response may speed pace of lung cancer prevention trials

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Testing medicines to prevent lung cancer requires treating many thousands of high-risk individuals and then waiting 5, 10 or 15 years to discover which of them develop cancer and which, if any, experience survival benefit from the treatment. A University of Colorado Cancer Center study recently published in the journal *Cancer Prevention Research* proposes a possible waypoint on the way to benefit, which if validated, could dramatically reduce the number of patients needed and time required to test drugs for lung cancer prevention.

"Chemoprevention is an important approach that has been way behind in terms of scientific advances for lung cancer," says Fred R. Hirsch, MD, PhD, investigator at the CU Cancer Center and professor of medical oncology and pathology at the CU School of Medicine. "If we could find a surrogate endpoint for lung cancer mortality – an intermediate endpoint – it would make it much easier to conduct smaller trials in much shorter time."

The original intent of the study was to discover certain microRNAs whose level of expression might predict patients likely to respond to the possible chemopreventive drug, Iloprost. If an especially high or low microRNA expression predicted response, it would allow researchers to test the drug only in the population most likely to benefit. Unfortunately, while levels of seven miRNAs were found to be correlated with the appearance of lung cancer, none predicted response to the drug.

It might have been a dead-end study if it weren't for microRNA-34c.

To a striking degree, changes in the expression of this molecule six months after treatment correlated with benefit from the drug seen much later. In those who later showed benefit, microRNA-34c expression was down six months after treatment; in patients who showed no benefit, microRNA-34c expression remained unchanged.

"Instead of waiting for an endpoint 15 years in the future, we could potentially discover the effectiveness of chemopreventive agents only six months after treatment. It would speed up the pace of discovery and eventually bring new chemopreventive agents much faster to the market," Hirsch says.

Hirsch cautions that his discovery, with CU Cancer Center colleagues including Celine Mascaux, MD, PhD, of this potential intermediate endpoint is just that: potential. Further work is needed to validate the predictive power of miRNA-34c in showing chemopreventive response. But Hirsch and colleagues are hopeful not only that miRNA-34c could be this predictive waypoint, but that the cutting edge technique of looking beneath genes, beneath even RNA and mRNA into the molecular world of microRNA will help them discover the roots of the disease.

"The approach is new and it needs to be further explored," Hirsch says.

Provided by University of Colorado Denver