Research targets metformin as breast cancer prescription

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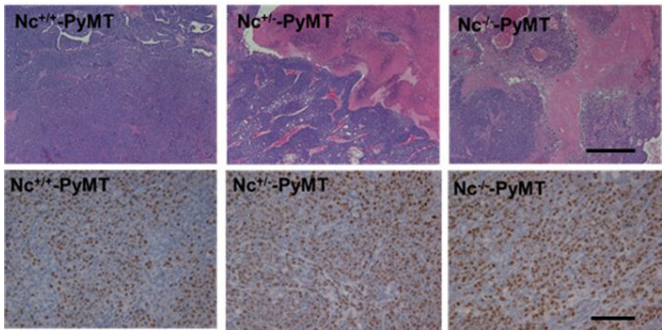

Credit: LSU Health

Research conducted by Suresh Alahari, Ph.D., Professor of Biochemistry and Genetics at LSU Health New Orleans School of Medicine, has found that metformin, a commonly prescribed drug for Type 2 Diabetes, may be effective in treating cancers that lack a protein called Nischarin. The findings are published online in the *International Journal of Cancer*.

Dr. Alahari discovered Nischarin, a protein involved in many biological processes that also acts as a tumor suppressor. Much of his research on this novel protein has been in breast cancer. In the current study, his lab showed that disruption of the Nischarin gene delays mammary gland development, enhances tumor growth and metastasis, and also decreases activation of an enzyme called AMPK. AMPK plays a major role in metabolism and is considered to be a therapeutic target for metabolic diseases and even some cancers. Metformin's precise mechanism of action remains unclear, but it appears to work at least partly through the activation of AMPK.

"The clinical documentation that diabetic patients on a metformin regimen display reduced risks of developing cancer poses the tantalizing possibility that this approach to treating cancer might prove to be an effective and unrealized therapeutic opportunity," says Alahari.

In this study, the researchers showed that metformin activates AMPK and has a strong inhibitory effect of growth on tumors that do not express functional Nischarin, suggesting metformin has a great therapeutic value in Nischarin-lacking tumors.

"We found that Nischarin-deleted tumor cells had lower AMPK activity than Nischarin-positive cells," notes Alahari, "and that metformin treatment activated AMPK more efficiently in Nischarin-deleted mice, and metformin suppressed tumor growth of Nischarin-deleted mice. Collectively, our data suggest that Nischarin disruption promotes breast tumor development, AMPK signaling is important for Nischarin-mediated suppression of breast tumors, and activation of AMPK by metformin suppresses breast tumor growth in Nischarin-lacking mice."

These findings have added clinical significance because Nischarin expression is frequently reduced in human breast cancer, especially triple negative breast cancers, and is associated with reduced long-term survival.

"The discovery that the effectiveness of certain drugs, such as metformin, are influenced by the level of Nischarin expression could help identify specific patients in whom it is most likely to prove beneficial," Alahari adds. "In this way, Nischarin expression could serve as a biomarker to help inform decisions in management by identifying a subset of patients most likely to benefit from AMPK activator therapies."

More information: Shengli Dong et al, Knockout model reveals the role of Nischarin in mammary gland development, breast tumorigenesis and response to metformin treatment, *International Journal of Cancer* (2019). DOI: 10.1002/ijc.32690

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