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Discovery means individualized ovarian, brain cancer therapies

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Mayo Clinic researchers have discovered that a molecular communication pathway—thought to be defective in cancer—is a key player in determining the effectiveness of measles virus oncolytic cancer treatment in ovarian and aggressive brain cancers. This discovery enabled researchers to develop an algorithm to predict treatment effectiveness in individual patients. The findings appear in the *Journal of the National Cancer Institute*.

"This discovery and algorithm will allow us to personalize cancer treatment by matching the most appropriate patients with oncolytic virus therapies," says Evanthia Galanis, M.D., senior author of the study. "We'll also know which ones can be helped by combining cancer virotherapy with other immune approaches.

This activation channel, known as the interferon response pathway, had been considered defective in cancer cells. Not so, according to the research team. They performed tests for gene variants and signatures that would identify pathways that resisted the effectiveness of the virus-based treatments that Mayo Clinic has long been developing.

The researchers tested their algorithm on human ovarian and brain tumors transplanted into mice and patients in phase one clinical trials. What they found is a weighted gene signature that could predict treatment sensitivity and resistance. Subsequent research also showed that repurposing ruxolitinib, a drug approved to treat malignant blood disorders, was able to overcome the resistance. This drug, which targets

the interferon response pathway, allows the measles virotherapy to increase effectiveness by a factor of 1,000.

The researchers say these findings will help select patients for future clinical trials involving oncolytic viruses and shape how those viruses are designed and used in medicine, including the development of effective combination therapies.

Provided by Mayo Clinic