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nature COMMUNICATIONS

CDK4/6 inhibitors target SMARCA4-determined cyclin D1 deficiency in hypercalcemic small cell carcinoma of the ovary

Yibo Xue, Brian Meehan, Elizabeth Macdonald, Sriram Venneti, Xue Qing D. Wang, Leora Witkowski, . . . Janusz Rak, Barbara Vanderhyden, William D. Foulkes & Sidong Huang

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SMARCA4 loss is synthetic lethal with CDK4/6 inhibition in non-small cell lung cancer

Yibo Xue, . . . Janusz Rak, William D. Foulkes & Sidong Huang

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Dr. William Foulkes, with collaborators at the Goodman Cancer Research Centre at McGill University, has shown that a drug currently in use against estrogen positive breast cancer may be effective in treating small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) and non-small cell lung cancer (NSCLC). The results are published simultaneously in two papers.

The breakthrough discovery launching this research came in 2014 when Dr. Foulkes showed that SCCOHT, a rare but highly fatal cancer which primarily strikes younger women, is caused by mutations in the gene SMARCA4. The challenge became how to knock out this particular gene in order to inhibit progression of the tumor. Subsequent work by Dr. Sidong Huang at McGill, identified that targeting the cyclin-dependent kinase 4/6 (CDK4/6) exposed a vulnerability in SMARCA4. What's clinically exciting about this work is that CDK4/6 inhibitors have been used for years, so they are very well known and their safety profile is established.