Small-cell carcinoma of the ovary, hypercalcaemic type

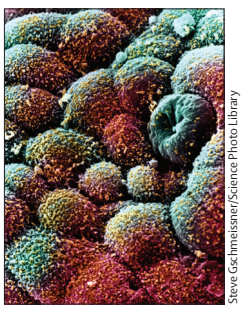
Next-generation sequencing has unequivocally associated the chromatin-remodelling gene *SMARCA4* with small-cell carcinoma of the ovary, hypercalcaemic type (SSCOHT). Roughly 13 women, with an average age of about 24 years, are diagnosed with this cancer every year in the UK, most of whom die within 1–2 years; indeed, mortality rates are high even for those who present with early-stage disease. The link of this disorder with *SMARCA4*, which has previously been associated with cancers of the lung, brain, and pancreas, might have a bearing on its resistance to platinum-based chemotherapy. "It is an Achilles' heel—we can use this information very rapidly to look for treatment options", affirmed co-author Jeffrey Trent (Translational Genomics Research Institute, Phoenix, AZ, USA). His paper was one of three published this week to reach the same conclusion about *SMARCA4*'s role as a genetic driver of SSCOHT.

Trent's group did whole-genome sequencing and whole-exome sequencing on tumours and germline samples taken from 12 patients with SSOCHT, and on the SSOCHT cell-line BIN-67. They identified inactivating germline and somatic mutations in *SMARCA4* in nine patients, and SMARCA4 protein loss in 14 of 17 tumours. For comparison, they analysed 485 primary ovarian tumours from other types of cancer—only two of which showed the same protein loss. "Loss of SMARCA4 protein expression is extremely specific to SCCOHT and can facilitate the differential diagnosis of SCCOHT", concluded the researchers. They added that their findings might suggest that the gene plays a part in tumour suppression.

"They've certainly proven that this technology has the ability to interrogate the entire genome at once and yield clear and unequivocal results", commented Steven Narod (University of Toronto, ON, Canada). "But one piece of the puzzle that is missing is how high is the risk of cancer for a woman with this mutation." Trent's group identified two patients, diagnosed at age 9 and 10 years respectively, with germline mutations. In theory, these cancers could have been prevented by a preventive oophorectomy; however, whether this procedure should be recommended for a child is unclear.

As for future research, Trent is in no doubt that we will see more of *SMARCA4*. "Expect this gene to have importance in other, more common cancer types. There is no question about that", he told *The Lancet Oncology*.

Talha Khan Burki



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DNA test offers new option for colon cancer screening

A multitarget stool DNA test has proven to be the most sensitive non-invasive test yet for detection of colon cancer and advanced pre-cancerous colorectal lesions. In a study of 9989 asymptomatic average-risk participants, screening for colon cancer was done for each person by three methods: stool DNA test, faecal immunochemical test (FIT) for haemoglobin, and colonoscopy. Colonoscopy results were used to identify the test's accuracy. The DNA test—which detects haemoglobin and cancer-related changes in DNA—had greater sensitivity than FIT for detection of colon cancer (92·3% [95% CI 83·0–97·5] *vs* 73·8% [61·5–84·0]) and advanced precancerous lesions (42·4% [38·9–46·0] *vs* 23·8% [20·8–27·0]). However, in participants with negative colonoscopy results (n=4457), 455 (10%) received a positive result with the DNA test versus 162 (4%) with FIT.

First author Thomas Imperiale (Indiana University Medical Center–Regenstrief Institute, IN, USA) said that, should the DNA test receive approval from the US FDA, "the next study that is most important to do is to determine the optimal frequency or interval for the DNA test; these data will likely surface in preliminary form in 2014." He added that investigators would also analyse the effectiveness and cost-effectiveness of the test, which will probably become available in 2014.

Douglas Robertson (White River Junction Veterans Affairs Medical Center, VT, USA; and Geisel School of Medicine at Dartmouth, Hanover, NH, USA), commented that, "these are encouraging results—they show a clear improvement in this technology, which is exciting". He cautions, "once this test becomes available, we'll need more real-world compliance data and effectiveness data. We don't yet know how this will translate into clinical practice…or what the impact of this test will be until those types of studies are done."

Incidence of colon cancer in the USA in 2001–10 decreased by 30% in people aged 50 years and older, according to a report from the American Cancer Society. This decrease was largely due to the increasing numbers of patients aged 50–75 years undergoing colonoscopy screening during this time. Imperiale said, "If the DNA test is approved, the hope is that it will enhance the uptake and adherence to colorectal cancer screening by providing another [screening] option….One in three Americans are not current with their colon cancer screening; we're hoping to bring this number down to 20% or less."

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