

To mimic what happens in actual tumors, researchers utilized a breast cancer cell line that created indolent tumors when xenografted into mice. From the same cell line, they generated a panel of 18 subpopulations, or subclones, by overexpressing in each subclone a different protein linked to cancer progression.

They then compared the phenotypic properties of tumors and clonal expansions in two experiments. In the first, mice were implanted with a single subclone that competed against its parental cells at a 1:18 ratio. In the second, mice were implanted with a mixture of the 18 different subclones. In both experiments, subclones that overexpressed the protein IL11 were able to drive tumor growth. In contrast, a subgroup that overexpressed the protein LOXL3 did not increase cancer growth despite taking over a large portion of the tumor.

“The minor subpopulation of IL11-expressing cells never grew to become a dominant clone, but it was still responsible for driving tumor outgrowth,” says Polyak, adding that IL11 appears to change the tumor microenvironment by recruiting stromal cells and promoting angiogenesis.

Researchers also observed that when all 18 subclones were present in the same tumor, they interfered with one another’s expansion. “Clonal interference can limit tumor growth,” Polyak says. “Decreasing heterogeneity—which sometimes happens in treatment—is not always good because you might be favoring the growth of cancer cells with less favorable properties such as those resistant to treatment.”

The best treatment approach, she says, would be to develop drug combinations based on the heterogeneity of the tumor. Currently available drugs could be applied more effectively if scientists better understood their effects on the tumor, says Polyak.

“Further studies will hopefully help us identify and target the true drivers and potentially slow down the growth of the tumor, even if we cannot cure it,” she says. ■

## Regulation May Stifle Research in Europe

The European Society for Medical Oncology (ESMO) is worried that a

proposed European Union (EU) General Data Protection Regulation about the handling of personal data could have unintended consequences for cancer research. Specifically, ESMO is concerned that the wording of the regulation might be interpreted as requiring a patient’s explicit—and repeated—consent prior to using their data or tissue samples in any new studies.

Such a stipulation “may put at stake the survival of retrospective clinical research, biobanking, and population-based cancer registries in the EU,” writes Paolo Casali, MD, author of the official ESMO position paper, published in August and endorsed by nine other European cancer-related organizations (*Ann Oncol* 2014;25:1458–61). Repeatedly needing to seek consent would be “time-consuming, administratively burdensome, expensive, and intrusive into patients’ lives,” he says.

Instead, ESMO calls for a “broad, one-time consent.” This way, fully informed patients could agree from the outset that their data and/or tissues can be used for future research unless they specifically withdraw their consent. This arrangement would mitigate the risk of cancer research grinding to a halt due to the need to obtain explicit consent for each new study.

The paper notes that existing safeguards at biobanks already adequately protect a person’s privacy, and that adapting those safeguards as new situations arise should provide continued protection. Furthermore, Casali says that the publication of research studies involves aggregate data, not individual results or identities.

When it comes to population-based studies, Casali argues that if individual patients are allowed to opt out, “the relevant registry will be incomplete or unrepresentative, and can lead to incorrect conclusions.” Even if the number of patients opting out is small, obtaining consent from everyone in a country or region “would be almost impossible.”

The European Commission, European Council, and European Parliament are still determining their respective positions on the regulation, after which joint negotiations over the final text will begin, likely in 2015. ■

## New Grants to Boost Genome Sequencing

The National Human Genome Research Institute (NHGRI), part of the NIH, awarded \$14.5 million in grants in August to eight groups of researchers in industry and academia who are working to make genome sequencing speedier, more accurate, and more informative.

Thanks to next-generation techniques, the cost of sequencing a human genome has plunged by more than 99% in less than 10 years, and now runs as low as \$1,000. Plummeting prices have opened up numerous opportunities for researchers, such as sequencing full tumor genomes to uncover gene variants that drive abnormal growth. But for clinical uses, “it’s still more expensive than you want it to be for an individual patient,” says Mark Akesson, PhD, of the University of California Santa Cruz Genomics Institute, who received one of the grants.

The awards are the most recent—and the last—from the NHGRI’s Advanced DNA Sequencing Technology program, which began in 2004. Over the last 10 years, the program “has in my opinion been just critical for advancing sequencing technology,” says Jay Shendure, MD, PhD, of the University of Washington in Seattle, who’s also a grant recipient.

Four grants went to researchers who are seeking to improve what may be the next big thing in genome sequencing: nanopore sequencing. Next-generation sequencing involves breaking up DNA into small chunks that can be less than 100 bases long. Copying and sequencing the pieces produces “reads,” and software assembles the jumble of reads into a full genome. Nanopore sequencing, in contrast, works by reeling DNA strands through tiny holes, or nanopores, in a lipid layer or other material. An electrical current passes through each nanopore, and as the DNA strand moves through the pore it causes characteristic changes in the current that allow researchers to determine the identity of the DNA bases.

Research labs already perform nanopore sequencing, and the first commercial device, the size of a flip phone, is being beta tested. The advantage of nanopore sequencing is that it