

Calling on the cancer sleuths: how cell biologists will do the detective legwork of the postcancer genome era

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High-throughput efforts of the past decade have afforded us with the first impressions of how the whole genome actually changes in a patient's cancer. Computational approaches are playing an integral role in tackling this flood of information, but it has also become clear that cancer will not be cured by improving p values, just like a Manhattan murder mystery will not be solved by going through the phone book.

This year's ASCB Minisymposium on Cancer and Cancer Microenvironment featured some insightful examples of how cell-based research can efficiently use whole-genome information and lead to "actionable intelligence" in our fight against cancer.

Euan Slorach, working in the lab of Zena Werb at the University of California, San Francisco (UCSF), identified a breast cancer oncogene in an amplified region on chromosome 8 that had been linked to disease progression and reduced survival. One of the genes,

Zeppo1, stood out as an orthologue of a gene for *Drosophila* trachea development. Because several such orthologues from *Drosophila* act in the developing mammary gland, they hypothesized that *Zeppo1* might regulate breast architecture. In mammary epithelial cells, the transcription factor induces epithelial to mesenchymal transition, and it causes tumors and metastatic spread in a xenotransplant model. Their data illustrate how a hypothesis derived from organ development in a different species can help solve a cancer problem: "I think it provides further support to the idea that cancer can be viewed as development gone astray," says Slorach. *Zeppo*-specific inhibition might even be beneficial beyond the context of the amplicon, according to their xenotransplant data. We will need to learn more about the role of *Zeppo1* in normal tissue as its suppression is entertained as a therapeutic approach. The derived preclinical mouse models will be key to answering such questions. There might even be benefits according to Groucho Marx, who said that "we're twice as funny without *Zeppo*."

When breast cancer metastasizes to the lung, the deposited cells often lay dormant for years at the distant site. **Hua Gao**, working with Filippo Giancotti at Memorial Sloan Kettering, expressed the transcriptome of a highly metastatic cell line in a dormant cell type to identify genes that trigger distant awakening in vivo. Their expandable method successfully identified genes that precipitate lung-specific metastasis and generate expression signatures that have been associated with metastatic relapse to the lung in patient samples.

Presentations focusing on the genetics of lethal prostate cancer (**Lloyd Trotman**, Cold Spring Harbor Laboratory), on the connection between breast tumor progression and mechanical cues (**Jose Lopez**, from the Valery Weaver lab, UCSF), the interplay of angiogenesis and cell adhesion in glioblastoma (**Joseph McCarty**, MD Anderson), and novel mechanisms behind attracting metastatic cells (**Dan Ishihara**, lab of Dianne Cox, Albert Einstein College of Medicine) perfectly illustrated how the cancer cell community is working on a seamless zoom—from a global view of the cancer genome down into the street view of molecular interactions—in unprecedented detail. It is also up to this community to ensure that we help translate these results into ever more faithful cancer models and cancer therapy.

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