Cancer: Getting the Big Picture

Outlining trends in cancer gene expression

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Genetic profiling is providing a new slant on cancer. In the July issue of *Genome Biology*, researchers in the Informatics Program (CHIP) at Children's Hospital Boston showed that cancers can be divided into three distinct groups, which could provide new insight into patient prognoses and possibly alter treatment decisions.

Traditionally, scientists studying cancer have devoted a great deal of attention to individual genes, boosting or suppressing their activity in the laboratory to tease out their respective roles in tumor formation. The CHIP researchers opted for a more holistic approach, systematically comparing the genetic profiles of a broad range of cancers to those seen during embryonic development, which allowed them to sort gene expression patterns in cancer along a continuum.

"Basically, there are three major groups in this continuum," says Kamila Naxerova, first author on the study and a graduate student working with CHIP director and senior author Isaac Kohane, MD, PhD. "The first has stem-cell-like and proliferative expression patterns similar to early development; another group expresses many genes linked to inflammation and is reminiscent of late development. The third is intermediate, falling somewhere between the other two."
The map describes three groups of human cancers, showing similarities in gene expression between different tumor-types and a range of developmental processes. Cancers in group 1 reactivate many early developmental genes; those in group 3 have gene activity patterns resembling late development. Red indicates a strong correspondence between gene expression in the cancer versus that in development, and green a weak relationship; black is intermediate.

Such "developmental timing" of tumors could potentially provide important information about a cancer's prognosis, adds Naxerova. Cancers with active genes characteristic of early development are generally undifferentiated and grow aggressively; cancers in the late developmental group are more indolent, with lower growth rates.

Naxerova and colleagues were surprised at some of the cancers that wound up in the same category. For instance, both adenocarcinoma--the most common form of lung cancer--and Wilms' tumor, a type of pediatric kidney cancer, landed in the early developmental group. "It's not what I would have expected, since these tumors arise under very different circumstances and are associated with different DNA alterations," says Naxerova. "But grouping cancers in this developmental context could provide a different therapeutic strategy."

In other words, as unlikely as it seems, drugs effective against lung cancer could well be used to treat kidney tumors in children.

"We're trying to capture a tumor's macroscopic properties," says Naxerova. "We're really going after the big picture here."

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Children's Hospital Boston is home to the world's largest research enterprise based at a pediatric medical center, where its discoveries have benefited both children and adults since 1869. More than 500 scientists, including eight members of the National Academy of Sciences, 11 members of the Institute of Medicine and 12 members of the Howard Hughes Medical Institute comprise Children's research community. Founded as a 20-bed hospital for children, Children's Hospital Boston today is a 397-bed comprehensive center for pediatric and adolescent health care grounded in the values of excellence in patient care and sensitivity to the complex needs and diversity of children and families. Children's also is the primary pediatric teaching affiliate of Harvard Medical School. For more information about the hospital and its research visit:
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