differentiated keratinocytes also had significant numbers of lung metastases.

Aware that melanoma cells express the Notch receptor, and that one of its ligands, DLL1, is expressed in differentiated keratinocytes, the researchers were not surprised to observe significant Notch activity when both cell types were co-cultured. Analyses of patient samples showed that melanoma cells far from DLL1-expressing differentiated keratinocytes remained noninvasive; on the other hand, direct contact between these cells induced Notch signaling and dermal invasion.

"Melanoma cells have to reach a particular microenvironment within the epidermis where Notch ligand–expressing cells reside," Levy says. "Once contact is made, it triggers an entire cascade of events, leading to metastasis."

Next, the researchers investigated this cascade in greater molecular detail. They found that in noninvasive melanoma cells, the proteins MITF and RBPJK cooperatively bind to and repress miR-222/221, two microRNAs in close proximity to each other. The Notch receptor's intracellular domain—cleaved when direct interaction of melanoma cells with differentiated keratinocytes activates Notch signaling—interferes with this repression by removing MITF; subsequently, miR-222/221 is activated and precipitates melanoma cells' ability to invade the dermis.

"This [study] sheds significant light on the complex relationships between malignant and nonmalignant cells in tumor microenvironments," says Marc Ernstoff, MD, director of the melanoma program at Cleveland Clinic's Taussig Cancer Institute, OH. "Understanding the pathways by which melanoma turns invasive, and how normal cells nearby contribute, will allow us to develop therapeutic strategies that can change the biological behavior of primary tumors."

For instance, Levy envisions delivering Notch inhibitors directly to the epidermis—perhaps via a skin cream. Then "patients with atypical moles could receive anti-Notch treatment, even while being monitored," she says.

"Melanoma's gestation is a lengthy one," Levy adds, "and as we uncover more of this disease's early events, we may someday be able to prevent metastasis altogether." ■

Five New Experts Appointed to NCAB

Five new cancer experts were appointed in June by President Barack Obama to serve on the National Cancer Advisory Board (NCAB).

Established in 1971, the NCAB consists of 18 members, including 12 distinguished leaders from health and scientific disciplines, and six representatives of the general public, including experts in the fields of public policy, law, health policy, economics, and management. Members serve overlapping 6-year terms.

The group advises the NCI director, the secretary of the U.S. Department of Health and Human Services, and the president on issues related to the NCI's operations, including its programs and future direction. According to its charter, the NCAB may also review applications for grants and cooperative agreements for research and training, and recommend the approval of "projects that show promise of making valuable contributions to human knowledge."

The NCAB's newest members are:

- Peter C. Adamson, MD, chair of the Children's Oncology Group at The Children's Hospital of Philadelphia, PA;
- Deborah Watkins Bruner, RN, PhD, associate director for outcomes research at Emory University's Winship Cancer Institute in Atlanta, GA;
- Yuan Chang, MD, chair of cancer virology at the University of Pittsburgh Cancer Institute, PA;
- Timothy J. Ley, MD, director of stem cell biology at the Washington University School of Medicine in St. Louis, MO;
- Max S. Wicha, MD, deputy director of the University of Michigan's Taubman Medical Research Institute in Ann Arbor.

Like his colleagues, Adamson is honored to be part of the NCAB. "Having a pediatric oncologist on board is important to the childhood cancer community," he says. ■

For more news on cancer research, visit *Cancer Discovery* online at http://CDnews.aacrjournals.org.

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- According to a published report on a phase III trial, **patients with metastatic prostate cancer who underwent six cycles of docetaxel chemotherapy along with a hormone blocker survived for a median of 57.6 months,** compared with a median of 44 months for those who received only the hormone blocker (N Engl J Med 2015;373:737–46). The results will likely change standard practice, which has been to withhold chemotherapy until hormone blockers become ineffective.
- **Seven congressional representatives introduced a bill to establish the nation's first registry to track patients with mesothelioma.** The registry would allow researchers, health care professionals, and patients to search information about diagnosis, disease trends, risk factors, treatment availability, and outcomes.
- **Bristol-Myers Squibb launched its Immuno-Oncology Rare Population Malignancy Program** in the United States. The program is a multi-institutional initiative with academic-based cancer centers to investigate immunotherapies for high-risk, poor-prognosis cancers, defined as a rare population malignancy. A rare population malignancy is a subpopulation within a higher-incident disease population, such as BRCA1 and BRCA2 breast cancers.
- **The FDA approved carfilzomib** (Kyprolis; Onyx Pharmaceuticals) in combination with lenalidomide and dexamethasone for the treatment of patients with relapsed multiple myeloma who have received one to three prior lines of therapy. The drug was previously approved as a monotherapy for a subset of patients with multiple myeloma.
- **A proposed rule in Massachusetts would limit prices on drugs,** especially very high-priced agents such as newer, targeted therapies for cancer. In addition, the law would "force biotechnology and pharmaceutical companies to justify their prices," *The Boston Globe* reported.
- A recent study found that **about 10% of serious and unexpected complications are not reported to the FDA by drug manufacturers within 15 days,** as directed by federal regulations, a delay that could compromise the safety of other patients (JAMA Intern Med 2015 July 27 [Epub ahead of print]).