Skin cells may provide early warning for cancer risk elsewhere in body

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(PhysOrg.com) -- While some scientists have argued that cancer is such a complex genetic disease that you'd have to sequence a person's complete genome in order to predict his or her cancer risk, a University of California, Berkeley, cell biologist suggests that the risk may be more simply determined by inexpensively culturing a few skin cells.

Harry Rubin, professor emeritus of molecular and cell biology at UC Berkeley, acknowledges that cancer cells have mutations in hundreds of genes, making it hard to determine which are the key triggers and making prognosis and treatment equally difficult. Even normal tissue differs from person to person because of a myriad of less disruptive mutations and because of different environmental exposures, both of which affect future cancer risk.

But in the September issue of the journal *Cancer Epidemiology, Biomarkers and Prevention*, Rubin argues that, while it may be hard to dissect the role of each of these mutations, their collective effect should be observable in tissue before any cancers develop.

Specifically, increases in how densely the cells grow, which Rubin argues are a prelude to cancer, may be detectable even before the cancer appears, warning of risks that could be lessened by behavioral changes.

"Over a 50-year career, I've worked with cells transforming (into cancer) in culture and seen the first step in a dynamic way, seen cells continuing to multiply when they should have stopped," Rubin said. "This is the first

step in cancer, though not yet cancer, and you can measure these changes quantitatively."

The problem, of course, is that it is impractical to test all the body's tissues to determine whether they have abnormal cell growth. But Rubin has found evidence from other studies that, in some cases, skin fibroblasts show these early changes even before cancer appears in other tissues, such as the colon.

"The abnormal growth behavior of skin fibroblasts in cancer-prone individuals has suggested that, at least in some cases, cancer can be considered a systemic disease and that this difference in the behavior of skin fibroblast cells from such individuals may be a practical basis for prevention, diagnosis and management of the disease," he concluded in his paper.

"It's a great idea, scientifically; the question is, 'Is it there clinically?'" said Douglas Brash, professor of therapeutic radiology, genetics and dermatology at Yale School of Medicine. "This is interesting enough that someone should look to see whether it is clinically reliable."

Dr. Stuart H. Yuspa, co-chief of the Laboratory of Cancer Biology and Genetics at the National Cancer Institute, agreed. "Harry's ideas are always amazing, and I admired the paper," he said. "His idea has scientific support, and if it turned out to be correct, it could be extremely valuable for people, assuming they would want to know their risk."

Rubin bases his argument on various studies over the past 50+ years that show that cancers grow from a larger "field" of abnormally multiplying cells that otherwise look normal. These "field" cells are generally ignored by surgeons when they remove solid cancers - in fact, the large size of the field would make its total removal impossible - but pathologists have shown that the cells are capable of again giving rise to cancers.

"These cells have early mutations that could lead to cancer," Rubin said. "Even though they look normal, they multiply in places where they shouldn't and eventually accumulate enough mutations to form a carcinoma. They are the first stage in cancer, but not cancer."

The inappropriate growth - called cancerization - is a sign that the normal processes that stop growth when cells contact one another have been disrupted, though not fully, because otherwise the cells would invade the underlying connective tissue and become cancerous.

Rubin showed in experiments 15 years ago that if you take cells that grow normally in cell culture and encourage mutations, then select for behavioral abnormalities involving growth, you can get proliferation of cells that behave like cancerization field cells.

Similarly, while normal skin fibroblast cells grow to a certain density and stop, fibroblasts from cancer-susceptible individuals grow to an unusually high density in a Petri dish. That difference between fibroblasts from normal and cancer-susceptible individuals can be amplified to improve identification of those at risk of cancer, Rubin said.

Rubin suspects that the growth change in skin fibroblasts heralds a general change in all the body's epithelial tissue, that is, the tissues that line all the body organs. The most prevalent cancers - including colon, breast, lung, skin, head and neck - arise from epithelial tissue. In certain cancer-prone families, for example, the same mutated gene is found in all tissues, and the fibroblasts grow to high densities in culture, just like epithelial cells in a precancerous field do in the body.

"If this works out after studying a large number of cases, then the people who are found to have a high probability of developing cancer would be more likely to pay attention to their diet, exercise, weight, smoking and

behaviors that are known to contribute to an increased risk of cancer," he said. "Basic studies of a cell culture model for field cancerization should reveal the conditions that drive or delay the process and could be applied in prevention of cancer."

Source: University of California - Berkeley (news : web)