Dear OncoLink “Ask The Experts,”

Do we know why people who didn't smoke get lung cancer?

Jared Weiss, MD Medical Oncologist & Assistant Professor at University of North Carolina's Lineberger Cancer Center, responds:

This is a great question because it gets to the very nature of what cancer is.

One of my patients once told me that she likened her cancer cells to misbehaving children and I think that this was a wise explanation. When a baby is born, it starts as a sperm fertilizing an egg, creating a single cell. That cell is pluripotent, meaning that it is capable of making all of the different kinds of cells that will ultimately be needed in the body. The cell will divide, then divide again, then divide again. In the process, the "daughter" cells become increasingly specialized. By birth, a baby has many different kinds of cells, each with very specialized functions and most of them have lost the ability to divide further or spread to other parts of the body. They are programmed to die in response to signals from other cells.

Each of these cells is a little factory, performing its specified functions. The tools that the cell uses to carry out these functions are called proteins. In order to make a protein, the cell starts with the DNA blueprint that is housed in a structure called the nucleus. The nucleus can be thought of as a little fortress-enclosed island containing stacks of blueprints in a big lake that is the cell. The DNA is transcribed (copied) into stuff called RNA, which travels out of the nucleus into the cytoplasm (which could be thought of like the water in the lake). In the lake, the RNA attaches to a structure called the ribosome (think of it as a small, floating protein factory) where it is translated into a protein.

Like a criminal, a cancer cell starts its life as a normal cell and then goes bad. It does so because of changes to its DNA that we call mutations. It takes multiple mutations for a cell to turn bad and become a cancer cell; the number probably varies greatly from one type of cancer to another. Thus, a person can be born with one or two of these changes, creating a genetic predisposition to cancer. Other changes come throughout life. Smoking is clearly the most important risk factor in lung cancer. Most lung cancer patients have smoked at some point in their life. However, it's clearly not the only factor; not all smokers get lung cancer and many lung cancer patients never smoked.

Other exposures that seem to be important include asbestos, radon, and cooking fumes. But, some patients have no history of major exposure. We're only just beginning to understand a bit about these cancers, but they seem to more of the adenocarcinoma (including BAC type) cell type and they seem to be driven by specific genetic changes. The most important of
these is the epidermal growth factor receptor (EGFR). Patients who have a mutation in this specific receptor tend to be never smokers (or former/light smokers) and they respond very well to the drugs erlotinib (tarceva) and gefitinib (iressa). More recently, we've learned about a translocation (when a piece of DNA moves to a place it doesn't belong) called EML4/Alk. Also much more common in never smokers, it predicts for efficacy of the new drug crizotinib. Lots more to learn, but these insights are a start to understanding lung cancer in never smokers.

This question and answer was part of the OncoLink Brown Bag Chat Series. View the entire transcript of the Lung Cancer Q&A Webchat.

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No