Cancer Genomics

Lynda Chin, from Harvard Medical School and Dana Farber Institute, gave a presentation on "Translating Cancer Genomics". Cancer is a disease of the genome, and understanding the human cancer genome is key to the prevention, detection, and treatment of cancer. Specifically, Dr. Chin is talking about recognizing the underlying genomic changes: that initiate and support cancer; that can lead to early intervention before cancer develops; that will promote early detection of the cancer; and that will point to targets for treatment. In the category of genomic understanding leading to treatment, Dr. Chin gave the example of the identification, in 2002, of the BRAF gene as a promoter of melanoma, and the development of a BRAF inhibitor in 2010 that has shown significant efficacy. Another example is the reformulation of the Pfizer drug, crizotinib, to target a specific mutation that is present in a small subset of non-small cell lung cancer patients. The drug has shown a 60-80% response rate in two trials. These successes have led researchers to focus on the cancer genome, which maps every mutated gene in each cancer. Advances in the latest gene sequencing technology have greatly assisted this effort. The cancer genome is quite complex, which has heretofore inhibited genetic research, but today's machines can sequence 50,000 times faster at 1/100,000 of the unit cost than machines of 10 years ago. Although this sounds impressive, the genome contains some 3 billion pieces of information, so the task is far from simple.

The field of cancer genomics is wide open and there is great deal of information still to be learned. For example, in 2007, a gene was found to be mutated in 9% of breast cancer patients, but in 2010, the same gene was found mutated in 84% of patients with a form of melanoma. This year, a gene called PBRM1 was found mutated in 41% of melanoma, and the development of a BRAF inhibitor in 2010 that has shown significant efficacy. Another example is the reformulation of the Pfizer drug, crizotinib, to target a specific mutation that is present in a small subset of non-small cell lung cancer patients. The drug has shown a 60-80% response rate in two trials. These successes have led researchers to focus on the cancer genome, which maps every mutated gene in each cancer. Advances in the latest gene sequencing technology have greatly assisted this effort. The cancer genome is quite complex, which has heretofore inhibited genetic research, but today's machines can sequence 50,000 times faster at 1/100,000 of the unit cost than machines of 10 years ago. Although this sounds impressive, the genome contains some 3 billion pieces of information, so the task is far from simple.

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There are hundreds to thousands of mutations in a single tumor. Therefore, a major objective is to identify the driver mutations (genes thought to have a role in the development of cancer) and perform functional analysis on the genes. In other words, the goal is to understand what processes they control and how the mutation interrupts it. A mutated gene can be oncogenic (promoting the formation of cancerous tumors) in one setting, and tumor suppressing in another, it is necessary to understand the cellular mechanisms that are influenced by the mutation. Dr. Chin referred to the Hallmarks of Cancer diagram, see below, remarking that many aspects of tumor functionality must be analyzed in order to understand how to approach patient treatment vis-à-vis specific driver mutations.

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