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It took nearly 13 years and cost over $3 billion to sequence the human genome for the first time, a task that was only completed a little over ten years ago. Today the cost is a four figure sum and falling, rapidly. We are approaching an age where it will be feasible to sequence the entire genome of a person, but how do we use this information? How does it help our doctors? How does it influence our lives?

Instead of our current one-size-fits-all treatment for most diseases, many envision a future in which we will be able to tailor medical treatment based on one’s underlying genetic information, a medical model known as personalized, or precision, medicine. This future is quickly becoming the present and the recent advances in cancer medicine and drug development demonstrate how precision medicine may be used by clinicians to treat patients. Cancer is principally the mutation of a cell’s genome leading to the uncontrolled production of cells and the ability of these cells to migrate and disrupt vital functions. Current cytotoxic chemotherapies have focused on eliminating the rapidly dividing cell populations, affecting both diseased and healthy cells in the process. These therapies result in incredible toxicities to healthy tissues and side effects that we know too well if we have personally experienced or watched a loved one battle cancer.

Newer therapies move away from this approach and focus instead on specific targets unique to cancer cells and their specific mutant gene expression. Doctors have been able to identify genes that cause cancers and markers on the surfaces of tumor cells that are ripe for target. For instance, drugs like Imatinib target a specific mutation on cell surfaces responsible for Chronic Myelogenous Leukemia, leading to incredible precision and successful treatment, dare we say “cures.” In addition, by understanding the responsible genes and the expressed products, the target for Imatinib was also identified in a completely different type of cancer, gastrointestinal stromal tumor (GIST). Although GIST is not categorized as a blood-related cancer, a targeted therapy for leukemia provides benefit for GIST patients, discovered because we understand the genome and the expression of these cancers.

By sequencing a patient’s tumor, we can anticipate which therapies have the greatest chance of success. Lymphoma is a perfect example of this approach. Lymphomas are classically divided into two groups: Hodgkin’s and non-Hodgkin’s lymphoma. With the advent of sequencing, the number of unique lymphomas has increased to nearly one hundred, which is important because different targets and different regimens are pursued depending on the type. This is where the personalization comes in: If you know the precise molecular trigger and the root cause, you can probably be more effective and have less collateral damage. It is rare that a cancer expresses a single mutant gene. Rather, several genes work together to promote tumor growth and metastasis. That means that treatment requires a better understanding of these factors, and a multi-disciplinary approach. In a cancer like glioblastoma (GBM), which is a primary brain tumor, several mutant cell lines can be identified in a single tumor mass. What looks like one disease is really several diseases occurring at the same time in the same place at the molecular level. This makes treating these tumors incredibly difficult because therapies targeting one cell population may find incredible resistance in another. GBMs are particularly challenging in this regard and personalized medicine will have a role in the future, although it currently has not found success for these patients. Progress has been slow because it takes a diverse field of researchers, clinicians, and data to tackle these difficult problems.

Genetic profiling of cancer cells is now standard practice across a wide variety of tumor types. It guides therapy, it allows the investigation of new targets, and it helps physicians tailor their treatments to the person. Personalization holds much promise for cancer medicine. We are on the cusp of an even larger revolution in genetics. It is an exciting time for the rising cadre of physicians looking to provide the best care for their patients. While it is much more complicated than finding the singular “cancer gene,” or the “intelligence gene,” or the “diabetes gene,” we are poised to use the data and the information now available to us to understand the interactions between our genome and the environment to advance clinical care. It’ll be a process, not a moment.
References