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When something is very big and moving very fast, the laws of physics tell us that it will strike with great impact. This could also hold true for personalized medicine, the application of genomic information to the understanding and treatment of medical conditions. “Personalized medicine represents a transformation of healthcare for humanity — and it’s happening faster than anyone ever anticipated,” declares F. Charles Brunicaudi, MD, Moss Foundation Chair in Gastrointestinal and Personalized Surgery.

While the field of personalized medicine is, according to Dr. Brunicaudi, still in its infancy, he and others are working to increase our understanding of genomic information and expand its use in providing clinical care. “A year ago, we had a portfolio of about eight genes that we could use to guide patient care; our portfolio now includes over 200.”

Examples from the field of digestive diseases include the CDH and APC genes. The CDH gene encodes for the E-cadherin protein. Patients with the CDH-1 gene are at increased risk for developing gastric cancer. Patients who are identified by their CDH gene can be put into a high-risk protocol and followed with regular biopsies, or treated prophylactically with total gastrectomy.

Mutations of the APC gene, which encodes a protein of the same name, along with a family history of

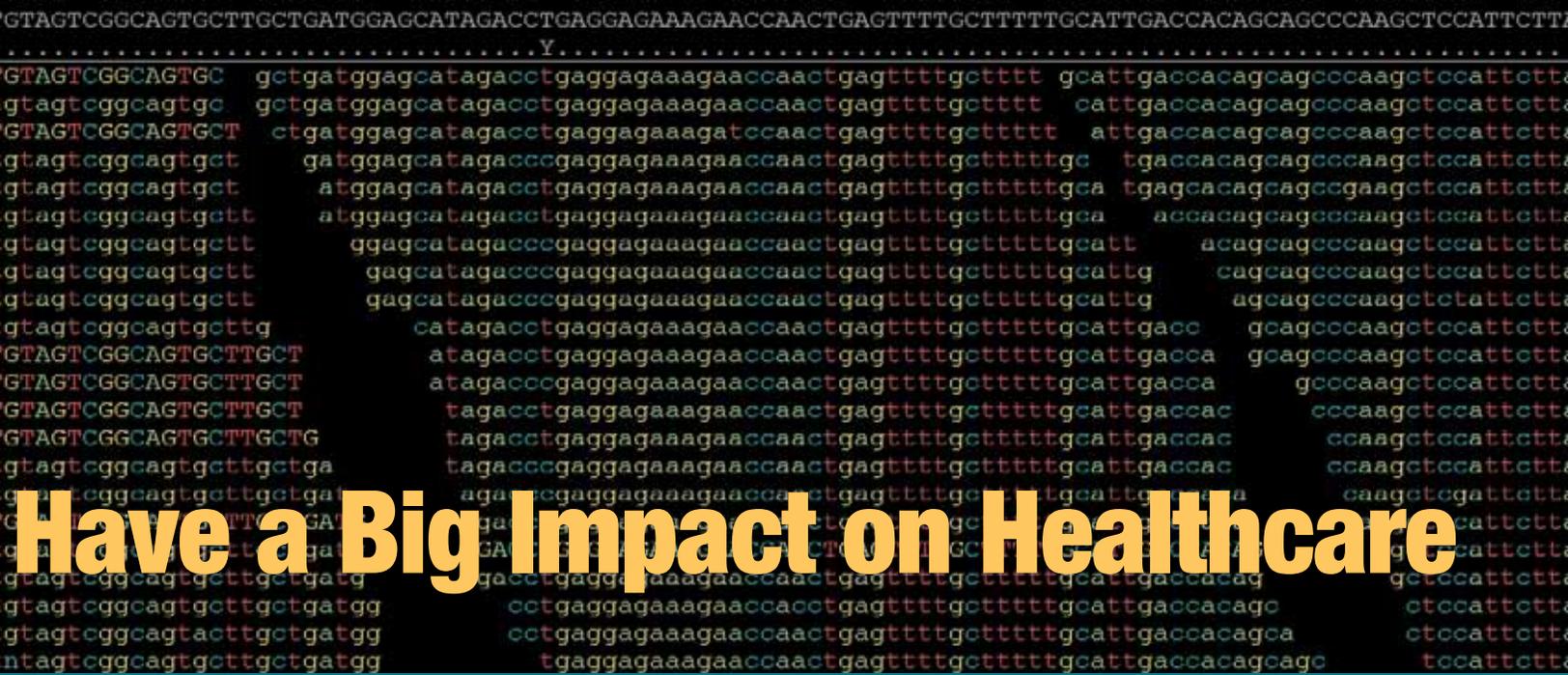
colonic polyps, are associated with a high risk of colorectal cancer. Again, patients identified by their APC gene can be followed in a high-risk protocol or can undergo total colectomy to prevent colon cancer.

In both cases, knowledge of the patient’s genetic code can lead to early cancer detection or preemptive treatment. A further step will be the development of targeted therapies that directly combat the disease based on the patient’s genomic profile, or even gene therapy to replace the defective gene.

To cite an example, Dr. Brunicaudi was part of a team whose analysis of pancreatic-cancer-patient genomes revealed aberrations in genes that control the axon guidance pathways. Those findings were recently reported in the journal *Nature*. “Our next step is to try to develop targeted therapies to the axon guidance genes that might be effective for pancreatic cancer,” states Dr. Brunicaudi.

New Center to Bring Personalized Medicine to Digestive Disease Patients

UCLA is launching a new treatment and research center, the UCLA-Santa Monica GI Neuroendocrine Center, that will focus on providing care guided by the patient’s GI neuroendocrine profile, including their genomic profile. Genomic sequencing of the patient’s blood and tumor tissue will augment standard immunohistochemistry and pathologic analysis of



disease specimens in determining which therapies are most appropriate for individual patients.

Research will include the use of genomic sequencing information to identify oncogenes and suppressor genes in order to develop targeted therapies. Another principal goal of the new center will be to develop targeted molecular imaging, such as PET-CT, optical imaging and radionuclide imaging to supplement current imaging modalities

A Furious Pace of Progress

Since the first draft of the human genome was sequenced in 2001, the speed of sequencing has increased by about 10,000 fold while the cost has decreased by about 10,000 fold. “Each run of our sequencing equipment takes about two weeks and generates about 20 times as much data as was generated during the entire 15-year period of the Human Genome Project,” states Stanley F. Nelson, MD, professor of human genetics and pathology and laboratory medicine.

Thus far, genetic testing has often been used to establish the genetic basis of rare and dramatic conditions, such as Mendelian genetic forms of diarrhea and malabsorption disorders. Dr. Nelson points out, “What these rare syndromes tell us about the genes and proteins needed to make the intestines fully develop and function normally

ultimately impacts more common diseases like Crohn’s disease, ulcerative colitis and diverticulitis.”

The next great step in personalized medicine will be to develop informatics tools to help physicians extract clinical meaning from the raw material of gene sequencing. “We know about 2,000 different locations in the genome that influence some health trait in everybody, but they each influence a person’s health only a little bit,” explains Dr. Nelson. The ability to effectively process all this information can ultimately yield insights about caring for individual patients — choosing and dosing medications more appropriately or knowing on an individual basis the risks of rare adverse drug reactions.

Bracing for Impact

“It’s been said that the genome is the anatomy of the 21st century. How can we take care of patients if we don’t know their anatomy?” asks Dr. Brunicardi. “To take the idea a step further, epigenetics and signaling pathways are the physiology of the 21st century. Physicians should know their patients’ physiology before they implement care.”

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