

The  
Power  
of  
Genetics  
and  
Medicine

**What  
Lies  
Within**



Medical genetics — a field that is not yet 50 years old — already is making an enormous impact on health care, as scientists discover that the key to sustaining health may lie beneath our own skins.

From familiar illnesses such as cancer and Alzheimer disease to rare inherited illnesses such as Charcot Marie Tooth Syndrome, scientists are discovering that our own genes provide important clues for identifying, treating and perhaps even preventing disease.

Genes are pieces of DNA that pass on the basic units of heredity from parent to child. By studying genes, physicians and researchers hope to understand what role defective genes play in the development of disease and how diseases could be prevented or cured based on genetic information. Scientists already have identified more than 500 gene defects that cause diseases such as cystic fibrosis, Huntington's disease and some types of breast cancer.

While impressive, these discoveries are just the beginning. A new era of genetic medicine has begun and promises to fundamentally change health care in the 21st century.

### How we got to today

Austrian monk Gregor Mendel discovered the general concepts of genetics in the 19th century. Based on his work with sweet pea plants, Mendel was able to describe how traits were inherited. The "Genetics Revolution" as it's been called, took off in 1953 when James Watson, an American biologist, and Francis Crick, an English physicist, discovered the structure of deoxyribonucleic acid, DNA. Known as the double helix, this was, Crick declared, "the secret of life." The double helix consists of two strands with adenine (A), thymine (T), guanine (G), and cytosine (C) nucleotides attached. One strand is the mirror image of the other strand, allowing duplication of hereditary information even if only one strand is present.

An explosion of discoveries have followed. In 1972, Stanley Cohen and Herbert Boyer invented a method that allows scientists to isolate and analyze genes. In 1977, Walter Gilbert and Frederick Sanger discovered methods for sequencing DNA, which means identifying in correct order the A's, T's, G's, and C's that make up DNA. Discoveries in genetic engineering (changing the genetic material of cells or organisms to enable them to make new substances or per-

form new functions), and DNA amplification (repeated copying of a piece of DNA) made possible isolating genes and reading the sequence of A, T, G, and C chemicals in the laboratory. Together, these and other discoveries made The Human Genome Project possible.

### The Human Genome Project — and beyond

In 1990, The Human Genome Project, an international research effort funded by the federal government, was established with the challenge of sequencing the entire human genome — the complete set of human chromosomes — by mapping human DNA. Chromosomes are microscopic units along which genes are arranged.

Results of the complete assembly of the entire human genome sequence were published in early 2001 with surprising results.

Scientists discovered that only about 30,000 to 40,000 genes actually are needed to make the human genome, far fewer than the original estimates of 70,000 to 150,000 genes. Even more remarkable was the finding that humans are 99.9 percent identical at the genetic level.

But our 0.1 percent genetic differences could provide valuable insight about people's susceptibility or resis-

tance to thousands of genetic diseases.

"I think genetic medicine will lead to predictive and preventative approaches to health care," says Margaret Kovach, Ph.D., a research instructor in the Department of Pediatrics, Division of Genetics, at the School of Medicine. "Treatments will be tailored based on patients' genetics that will determine individual response to drugs."

Dr. Kovach adds that "gene therapy, a technique for introducing 'good' gene(s) into a patient's cells in order to compensate for a defective gene, is a promising future application developing from our understanding of the human genome. Diseases targeted for gene therapy include those that stem from single gene defects, such as cystic fibrosis, as well as vascular (blood vessel) disease, cancer, AIDS, and more." Dr. Kovach's research investigates the molecular basis of unique genetic disorders.

### One family's case

Dr. Kovach, working with former SIU assistant professor Dr. Virginia Kimonis, has studied one family with Hereditary Inclusion Body Myopathy (HIBM), which is characterized by adult onset of muscle weakness, particularly of the shoulder and pelvic girdle. The affected members of this

family also suffer from Paget disease of bone — a chronic skeletal disorder that can result in enlarged or deformed bones — and had a higher incidence of early onset dementia.

“We mapped this complex disorder to a region of chromosome 9 near the centromere. That’s a big region, but it’s still progress,” says Dr. Kovach. Now that the neighborhood of the diseases have been pinpointed, researchers can begin to look in the individual houses — genes — to discover which mutate to cause this syndrome. Dr. Kovach is examining candidate genes within this region for mutations that might explain the syndrome’s pathology. She and Dr. Kimonis have made progress in this area too.

“Our intent is to identify the gene responsible for HIBM, determine its function and eventually apply this knowledge toward development of effective therapies.”

Drs. Kimonis and Kovach have received funding from SIU’s Central Research Committee, Excellence in Academic Medicine, and two National Institutes of Health grants for the initiation and continuation of these studies, and their research has expanded from one local family to four families nationwide.

“With so much information being discovered, the possibilities are limitless right now,” says Dr. Kovach, “But the ethical use of genetics in medicine must be carefully considered.”

### **Dealing with genetic destinies**

The staff of the Clinical and Metabolic Genetics Division at SIU School of Medicine carefully consider the implications of genetic information as they ensure that their patients get answers to their health-related questions.

The genetics division provides services for high-risk pregnancies and the diagnosis, evaluation, and management of children, adults, and families with diverse inherited conditions or

congenital malformations, including inherited metabolic disorders, familial cancer syndromes, chromosomal disorders and disorders associated with multiple congenital anomalies.

“Most genetic disease first becomes apparent in the newborn or pediatric periods,” says clinical geneticist and researcher Michael Schneider, M.D., assistant professor in the Department of Pediatrics. He emphasizes the importance of talking with patients about genetic risk.

“We consider the benefits and limitations of the resources available,” says Dr. Schneider. “The question is, how is this information going to alter their lives?” He cites an example: “One in 25 people of Northern European descent are carriers of the cystic fibrosis gene. Some national organizations recommend preconceptual genetic testing for these couples. However, we must fully educate patients regarding the implications of the test results for themselves, their offspring and their extended families. Patients must have the ability to make informed decisions about genetic testing.”

This dialogue is known as genetic counseling, a private interview and discussion with a health care professional who specializes in helping people assess their genetic risks.

“Genetic counselors gather and provide information while working to assess and provide for the psychosocial needs of the patient and their family,” summarizes certified genetic counselor Shawnia Forrester, M.S., who works closely with Dr. Schneider.

Telling people about their disease or their likelihood of disease in themselves or their offspring can help people modify their lifestyle and manage their health, while letting them make more informed reproductive decisions. “It gives them an insight into their future,” says Forrester. “We provide education and support for the decisions they make.”

Learning about the patient’s fam-

ily history is an important piece of information in a genetic evaluation. This information, along with the detailed medical histories, allow Dr. Schneider and Forrester to counsel their patients about pursuing the next step, genetic testing — an analysis of the DNA in your blood or tissues — to determine further risk. Counseling also helps people accept their genetic diversity. “A mother may mourn when her child is diagnosed with Down Syndrome, but we point out that the child can be a happy and productive member of society,” says Dr. Schneider. “This kind of genetic counseling helps society reassess its humanity.”

For patients diagnosed with genetic illnesses or identified as genetic carriers of a disease, Dr. Schneider and Forrester inform the patient and their families about the genetic principles involved, the patient’s prognosis or chance of developing symptoms, and treatment options. They also provide information about support groups and other families with the condition. “It lets them know they’re not alone,” says Forrester. “They can talk to other families and know that someone else has gone through what they’re going through.”

### **A weapon against cancer**

The genetics division also sees a growing number of patients who want to know their genetic risk for certain cancers. Known as cancer risk assessment, it consists of a family history and blood tests to “give patients an education,” says Dr. Schneider. He and Forrester recommend that patients pursue assessment if they are concerned about their genetic predisposition or if the information gained will modify medical management or lifestyle choices for them or their children.

Cancer is the reproduction of damaged cells, a mutation of the genetic

code in a cell that divides uncontrollably. Whether involving hereditary factors or resulting from the body's response to environmental viruses or toxins, cancer is a genetic disease, making genetic testing an increasingly useful tool.

From a patient's perspective, this could mean that in the future a simple genetic test at a young age will predict an impending cancer, which could then be addressed before symptoms occur. Some experts say that genetic engineering could replace surgery or radiation to treat cancer, and that chemotherapy would kill only the cancerous cells, leaving patients healthier.

SIU researchers like Kounosuke Watabe, Ph.D., are hunting for genes to suppress the spread of cancerous tumors. He has identified a link between two genes, the KAll gene and the p53 gene, which together could be a marker to distinguish between tumors that will spread and tumors that won't. He has concentrated his studies on prostate cancer, which kills more than 40,000 men each year.

Dr. Watabe also has identified four chromosomes in the human body — 2, 9, 16 and 20 — that contain some genetic material that may suppress tumor metastasis. He also is studying a gene that may suppress lung cancer metastasis. "Our long-term goal is to construct a molecular map of metastasis suppressors and to make clear the mechanisms of tumor metastasis in the prostate tumor, which can eventually lead to better diagnostic markers and therapeutic remedies for this devastating disease."

### **Beyond the genetics map**

With the completion of the human genome sequence, scientists now have a powerful tool to further explore the secrets of genetics.

Beyond the map of the 30,000 human genes lies an intricate net-

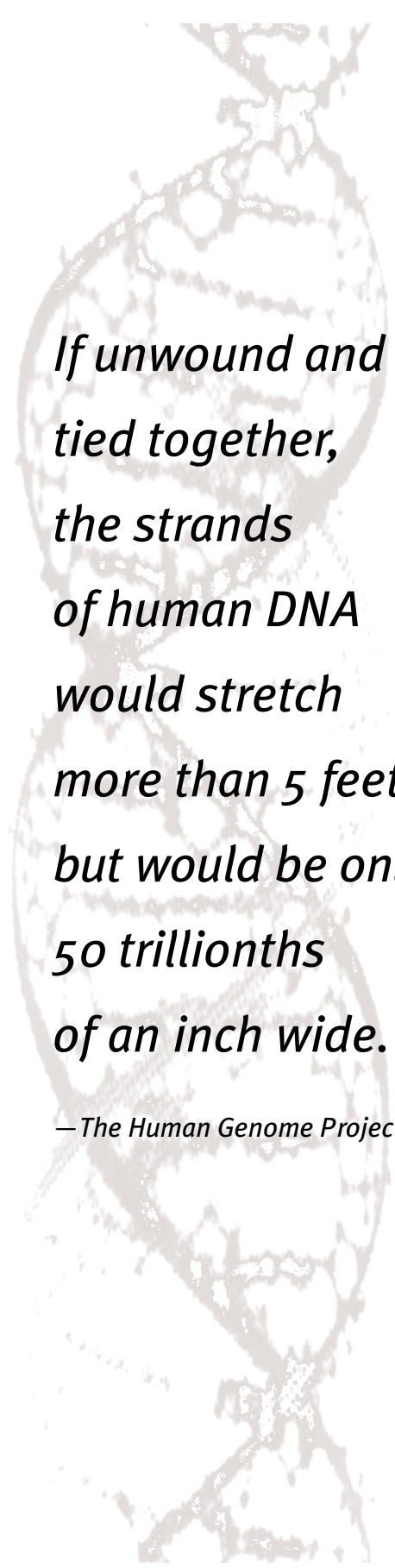
work of proteins, large, complex molecules within genes that determine how well cells in the body will operate. As the products of genes, proteins serve as the engineers of cellular health and may begin the chain reaction that leads to disease.

Analyzing each of the body's proteins, which could number well over 300,000, is the next challenge for researchers in a field called "proteomics" — the study of the expression and function of biological proteins in relation to the normal function of cells and their role in health, disease and therapy.

"Understanding the functions of the proteins will give scientists a better understanding of the mechanisms underlying neurodegenerative disease and could help scientists regulate the proteins, leading to earlier detection and better treatment of diseases with new drugs or therapies," says R. Stanley Burns, M.D., professor of neurology and director of the SIU Parkinson Disease Center.

SIU School of Medicine has responded to these challenges by establishing the Laboratory of Gene Expression and Proteomics, which focuses on proteins expressed in nerve cells. "The goal is to identify unknown proteins and characterize the changes they undergo in a diseased state," says Dr. Burns. He is focusing his research on the potential for improved treatments and understanding of the neurological diseases that plague millions of people and their families every year who face illnesses such as Parkinson's disease, Alzheimer disease, ALS (Lou Gehrig's disease), ataxia and others.

Though impressive achievements have been made, the field of genetic medicine is young, and decades of work lie ahead for physicians and researchers who believe that the key to health lies within. ■



*If unwound and  
tied together,  
the strands  
of human DNA  
would stretch  
more than 5 feet  
but would be only  
50 trillionths  
of an inch wide.*

— *The Human Genome Project*