patients. “He continues to be an outstanding role model for physician-scientists,” says Brenda Sandmaier, MD, a professor and member of the clinical research division at the Fred Hutchinson Cancer Research Center and a former Storb mentee. Most recently, the pioneer helped to lead the recruitment of 6 young assistant professors to the transplant program at the Fred Hutchinson Cancer Research Center: 4 women and 2 men from “very diverse backgrounds,” he says.

“[Dr. Storb] takes great pride in training researchers, many of whom have become leaders in transplantation centers throughout the U.S. and Canada,” shares Dr. Sandmaier. “One thing he taught me is to be data-driven when treating patients. Sometimes you’ll be surprised during a randomized study—your first impressions aren’t always correct.”

**Evolving a Regimen**

Dr. Storb’s path to his groundbreaking work in Seattle was a fortuitous one. Born and raised in Germany, he weighed pursuing engineering or architecture before settling on the “family tradition” of medicine. He obtained his medical degree from the University of Freiburg, an institution known for a strong focus on hematology. Dr. Storb soon became intrigued with bone marrow transplantation. Inspired by the work of Dr. Thomas in Seattle, he came to the United States on a Fulbright Scholarship in 1965 and began working in the “tiny lab.”

Dr. Storb and his colleagues performed their first transplants in the late 1960s, one on a leukemia patient and another on a patient with aplastic anemia. The regimen that they introduced for treating the latter disease is still used today and boasts a survival rate that has improved more than 100% over the past 18 years, Dr. Storb reports. Years later, the acclaimed physician became one of the founding members of the Fred Hutchinson Cancer Research Center and helped it evolve into a leading cancer institution known worldwide for its expertise in bone marrow transplantation.

Over time, Dr. Storb and his colleagues have recognized the importance of developing less toxic conditioning regimens for patients older than 60 years and others not considered healthy enough for conventional high-intensity transplantation. Thus, they have worked to develop mini or “reduced-intensity” transplants that rely largely on the donor’s immune system to attack and destroy the patient’s cancer cells.

“The original concept with conditioning treatment was always to be ‘at the brink’ of what most patients could tolerate,” Dr. Storb explains. “The problem was that therapy was not tolerated well by older patients with hematologic cancers; however, most acute and chronic leukemias, myelomas, and non-Hodgkin’s lymphomas occur in patients ages 65 to 70. As a result, we missed most of these groups.”

The challenge in using milder conditioning therapy and donor cells to reduce the risk of relapse often resulted in increased graft-versus-host disease in patients. However, in 1997, Dr. Storb and his colleagues developed a promising drug regimen that would prove effective on both fronts. Today, they continue to conduct clinical studies to improve mortality rates and reduce graft-versus-host disease. In a *Journal of Clinical Oncology* study published in 2013, they showed that depending on the disease risk, comorbidities, and graft-versus-host disease, lasting remissions were seen in 45% to 75% of allogeneic transplant patients with advanced hematologic malignancies who were treated with minimal-intensity conditioning regimens for allogeneic transplant patients with advanced hematologic malignancies. The 5-year survival rates ranged from 25% to 60%.

In July 2016, the team entered 168 patients into a new phase 3 clinical trial analyzing double- and triple-drug regimens to reduce graft-versus-host disease in patients treated with minimal-intensity transplants. The Food and Drug Administration closed the study early because one trial arm did significantly better than the other and led to a reduction in the graft-versus-host disease rate from 55% to 23%, Dr. Storb reports.

Currently, Dr. Storb and his colleagues are developing a method of targeted radiotherapy treatment of patients with hematologic malignancies that includes the use of the anti-CD45 monoclonal antibody, which binds to the CD45 protein. This protein is expressed in most blood cells and some types of leukemia and lymphoma cells and is believed to help the immune system kill cancer cells. Working in concert with radiation oncology colleagues and physicists at the University of Washington, the researchers were planning at press time to enroll their first patients. The study’s goals are to intensify conditioning regimens without increasing toxicity and, ultimately, further reduce relapses.

“We hope we can reduce relapse rates from 34% in 5 years to 15 or 20%,” says Dr. Storb, who at 82 is showing no signs of slowing down. A long-time athlete, he still rows regularly with his son and even participates in open-water races. “I still do a lot of sports—it balances your life,” he says. “You’re doing something intellectual all day at work, and then getting out on the water is really great.”

**Reference**


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**Largest Brain Cancer Study Offers Clues to Inherited Risk**

Scientists have gleaned new information about the genetic causes of brain cancer in the largest study to date of the disease.

The research, published in *Nature Genetics*, uncovered 13 new genetic errors associated with an increased risk of glioma, the most common form of brain cancer. One of these changes increases the risk by as much a third, whereas the other errors increase the risk by at least 15% each. The new information can assist physicians in identifying people who are at significantly increased risk of developing the disease.

The study, led by researchers at the Institute for Cancer Research, London, along with colleagues in Europe and the United States, included more than 30,000 people with and
without glioma. The disease, which accounts for 40% of all brain tumors, presents challenges to health care providers on a number of fronts; this is mainly related to the fact that there are no reliable means of early detection, and current treatments are not very effective.

The gathered data provide extensive information about what predisposes people to gliomas and thus could enable physicians in the future to monitor those patients most at risk and diagnose the disease earlier and also lead to new drug discovery, the authors say. In their research, scientists conducted 2 new genome-wide association studies and combined the results with those of 6 previous studies in a “meta-analysis” comprising 12,496 cases with glioma and 18,190 cases without it.

This large study led to the detection of 13 previously undiscovered genetic changes that increase glioma risk. The errors were found to affect a number of cell functions, including cell division, DNA repair, cell cycle control, protein production, and inflammation. Researchers also learned that different sets of genes affect a person’s risk of developing the 2 glioma subtypes: glioblastoma and nonglioblastoma.

One example of their findings is a DNA change that influences activity of the gene HEATR3, which increases the risk of glioblastoma, a very aggressive type of glioma associated with an average survival of just 10 to 15 months after the diagnosis. The particular error discovered in this gene increases glioblastoma risk by 18%, researchers found. However, the error has a much smaller effect on the risk of developing nonglioblastoma.

Scientists also gained additional knowledge about the roles of DNA errors in genes that they had previously identified as being associated with glioma and other cancers, including p53 and EGFR as well as TERT and RTEL1, which protect the ends of chromosomes. Their newest findings double the number of genetic changes associated with glioma risk and bring it up to 26.

Richard Houlston, MD, PhD, a professor of molecular and population genetics at the Institute of Cancer Research, London, notes that understanding the genetics of glioma in new and better detail has helped researchers see that what they had considered 2 related subtypes of the disease (glioblastoma and nonglioblastoma) have very different genetic causes and may require different approaches to treatment.

Reference

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**Sulfide-Producing Bacteria Linked to Higher Colon Cancer Risk in African Americans**

A study reported in the journal *Gut* finds that in comparison with non-Hispanic whites (NHWs), African-Americans (AAs) harbor higher amounts of sulfide-producing bacteria that live in the colon, and those differences are related to a higher-than-average colon cancer risk in AAs.1

The study was led by H. Rex Gaskins, PhD, of the University of Illinois at Urbana-Champaign, and Nathan Ellis, PhD, formerly of the University of Illinois at Chicago and currently scientific director of the cancer biology research program at the University of Arizona Cancer Center in Tucson. Researchers analyzed colonic tissue biopsies from 197 AAs and 132 NHWs collected over a 2-year period. They determined the amounts of various types of microbes in the samples. Findings revealed greater amounts of hydrogen sulfide-producing bacteria in the colons of AAs versus NHWs. Although these microbes are a normal part of the gut ecosystem, too much sulfide in the colon can lead to inflammation and damage DNA, researchers state. Dr. Gaskins notes that he and his colleagues demonstrated more than a decade ago that hydrogen sulfide is a potent genotoxin.

Researchers also found that *Bilophila wadsworthia*, a bacterium that produces hydrogen sulfide from the amino acid taurine, was significantly more abundant in AAs with colon cancer than in their healthy counterparts. The bacteria use nutrients associated with an animal-based diet, points out Dr. Gaskins. The same relation between the amounts of *B. wadsworthia* and colon cancer risk was not observed in NHWs.

Approximately 85% to 90% of colon cancer cases are sporadic rather than familial, Dr. Gaskins says, and he adds that although there may be a genetic element involved, environmental factors such as pollutants or dietary components also contribute to the onset of cancer.

Researchers report that the incidence of colorectal cancer is higher in AAs versus other Americans. In 2013, there were 33.5 colon cancer cases per 100,000 AAs but only 26.8 colon cancer cases per 100,000 whites. Investigators have observed that the incidence of colorectal cancer in Native Americans is dramatically lower than that of AAs, seeming to indicate that dietary factors may play a role along with genetics. A diet high in red meat and animal fat has previously been linked with increased colon cancer risk, Dr. Gaskins says. He adds that microbes inhabiting the colon should now be considered to be playing a potential role in the equation.

Reference

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