Top Cancer Researchers Finding Genes for New Therapies

There is new hope on the horizon in cancer research, according to two of the top scientists in the field who presented their latest work at McLaughlin Research Institute’s annual Biomedical Sciences Workshop in September. Nancy Jenkins and Neal Copeland, directors of the Institute of Molecular and Cell Biology in Singapore, are longtime members of MRI’s Scientific Advisory Committee. The husband-and-wife researchers have been called “the founders of modern mouse genetics” for combining molecular biology with formal genetics in 1980.

Using a powerful new technology they developed, Drs. Copeland and Jenkins are discovering cancer genes that can be used as targets for drug therapies. The new trend in cancer research is to develop drugs that stop the mutated genes from driving the disease, even in its late stages, when chemotherapy is often ineffective. “It’s a paradigm shift,” Dr. Jenkins said, explaining that in the past, the pharmaceutical industry looked only at therapies that attack rapidly dividing cells, a characteristic...
of cancer cells. One problem with this “sledgehammer approach” is that many of the body’s normal cells are also rapidly dividing, including those in hair follicles and the gastrointestinal lining. The destruction of these cells causes chemotherapy’s side effects.

The new direction—toward therapies that target genes—has prompted the formation of an international consortium dedicated to identifying cancer genes by sequencing the genomes of 25,000 tumors, Dr. Copeland said. He and Dr. Jenkins are taking a complementary approach to this time- and labor-intensive search for human genes by developing mouse models for many types of cancer. They use a jumping piece of DNA that moves around the mouse genome, mutating genes and inducing cancer. As the mobile DNA mutates a gene, it tags it, enabling the scientists to identify cancer-causing genes far more rapidly than can be done in humans. So far, their results show that the known cancer genes are the same in humans and mice, and new genes they’re finding promise to follow suit.

Scientists have recently learned that Copeland and Jenkins were right early on when they said there would be hundreds of cancer genes, rather than the handful researchers were looking for.

“‘It shows you the value of the mouse model,’” Dr. Jenkins said. “These models were highly predictive all along.” Now that it appears there are roughly 200 varieties of cancer, caused by particular combinations of mutated genes, treatment development becomes even more challenging. Drugs need to be tailored to each cancer’s genetic profile. “Cancer has turned out to be far more complicated than anyone thought,” Dr. Jenkins said.

A recent clinical trial for a drug targeting a known cancer gene showed that it can dramatically reverse the course of even very advanced cancer, but only temporarily. After a number of months, the cancer spread again, indicating that additional mutated genes took over where the targeted one left off. According to Dr. Copeland, this corresponds with the evidence that a number of genes are involved in each type of cancer and that a “cocktail” approach to targeted cancer drugs is likely called for.

He and Dr. Jenkins are talking with two major pharmaceutical companies about collaborating on their mouse models for pancreatic and prostate cancer. They are also developing models for melanoma, breast cancer, liver cancer, and a list of others. “Pharma is very interested in preclinical testing on our mice,” Dr. Jenkins said.
“We’re at the stage where we’re ready to take advantage of stem cell biology and move into therapies,” Irving Weissman told a Great Falls audience at a public lecture in May.

Dr. Weissman’s discovery of the stem cell in the 1980s opened many new avenues for medicine. He and his colleagues are now transplanting brain stem cells into children with a fatal brain disease and will soon begin similar clinical trials for spinal cord injuries, along with trials using blood-forming stem cells to treat several cancers. Meanwhile, they are developing promising treatments for muscular dystrophy, juvenile diabetes, and a number of autoimmune disorders.

Dr. Weissman is director of Stanford’s Institute for Stem Cell Biology and Regenerative Medicine. His labs have identified and isolated the human stem cell that makes blood and the one that makes the brain, as well as the muscle-forming and the bone-forming stem cells. As Dr. Weissman said, scientists have learned in recent years that “once a stem cell is specified for a particular tissue, it can make only that tissue.” In the early days of stem cell biology, there was hope that any stem cell could make tissue for any part of the body.

“Stem cells are the rare cells that are entirely responsible for the original generation of all body tissues and regenerate them throughout our lives,” he said. Scientists are working to harness this ability of the stem cell in order to regenerate healthy new tissue in the case of disease.

The progress of stem cell therapy has been slowed by significant barriers, beginning with the national debate over the research. In addition, Dr. Weissman said, pharmaceutical companies don’t want to fund these therapies, since they prefer drug therapy to cures. And clinical trials, which are long, drawn-out, and rigorously regulated, are made more difficult in the U.S. by negotiating with many different insurance companies.

Another problem is that an alarming number of companies are taking advantage of the promise of stem cell therapy to offer fraudulent treatments. Often in countries with fewer regulations than the U.S., these companies take large sums of money from desperate patients hoping to be cured. As president of the International Society for Stem Cell Research, Dr. Weissman encouraged people to use the website created by the Society at www.closerlookatstemcells.org to help distinguish between legitimate and illegitimate therapies.

Irv Weissman was MRI’s first student intern in the 1950s. His internship began the education program at McLaughlin that has grown to be, in his words, “the most innovative research training program in the country for high school and undergraduate students.” That program, in partnership with the Howard Hughes Medical Institute, sponsored Dr. Weissman’s lecture in order to promote public education about science.

Dr. Weissman is also the longtime Chair of McLaughlin’s Scientific Advisory Committee. He acknowledged MRI’s continuing role in his research, through collaborations, and told his audience, “This seminar was put on by a research group that does biomedical research that will be translated into treatments, in the auditorium of a hospital that needs desperately to see these translations, so I hope everyone here will help us—McLaughlin and Benefis—find a way to work together so it works even faster, here in Great Falls.”

Dr. Irv Weissman
For more than twenty years, award-winning CBS News Correspondent Barry Petersen’s wife, Jan, was all he wanted in life. The two shared adventurous careers as television journalists based in Tokyo, Moscow, London, and Beijing. Now, he says, Jan is all but gone to him, stolen by what he calls “this horror of a disease”—early onset Alzheimer’s. The couple’s ordeal has given Barry, a former Montana resident, the urge to tell his story so that others may benefit. He spoke at the annual meeting of McLaughlin Research Institute’s National Development Council in June, just after the publication of his book, Jan’s Story: Love Lost to the Long Goodbye of Alzheimer’s.

Barry described the nightmare of watching the woman he loved lose her mind and much of her personality. First affected as early as age 40, Jan Chorlton Petersen received the dreaded diagnosis at 55. Five years later, at just 60 years old, she is in an assisted living facility and does not know her husband. The former dynamic TV reporter struggles to communicate and has disappeared into “a fog.” Barry’s grief, as a friend of his describes it, is “like going to the same funeral over and over.”

Jan’s Story is a harrowing and deeply personal account of the private war Barry and Jan have waged against “The Disease,” as he calls it. And with “no cure, no known cause, and no way to prevent it,” Alzheimer’s makes a formidable enemy.

With his book, Barry Petersen has opened a conversation with the country, calling attention to the alarming reality Alzheimer’s presents for his generation. By age 85, half of Americans will have Alzheimer’s, and, as Barry pointed out, the other half will be caring for them. As the baby boomers age, the number of people with the disease is expected to triple by 2050, to 16 million. The disease is expected to cost the government and private citizens a total of $20 trillion between now and then.

Barry Petersen has reported with composure from Bosnia, Rwanda, and Tiananmen Square on some of the past 30 years’ most disturbing events. For the McLaughlin audience, watching this familiar television broadcaster wipe away tears over his own story, his resonant voice breaking, brought home the tragedy of Alzheimer’s disease. “I was terrifically moved by his talk,” said Lorena Lauritzen of Great Falls. “Everyone was mesmerized.” As she listened to Barry’s story, she was also struck by the relevance of MRI’s research to the devastating disease. “This is what they’re dealing with at McLaughlin,” she realized. “This is what they’re trying to solve. We should support this more than we do.”

While documenting the sad disappearing act of a charming woman in the prime of her life, Jan’s Story also reveals the plight of the caregiver. After a live-in nurse told Barry he would die if he continued to keep Jan at home, he had to let go of the life they had shared. Another agonizing decision he made was to move on with his own life and begin a new relationship. “I will not let two lives be lost to Alzheimer’s,” he explained. Now he and Mary Nell visit Jan together: “We’re a family of three.” Barry suggests many of us will be faced with such unconventional family arrangements as Alzheimer’s tears apart the traditional structure of millions more American families.
Alzheimer’s Research Making Slow But Sure Progress

A cure for Alzheimer’s disease—using brain stem cells—could be in the making, Irving Weissman told Barry Petersen’s audience after Petersen spoke about the impact of the disease on his life. (See article on preceding page.) Transplanting brain stem cells into people who are genetically susceptible to Alzheimer’s could produce enough new brain cells to prevent or disrupt the progress of the disease, Dr. Weissman said. “We plan to test this idea in special mice bred at MRI, and if the test is positive, we’ll move forward, but developing this therapy will take time,” he said after the symposium.

Dr. Weissman spoke as a member of a panel of scientists who discussed various approaches to Alzheimer’s research. He is director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine and co-founder of StemCells, Inc., where his wife, Ann Tsukamoto Weissman, is Executive Vice President of Research. Dr. Tsukamoto Weissman explained how the company applies basic research to human disease through clinical trials. After isolating and growing human brain stem cells, she said, StemCells, Inc. collaborated with George Carlson’s lab at MRI to show that the human cells would survive in mice whose brains are riddled with the plaques associated with Alzheimer’s disease. “We’d like to do further studies with other models and show that transplanting these human cells produces proteins that will protect the cells that are resident in the brain from dying.” The company is conducting clinical trials of a similar treatment for another brain disease called Batten disease, but the Food and Drug Administration’s regulatory process is painfully slow and cumbersome.

George Carlson discussed the challenge he and other scientists face in developing a good mouse model for Alzheimer’s disease. While mice are genetically similar enough to humans to make them a good model for many human diseases, Alzheimer’s behaves differently in the two species. Dr. Carlson and others are working with those differences to find a missing link in the scientific understanding of the disease process.

That is the role of basic research, as MRI’s Teresa Gunn pointed out. “A lot of what we’re doing at this basic level is looking at what is going wrong in the brain,” she said. “Without understanding the underlying biology, scientists can’t come up with effective treatments or prevention.”

Another panel member, Deborah Cabin, studies Parkinson’s disease at McLaughlin. She drew parallels between her mouse models for Parkinson’s and those for Alzheimer’s. The two brain diseases are in the same class, so there is some overlap in the research, although the Parkinson’s mouse model has been more successful. According to Dr. Cabin, who came to MRI from the National Institutes of Health (NIH), the NIH has a bank of chemicals available for testing as therapies. “They’re begging for animal models to test their compounds on,” she said.

While a better mouse model for Alzheimer’s remains a goal for Dr. Carlson, his lab does have a pre-clinical mouse model for the disease that is promising. The mice show small, accumulated changes over time, long before symptoms would appear. “If we could identify people very early on who are destined to develop Alzheimer’s—decades before the plaques and tangles appear—we could start developing preventive measures,” he said. “If we could even delay the onset of the disease by five or ten years, people could have a chance at enjoying their remaining years. It would also save trillions of dollars in medical costs.”

“This is what they’re dealing with at McLaughlin. This is what they’re trying to solve. We should support this more than we do.”

—Lorena Lauritzen on Alzheimer’s disease
Students Help Make Science Fun

In high school science classes across Great Falls, and wherever they have Internet access, students are being engaged by fun new educational tools their teachers developed over the summer at McLaughlin Research Institute.

- A video podcast on YouTube called Hodges & Sully on Science, created by Great Falls High teachers Mike Hodges and Brian Sullivan to translate what they’ve learned at McLaughlin into accessible terms.

- Simulated high-tech lab procedures like polymerase chain reaction, brought to Nathan Greiger’s students at CM Russell High School via Moodle, an online virtual learning environment.

- A music video called Chromosome, a creative educational spoof of the wildly popular Lady Gaga video Telephone.

The audience at the Institute’s Summer Intern Symposium in August was treated to presentations of these hip teaching methods by a team of teachers and students who developed curriculum that will encourage students to explore science. Jojo Coburn, who created Chromosome on her own time, was one of the students on the curriculum team. She graduated from CM Russell High School last spring and now studies molecular cell biology at UC-Berkeley. Jojo is considering careers in both education and research. “I think it’s important to share the love of science with those who don’t have it,” she said. According to her, one way to do that is by making science “cool.”

Tom Cubbage, a science teacher at CM Russell High who has spent a handful of summers working in labs at McLaughlin, was the lead teacher in the curriculum group this year. Before his colleagues presented their flashier, high-tech projects, he laid the groundwork with a model for argumentation and analysis that he said will help students “test the reliability of knowledge” by using critical thinking in science class and beyond.

MRI added the curriculum group to its education program three years ago with a five-year grant from the Howard Hughes Medical Institute. HHMI’s program is part of a national effort to address the shortage of scientists in the U.S. by making science more appealing to students. That effort includes a trend toward inquiry-based science education, which emphasizes critical thinking and exploration over textbook memorization. Great Falls Public Schools is making the transition to an inquiry-based science curriculum, and the partnership with McLaughlin is playing a key role.

Last summer was Jojo Coburn’s second summer at MRI. The previous year she worked in Dr. George Carlson’s lab learning how to perform research. Each year for more than 50 years, high school and college students have spent their summers in the Institute’s labs, studying the molecular mechanisms of diseases—and, along the way, boosting their chances at getting into their preferred college, graduate school, or medical school. The 2010 student and teacher interns presented their research at the August symposium.

Great Falls Public Schools’ Assistant Superintendent Tom Moore was impressed by the presentations. “It’s amazing that our high school students are working on research as important as this—studying diseases like Parkinson’s and Alzheimer’s disease,” he said. “We’re so thankful to McLaughlin for the ability to do something like this locally. This is a perfect use of a tremendous asset in our community as a vehicle for bringing new relevance to the classrooms.”
“I think it’s important to share the love of science with those who don’t have it.”
–Summer Student Jojo Coburn

High School Program
Supported by the Howard Hughes Medical Institute

Students
Kaitlyn Carlson .......................CM Russell High School
Jojo Coburn ............................CM Russell High School
Severin Gilbert ..........................Cascade High School
Dora He ..................Mira Loma High School, Sacramento, CA
Will Strauss ...............................Great Falls High School
Chelsea Xu ............Stuyvesant High School, New York, NY

Teachers
Tom Cubbage ............................CM Russell High School
Brittany Deffinbaugh ....................CM Russell High School
Sara Farr .................................North Middle School
Nathan Greiger ..........................CM Russell High School
Mike Hodges .............................Great Falls High School
Carolyn Prill .............................Central Catholic High School
Brian Sullivan ...........................Great Falls High School

College Interns
Supported by MRI’s generous contributors
Larissa Donahue ..........Montana State University, Bozeman
Chris Peck ............................Montana State University, Bozeman
Kelsey Schweitzer ..........Pacific University, Forest Grove, OR

Mike Hodges, Brian Sullivan, Kaitlyn Carlson, Kelsey Schweitzer, Dora He, Larissa Donahue, Chelsea Xu, Carolyn Prill, Will Strauss, Chris Peck, Severin Gilbert, Nathan Gregier, Jojo Coburn, Tom Cubbage
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Principal, James C. Soft and Associates
Certified Financial Planner, MS in Personal Finance, College of Financial Planning

Gift Annuities, Business Contributions and Paid-up Insurance
Presented by Gary Bjelland
President of Jardine, Stephenson, Blewett, and Weaver, PC
Specialist in trust and estate work, tax law and creating business entities

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Certified Financial Planner - 2 CE credits
(CFP Board has accepted Program)

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