



STANFORD UNIVERSITY SHARES IN \$540 MILLION GIFT FROM LUDWIG CANCER RESEARCH

Ludwig Center at Stanford receives \$90 million

Stanford, Calif. (January 6, 2014) – The Stanford University School of Medicine has received \$90 million from Ludwig Cancer Research on behalf of its founder, Daniel K. Ludwig, to support the school's innovative work in cancer stem cells, which are believed to drive the growth of many cancers.

Stanford is one of six institutions to share in Ludwig's \$540 million contribution to the field of cancer research. Announced today, the gift is one of the largest ever made to the field from an individual donor.

The funding will augment the existing endowment for the Ludwig Center for Cancer Stem Cell Research and Medicine at Stanford, established in 2006, where scientists already have discovered some promising therapies that are moving into clinical trials.

"Today's gift from Ludwig Cancer Research is truly historic," said Stanford University President, John Hennessy. "Over the years, Ludwig has been a generous supporter of cancer research, and through its support changed the course of cancer treatment. But this extraordinary gift will spur innovation well into the future. Stanford is distinguished for its cancer research and has assembled a 'dream team' of dedicated scientists at the Ludwig Center for Cancer Stem Cell Research and Medicine at Stanford. This gift is a tremendous vote of confidence in the work they and their colleagues at other Ludwig Centers are doing and will provide essential support as they pioneer new treatments and therapies."

The Ludwig gift will complement Stanford's Cancer Initiative, a \$250 million effort to advance research and improve patient care, said Lloyd Minor, MD, dean of the Stanford School of Medicine.

"We are very grateful to Ludwig Cancer Research for this exceptional gift, which will provide momentum for further discoveries in cancer stem cells and spur the development of new therapies," Minor said. "Together with our Cancer Initiative, it represents an opportunity to truly transform cancer research and treatment."

With his latest gift, Ludwig has now committed \$150 million to Stanford. The university's Ludwig Center, the only cancer stem cell center of its kind, is directed by Irving Weissman, MD, also the Virginia and D.K. Ludwig Professor for Clinical Investigation in Cancer Research at Stanford.

The first evidence of cancer stem cells was found in acute myeloid leukemia in 1994 by Canadian scientist John Dick, PhD. Weissman and his colleagues purified human blood forming stem cells in 1992 and human leukemia stem cells in 2000 and later identified potential therapeutic targets on them. Since then, Michael Clarke, MD, professor of medicine at Stanford



and a Ludwig Center deputy director, isolated cancer stem cells in breast cancer, pancreatic cancers, and colorectal cancer, and with Weissman head and neck cancers, bladder cancer, myelomas and other cancers.

These specialized stem cells are believed to both self-renew and generate new cancer cells. Thus, any treatment that leaves behind residual cancer stem cells will inevitably lead to a patient's relapse.

Weissman, who was the first scientist to isolate blood-forming stem cells in humans and mice, said Ludwig took a bet on Stanford when the field of cancer stem cells was very new.

"Ludwig funded cancer stem cell research at a time when it was unpopular and disbelieved," he said. "Its support has enabled us to take a discovery that was first made in leukemia and apply it to all cancers and to develop new immunotherapies to targets revealed in these cancer stem cells. Several of these approaches will be clinically tested in patients with various types of cancers."

In his studies of blood-forming stem cells and leukemia in the late 1990s, Weissman and his colleagues found that mice prone to the blood disease overexpress a protein known as CD47. They would later discover that virtually all cancers express CD47, which essentially functions as a "don't-eat-me" signal to fend off potential attacks from the body's immune system.

The Stanford researchers at the Ludwig Center have developed an antibody against CD47 that, when transplanted in mice, causes human tumors to disappear or shrink. It is the first antibody to be shown to be broadly effective against all tested human solid tumors. Most recently, the researchers found that the CD47-blocking antibody wages a two-pronged war on cancer cells; it first enables macrophages, key immune system cells, to grind up the malignant cells, then can stimulate killer T-cells to continue the attack. Because T-cells are constantly patrolling the body for foreign invaders, their presence presumably could keep cancer cells permanently in check, Weissman said. The group, led by Weissman and Ravi Majeti, MD, assistant professor of medicine at Stanford and member of the Ludwig Center, now plans clinical trials with the antibody in 2014 in patients with various types of cancer.

"The process of discovery has been very fast track — from the first paper in 2009 to a planned clinical trial in 2014," Weissman said. "There is no question that without funding from Ludwig, as well as the California Institute for Regenerative Medicine, it would not have happened."

Stanford scientists within the Ludwig Center have been building on the work to create other new approaches to immunotherapy. For instance, Christopher Garcia, PhD, professor of molecular and cellular physiology at Stanford, and two MD/PhD students, Kipp Weiskopf and Aaron Ring, collaborated with Weissman to develop a version of a naturally occurring protein that binds more tightly than the antibody does to CD47. Just recently, Weissman and his colleagues reported in the journal *Science* that this protein works particularly well when used in combination with other known anti-cancer agents, such as rituximab (a lymphoma drug) and trastuzumab, also known as Herceptin (a breast cancer drug), effectively reducing or eliminating tumor growth entirely in a mouse model.



With Ludwig support, Weissman is also pressing forward with clinical trials for a therapy that could dramatically improve survival rates for women with metastatic breast cancer. More than 15 years ago, he and his colleagues Judith Shizuru, MD, an associate professor of medicine, Robert Negrin, MD, a professor of medicine, and the late Karl Blume, MD, conducted a small clinical trial in women involving a novel approach to bone marrow transplantation. In the trial, the researchers removed bone-marrow-rich blood from the women and then purified the stem cells in the lab. These cancer-free stem cells were infused back into the patients to reconstitute their blood and immune systems, which had been destroyed by high doses of cancer-killing chemotherapy.

After 15 years, 33 percent of the women were still alive and well. Among women who receive the standard treatment, the survival rate after 15 years is just 7 percent, Weissman said. The trial was discontinued by the sponsoring company, but with Ludwig support, Weissman and Shizuru have obtained the rights to the process and plan a larger clinical trial at Stanford in 2014.

“If this works as it did before, one third of women will be alive and will never see doctors again for breast cancer,” Weissman said. “We have talked to these women who were in the trial, and they are hopeful and have families, maintain jobs and lead normal lives. We need to do the pivotal trials to extend and expand the original study.”

Ludwig Cancer Research, which includes six Ludwig Centers as well as the Ludwig Institute for Cancer Research, has committed \$2.5 billion in cancer research to date. At Stanford, Ludwig has funded the work of some 10 to 15 laboratories and has helped support an international collaboration with the University of Oxford in London, which will conduct CD47 trials in patients with leukemia and solid tumors. The trials are also being done in collaboration with Brandy Sikic, MD, professor of medicine, and Bruno Medeiros, MD, assistant professor of medicine, both at the Stanford Cancer Institute.

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