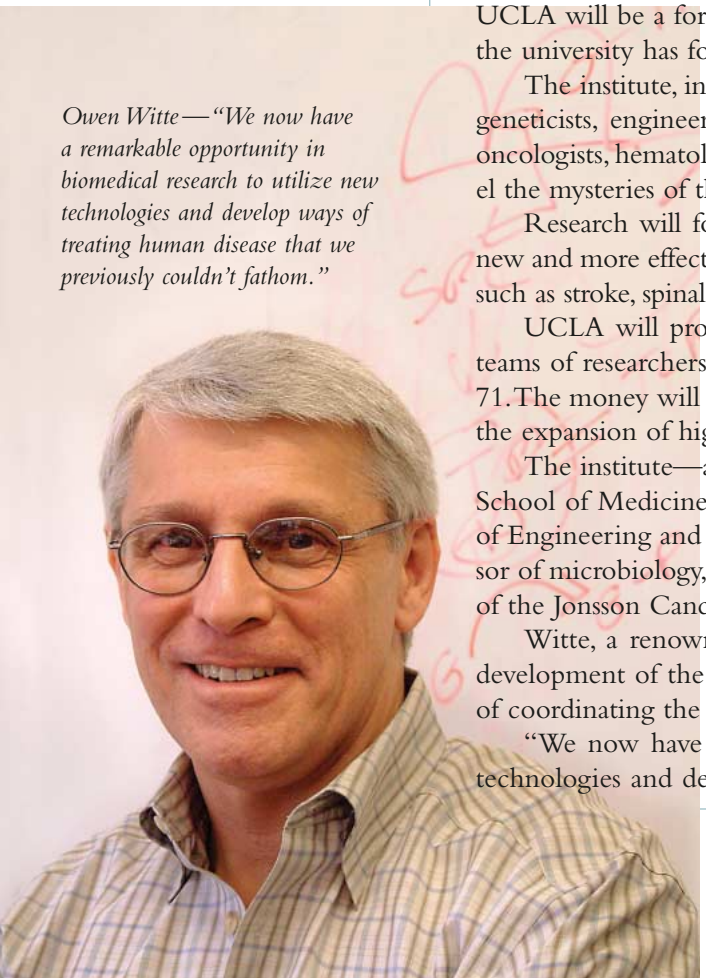
First Steps in a Bold Scientific Adventure

The College is taking a leading role in UCLA's broad new initiative to explore the scientific and medical potential that is emerging from research on stem cells.

By Dan Gordon

"We're seeing a concerted effort to build a scientific culture founded on ties between investigators interested in clinical and biomedical research, basic life sciences, engineering and the physical sciences."



Owen Witte—"We now have a remarkable opportunity in biomedical research to utilize new technologies and develop ways of treating human disease that we previously couldn't fathom."

They are the source of all we become—the unspecialized cells that give rise to the human body's tissues: lungs, liver, brain, hair, heart—and the source of great excitement among scientists.

Armed with ever more powerful tools, researchers from a wide array of disciplines are exploiting the power of stem cells to reveal vital information about human development, including the events that lead to serious medical conditions such as cancer and birth defects. Such study could uncover new avenues for treating numerous diseases, or may lead to a renewable source of replacement cells and tissue to treat degenerative diseases such as Alzheimer's, heart disease or diabetes.

Recently, the non-scientific public expressed its own enthusiasm for this research. Last November, California voters approved Proposition 71, which provides $3 billion in bonds to create the California Institute for Regenerative Medicine—an agency that will regulate human embryonic stem cell research and provide funding through grants and loans for stem cell science at institutions across the state.

The funding boon places California in the forefront of stem cell research, and UCLA will be a formidable player—especially with the announcement in March that the university has formed the Institute for Stem Cell Biology and Medicine.

The institute, in which the UCLA College is taking a leading role, brings together geneticists, engineers, ethicists, chemists, policy experts, pathologists, immunologists, oncologists, hematologists and scientists from other disciplines in a joint effort to unravel the mysteries of the growth and development of adult and embryonic stem cells.

Research will focus on translating fundamental observations about stem cells into new and more effective ways to treat and prevent HIV, cancer and neurological disorders such as stroke, spinal cord injury, brain tumors, multiple sclerosis and genetic diseases.

UCLA will provide $20 million over five years to launch the institute, enabling teams of researchers to compete for state grants created by the passage of Proposition 71. The money will fund the recruitment of a dozen new faculty positions, salaries and the expansion of highly sophisticated laboratory space, infrastructure and supplies.

The institute—a collaboration between the UCLA College and the David Geffen School of Medicine, UCLA's Jonsson Cancer Center, and the Henry Samueli School of Engineering and Applied Science—is headed by the College's Owen Witte, professor of microbiology, immunology and molecular genetics, with Judith Gasson, director of the Jonsson Cancer Center, serving as co-director.

Witte, a renowned scientist whose laboratory research laid the groundwork for development of the targeted leukemia therapy Gleevec, has begun the important task of coordinating the efforts of researchers from a wide array of disciplines.

"We now have a remarkable opportunity in biomedical research to utilize new technologies and develop ways of treating human disease that we previously couldn't

fathom," said Witte. "As someone whose entire career has been about finding ways to apply knowledge of the basic pathobiology of disease to devise new therapeutic strategies, I am very excited to be involved in this effort."

Under Proposition 71, priority for grants will be given to stem cell research that meets the state institute's criteria and is unlikely to receive federal funding. That means that in addition to studies with adult stem cells and so-called presidential stem cell lines—the embryonic lines created before April 9, 2001, the only ones available for federally-funded investigations—researchers eventually hope to be able to work with previously unavailable embryonic lines.

"It will be very helpful to study new embryonic stem cell lines," Witte said. "Many of these lines have unique characteristics, so we need to study lots of different ones in order to learn how things work."

Adult stem cells, which help the body replace tissues that must be renewed continually throughout life, are descended from embryonic stem cells—the cells that give birth to those that become the different parts of the body. Scientists obtain adult stem cells for research from many organs and tissues in the body, including the brain, blood vessels, skin and bone marrow.

Adult stem cells generally are limited to becoming the cell type of their tissue of origin. Embryonic stem cells can be found in an embryo—a fertilized human egg—five to seven days after conception; typically, they are extracted from embryos that have been donated to research by parents undergoing fertility treatments. In vitro fertilization clinics prepare many cells that are not used for the initial impregnation, and the unused or surplus cells are kept frozen as human tissue in case they are needed. When the tissue is no longer needed for pregnancy, it is available for life-saving stem cell research.

Although adult stem cells offer potential benefits and will continue to be studied, most scientists agree that with what is known today, there is much greater promise in embryonic stem cells, given their potential to develop into every type of cell in the body. Jerome Zack, professor of medicine and of microbiology, immunology and molecular genetics, and the associate academic director of UCLA's new stem cell institute, has been involved in clinical trials of a strategy that treats adult stem cells with antiviral genes to provide protection from HIV infection.

The adult stem cells can differentiate to become the blood-forming stem cells infected by the AIDS virus. But the inherent drawback to the approach is that it requires patients to go through the arduous process of having their own stem cells isolated, treated with the genes, and then re-implanted.

Jeffrey F. Miller—"The stem cell institute is designed to take advantage of the full range of expertise available on this campus."

"The beauty of embryonic stem cells, assuming we can get them to develop into blood-forming lineage, is that we could engineer cells to be universally transplantable without having to remove the patients' adult cells and manipulate them in culture," Zack said.

Given the ambitious nature of the task, capitalizing on the public's support requires harnessing expertise from academic fields all over the university.

"UCLA encourages strong collaborations between faculty in the life sciences and the health sciences," said Patricia O'Brien, executive dean of the UCLA College. "As biomedicine grows increasingly complex, new academic partnerships hold the key to discovery; this institute will create novel opportunities for research that span many disciplines."

Said Witte, "There will be opportunities for collaborations that otherwise would not have occurred, simply because faculty from different disciplines are meeting and talking to each other about their work for the first time." Witte has initiated a series of workshops designed to facilitate such discussions.

Within the College alone, researchers with diverse interests are becoming involved. Many faculty in the Department of Molecular, Cell, and Developmental Biology use model systems to understand genetic regulations needed for cells to go into differentiated states.

"In that sense, a stem cell is an ideal system for study," said Utpal Banerjee, the department's chair. Banerjee sees his department's faculty providing fundamental information on non-human organisms that can be applied by translational researchers.

Jeffery F. Miller, chair of the Department of

Microbiology, Immunology, and Molecular Genetics, points out that the multidisciplinary nature of his department—which includes researchers who cover areas ranging from immunology, virology, bacteriology and cell biology to regulatory mechanisms, molecular biology and the study of single cells—makes it ideal for faculty to work with researchers on other parts of campus to better understand and manipulate stem cells.

"This is an exciting time on campus, a time when we're seeing a concerted effort to build a scientific culture founded on ties between investigators interested in clinical and biomedical research, basic life sciences, engineering and the physical sciences," Miller said.

"The stem cell institute is clearly designed to take advantage of the full range of expertise available on this campus and our ability to effectively collaborate in an effort to solve complex biological problems."

Outside the College, the Jonsson Cancer Center features an established clinical trials infrastructure that can be used to test applications that come out of collaborations with biological researchers.

"More and more evidence suggests that cancer is a stem cell disease," said institute co-director Gasson, the cancer center's director and a professor of medicine and biological chemistry. "Many of our current therapies are not effective because they don't target the cancer stem cells."

Meanwhile, faculty in the engineering school with expertise in microfluidics and nanosystems will be counted on to develop new technologies to help accelerate the pace of progress in embryonic stem cell research.

"Every major advance in science that I'm aware of these days is coming from interdisciplinary work," said Witte, who is also looking beyond the College's medical school and engineering partners to other campus departments and schools—future collaborations are envisioned with ethicists, social scientists and experts in business and public policy, among others.

"The image of the solitary scientist is no longer relevant," said Witte. "Stem cell research cuts across every scientific discipline one can imagine—from fundamentals of developmental, cell and molecular biology into applied issues such as how to introduce new or altered genetic information, up to engineering questions of how does one grow and manipulate these cells at scale, and into medical issues of how do you apply this knowledge in the clinic. It's a unifying science that requires different kinds of people to work together."

If the passage of Proposition 71 makes California the focal point for stem cell research in the United States, UCLA appears ideally positioned to take on a central role in the state. Even before the recruitment of new stem cell researchers to the faculty, the campus already boasts experts in adult human stem cells and experts in mouse embryonic stem cells; the two sides will share knowledge as the institute delves further into human embryonic stem cell research. UCLA is also the only public university in California with a Good Manufacturing Practice suite, a specialized laboratory that is critical for the safe growth and manipulation of stem cell lines.

Utpal Banerjee—To understand genetic regulations needed for cells, "a stem cell is an ideal system for study."

As with any relatively new scientific endeavor, researchers are quick to caution that the revolutionary new treatments they hope will eventually evolve for Parkinson's, spinal cord injuries, Alzheimer's, cancer and other diseases may be years or even decades away. But they are also optimistic about the gains that can be realized from this new frontier.

"Technology is such now that with scientists working together, we should be able to determine the signals and conditions that tell these cells what to become," said Zack. "And if we can do that, it opens up a floodgate of therapeutic possibilities."

Dan Gordon is a Los Angeles-based writer who contributes frequently to UCLA publications.