Big Advances Coming in Precision Medicine

Major NIH grant is a coup for UCSF

In the not-too-distant future, thanks in part to advances expected from UCSF scientists collaborating in a major new campuswide NIH-funded initiative, therapy for many rheumatic diseases will be more individualized and precise, based on understanding the unique features of each patient’s disease.

The grant focuses on “precision medicine.” The vision is that physicians will be reasonably confident, perhaps as early as the initial clinic visit, in predicting how an individual patient’s disease will behave, the expected long-term outcome, and what drug regimen will be most effective.

This is in contrast to today when treatment is largely a process of trial and error over many months before identifying the optimal therapy.

Through the new UCSF Center for Advances in Precision Medicine in Rheumatology, UCSF’s key leaders, thinkers, and investigators in a wide variety of fields will concentrate on autoimmune rheumatic diseases, says Dr. Criswell, center director and chief of the UCSF Division of Rheumatology.

She expects the effort to especially accelerate progress in the diseases where UCSF is particularly strong: rheumatoid arthritis, systemic lupus erythematosus, vasculitis, scleroderma, and ankylosing spondylitis, as well as pediatric rheumatic diseases.

“There is tremendous expertise in precision medicine throughout this campus and real excitement about focusing on rheumatic diseases,” says Dr. Criswell. “But the people developing the new technologies are usually not in a position to apply them. They’re not clinical investigators, and they don’t have access to patients, patient samples, and patient data. At the same time, there are outstanding clinical investigators who don’t know what new technologies are out there and how best to apply them to improve diagnosis and treatment of rheumatic diseases.

“Our role is to be a kind of matchmaker enabling these people to work together efficiently and easily. We’re also integrating special experts in bioinformatics to extract and interpret data from multiple types of highly complex data on carefully characterized patient cohorts.”

UCSF is already a leader in precision medicine in rheumatology. One example is what happened after UCSF physicians diagnosed a number of patients with a previously unknown form of rheumatoid arthritis, which always presents with severe lung disease. Working together, pulmonologists, rheumatologists and research experts in genetics and bioinformatics discovered the underlying genetic mutation, in the COPA gene, that causes the disease.

The new NIH grant will support similar discoveries that will lead to more precise diagnoses and treatment approaches.

Precision medicine cured 10-year-old Yasmine Morsy of a debilitating, life threatening rheumatologic autoimmune condition. Her UCSF medical team identified a rare abnormality that caused Yasmine’s disease and corrected it by giving her a new immune system through a bone marrow transplant. The outcome was uncertain. Severe side effects were possible. “We took a leap of faith,” says May Morsy, Yasmine’s mother. Her father, Loay, says, “Five miserable years filled with worry are behind us. Yasmine is off all her medications and doing great.”

It was a major coup for UCSF to attract this funding, which totals $4 million over five years. Because the NIH supports only four centers for this kind of research, the award represents recognition by the NIH of the great promise at UCSF, says Dr. Criswell.

“We’re thrilled,” says Dr. Criswell, “and we’re confident that we’ll make major contributions to this new field. Precision medicine is coming. The only question is how soon.”
A unique rheumatoid arthritis research collaboration between the UCSF and Stanford rheumatology divisions, now in its fourth year, has produced two important results. First, very real progress has been made toward improving the diagnosis and treatment of RA and other rheumatic diseases. Second, each institution has leveraged the studies into very substantial new funding.

The joint venture, called the Center of Excellence (COE), operates through a novel funding model. It is supported by the Arthritis Foundation via gifts to the former Northern California chapter and by both UCSF and Stanford. The Russell/Engleman Center has provided UCSF’s investment.

This shared funding overcomes “one of the weaknesses of U.S. biomedical research,” wrote a member of the expert international panel of scientists who endorsed the initial COE grant proposal. While NIH funding of individual institutions “tends to inhibit collaboration . . . (this) grant does the reverse. It clearly promotes the interaction of scientists at two leading institutions.”

Looking ahead, COE studies might help:

Predict serious bone loss. Autoimmune and inflammatory disease patients with greatly excessive bone degradation are at high risk for fractures and limited mobility. If physicians could predict bone loss, they could mitigate it by modifying therapy. A COE team is experimenting with novel imaging technologies using MRI and high-resolution CT scans that would be the first predictive tools of their kind. (Lead UCSF radiology investigator: Dr. Xiaojuan Li.)

Vastly expand genetic studies. The major obstacles to investigating epigenetics—how environmental factors such as diet, aging, and chemical exposure turn on genes that trigger autoimmune forms of arthritis—are the logistical challenges and the high cost of collecting the required cells from patients’ joints. A small COE study suggests that blood samples are a reliable proxy. Because blood tests are routine and inexpensive, this could exponentially increase epigenetics studies. (Lead UCSF genetics investigator: Dr. Lindsey Criswell.)

Reduce cardiovascular deaths. Many rheumatoid arthritis patients don’t realize that having the disease is, in itself, a risk factor for heart disease. A COE team will answer this question: Do patients who responded well to therapy and whose disease is well-controlled—with only a few tender or swollen joints—have the same elevated cardiovascular risk as those with more severe RA? Early data suggests the answer is yes. The scientists hope to determine what drugs lower the risk. (Lead UCSF cardiovascular investigator: Dr. Jonathan Graf.)

COE work played a key role in the NIH awarding a $4 million, five-year grant to establish the UCSF Center for Advances in Precision Medicine in Rheumatology. (See front page.) “The NIH was intrigued by some of our preliminary data from a small number of patients, and they want us to advance our studies, which are needed to truly enable precision medicine for our patients,” says Dr. Mary Nakamura, site director of the COE.

UCSF rheumatology investigators were awarded additional grants totaling more than $2 million in funding based on new knowledge from COE research.

The COE has funding for one more year.