

Ochsner Research Update

Richard N. Re, MD

Scientific Director, Ochsner Clinic Foundation, New Orleans

Academic year 2010-2011 saw significant progress from Ochsner research in the basic, translational, clinical, and health science research areas. These efforts, as always, are patient centered in their goals of investigating clinical disorders and providing new insights into therapeutic options. And, as in the past, Ochsner research is ongoing in virtually every clinical department.

In the area of basic science, our internationally recognized Laboratory of Cellular Immunology, under the direction of Yong Sung Choi, MD, PhD, has made significant progress in several areas. Dr Choi's efforts have further identified the chemical factors (cytokines) that direct both normal and cancerous B-lymphocyte development. B-lymphocytes are necessary for mounting a normal antibody response to infection but, when abnormal, produce a common form of leukemia. Therefore, understanding how these cells grow and develop in both health and disease is of great importance. Most recently, this laboratory has shown that the cytokines interleukin-10 and interleukin-21 are important regulators of this developmental process. These investigators have also demonstrated that the cell marker CD9 is depleted in aggressive B-cell lymphomas, providing new insight into possible therapeutic approaches. In addition, the laboratory is working closely with the staff and fellows of the Section on Rheumatology to identify abnormalities of B-cells in patients suffering from systemic lupus erythematosus. This work could provide important new insights into the causes and treatment of this debilitating disorder. Others in the laboratory are collaborating with the Department of Colon and Rectal Surgery to identify so-called cancer stem cells in human colon cancer using techniques they previously employed successfully in their studies of B-cell development. These latter two projects in Rheumatology and Colon and Rectal Surgery are prime examples of translational research: the close linking of basic and clinical scientists to address issues of immediate clinical importance.

Julia Cook, PhD, codirector of the Laboratory of Molecular Genetics, and her team have made important advances in the study of the peptide hormone angiotensin II, a powerful regulator of blood pressure and cardiovascular structure. They discovered new actions carried out by the receptor for this hormone. While it has been known that interaction of angiotensin II with its receptor could lead to cell

growth and participate in such processes as enlarging the heart in patients with high blood pressure or those who have suffered a heart attack, Dr Cook found that in some cases binding of the hormone resulted in cleavage of the receptor on the cell surface, the transfer of part of the receptor to the cell nucleus, and the induction of apoptosis—that is, programmed cell death. This observation is important because progressive cell death is a key feature of disorders such as heart failure, a condition that has already been shown to benefit from drugs that block angiotensin action. The laboratory's investigation suggests why these drugs work. Moreover, additional observations have identified mechanisms that control the movement of the receptors within the cell, suggesting ways to prevent the receptor from reaching the cell surface and therefore blocking the detrimental effects of angiotensin II. Finally, the laboratory continues its groundbreaking studies of the intracellular—that is, the intracrine—actions of angiotensin and other hormones. Transgenic animals expressing intracellular angiotensin have been shown to develop a particular form of hypertension and kidney disease; this sheds light on the potential of intracrine angiotensin to produce disease.

The Hypertension Research Laboratory under the direction of Edward Frohlich, MD, Alton Ochsner Distinguished Scientist, continues its nationally recognized research on the adverse effects of salt on health. It has long been known that high salt intake can produce high blood pressure in susceptible people and make hypertension harder to control in patients. However, work beginning about 10 years ago suggested that high salt intake could be harmful even if it does not produce high blood pressure. Dr Frohlich's group has expanded this research not only by showing an adverse effect of high salt on the health of laboratory animals but also by demonstrating that inhibitors of angiotensin II action can prevent these effects. These findings have important medical and public health implications. Dr Frohlich's research contributed to the recent American Heart Association recommendation that sodium intake be reduced to 1,500 mg/d for everyone. As a nation, we have been mobilized to fight a growing epidemic of obesity, and the wisdom of this course of action is unassailable. However, the findings of Dr Frohlich's group point out the importance of not substituting salt for calories in order to make food taste better.

The Cardiology research effort headed by System Cardiology Chairman Christopher White, MD, also continued to make significant progress in its translational research initiatives. A major effort of this group is to improve the cure rates for patients undergoing renal artery stenting for narrowing of the artery, a condition that can produce severe hypertension and can also lead to kidney failure. Working in tandem with basic scientists, the team is developing biochemical markers to help predict which patients are likely to benefit from therapy and is testing devices that could increase cure rates by limiting any procedure-related renal damage. This group also continues its basic science efforts to determine why stent restenosis occurs more frequently in patients with diabetes.

The Center for Health Research, headed by Marie Krousel-Wood, MD, MSPH, continues to investigate the factors that determine patient adherence to medical therapy. This is an important area because it is becoming clear that lack of patient adherence to therapy is a major cause of preventable morbidity and healthcare costs. Other ongoing representative projects in the Center include the effect of natural disasters on patient health and methods to improve compliance in diabetic and depressed patients. The Center is currently expanding so it can address a wide range of clinical outcome questions and has recently established a close working relationship with researchers at Tulane University Medical Center.

As in the past, clinical research projects are ongoing in virtually every clinical department. For example, Jonathan Nussdorf, MD, Chairman of

Ophthalmology, is collaborating with neuroscientists at Louisiana State University Health Sciences Center on the potential utility of a novel nerve cell protective factor in the treatment of eye disorders. Significant clinical research expansion is continuing in many clinical departments, particularly in Anesthesiology, Colon and Rectal Surgery, Endocrinology, Nephrology, Hematology-Oncology, Cardiology, Infectious Diseases, Transplantation, Neurosciences, Rheumatology, and Nursing, among others. Not surprisingly, several of these research programs—such as Nephrology, Anesthesiology, Cardiology, Infectious Diseases, Transplantation, Neurosciences, and Hematology-Oncology—have dedicated basic science research components as well.

An additional and growing facet of Ochsner research is the collaboration with The University of Queensland. Jawed Alam, PhD, Deputy Head (Research), The University of Queensland, Ochsner Clinical School, directs the Ochsner effort in forging this collaboration. Face-to-face meetings between scientists in both organizations are occurring regularly. In due course, collaborative research efforts are bound to develop—an extraordinarily bright prospect. Finally, 81 posters were presented at the 2011 Research Night. A new feature this year was the awarding of a prize by the Ochsner Alumni Association to the best resident research poster. This is yet another sign of the campus-wide interest in this activity and in Ochsner research.

In sum, the Ochsner research enterprise continues to make good progress and looks forward to additional growth next year.