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Ochsner Research Update

Richard N. Re, MD

Scientific Director, Ochsner Clinic Foundation, New Orleans, LA

Research activities at Ochsner Clinic Foundation (OCF) continue to make progress in clinical, basic science, and translational investigation. Here several activities are highlighted as part of an ongoing series describing research at this institution.

Dr Li Li of the OCF Cellular Immunology Laboratory has long worked with the laboratory director, Dr Yong Sung Choi, in the area of B-lymphocyte differentiation. Together these investigators have identified a novel cell surface protein, CD320, which appears to be important in the maturation of normal lymphocytes and in the growth of malignant lymphoma cells. The prospect that interruption of the activity of this protein can blunt lymphoma growth gains support from the fact that a monoclonal antibody directed to this factor slows the growth of lymphomas in animal models. These investigators and their colleagues also have found evidence to suggest that the factor plays a role in the proliferation of other tumor cells residing in lymph nodes. Therefore, this work has implications for the treatment of metastatic disease. Recently, Dr Li Li began studies in the emerging field of cancer stem cell biology. It appears that rapidly dividing cancer cells in many instances are the daughter cells of slowly dividing stem cells, and—unlike the daughter cells—are extremely long lived. Thus, therapies directed at destroying rapidly dividing cells may reduce the body's burden of damaging daughter cells but are unlikely to eliminate the slowly dividing stem cells, making these therapies less effective in tumor eradication. Dr Li Li is well on the way to isolating follicular lymphoma stem cells, and the identification and study of these cells will have important implications for the design of effective and less toxic therapies.

Address correspondence to:
Richard N. Re, MD
Research Operations
Ochsner Clinic Foundation
1514 Jefferson Highway
New Orleans, LA 70121
Tel: (504) 842-3562
Fax: (504) 842-3899
Email: rre@ochsner.org

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Dr Marie Krousel-Wood and colleagues have been conducting a long-term project studying the factors that determine adherence to medication regimens in patients with hypertension and, likely therefore, in patients with other chronic conditions. The occurrence of Hurricane Katrina during the study offered the opportunity to investigate the effects of disasters on compliance. The study involved identifying more than 2000 patients in the OCF health system with hypertension. Patients completed detail questionnaires on their health conditions and medication use at the start of the study and regularly thereafter. Medication use was also determined by examining prescription refill records. A variety of validated instruments were employed to assess demographic, financial, and health determinants of compliance. The results of the study will be available in 24 months, although interim analysis is already shedding new light on why people sometimes fail to take their medicine either in normal times or following a disaster.

Drs Julia Cook, Jawed Alam, Richard Re, and their colleagues have for some time studied the intracellular workings of the peptide hormone angiotensin (AT). The so-called AT-1 receptor for angiotensin II can be shown to traffic from its usual position on the cell membrane to the nucleus following binding of externally applied angiotensin to the cell surface. Indeed, angiotensin II can also traffic to the nucleus as part of this *intracrine* system. Recently, Dr Cook identified two proteins that bind to the intracellular tail of the AT-1 receptor and appear to influence its trafficking from intracellular sites to the cell membrane and possibly from the cell membrane to nucleus. These proteins represent possible targets for drug development because knocking them down results in less membrane AT-1 and therefore less angiotensin stimulation of cells. Because of the role angiotensin II plays in hypertension and cell proliferation, this could have important therapeutic applications.

Drs Edward Frohlich, Dinko Susic, and their colleagues continue animal studies aimed at determining whether or not and how salt intake can produce cardiovascular disease independent of sodium-induced raises in arterial pressure. There is a small, but growing, body of evidence to indicate that whereas salt intake correlates with blood pressure across populations, particularly when societies with very high and very low salt intake are included, the

effects of salt intake on blood pressure are modest within populations. Yet epidemiologic evidence strongly suggests that high salt intake is associated with cardiovascular morbidity in Western populations. Because pharmacologic inhibition of the renin-angiotensin system, even in the presence of suppression of circulating renin by salt, mitigates the pathological effects of salt intake in animal models, these OCF investigators posit an effect of salt intake on tissue-based renin-angiotensin systems in the heart and vasculature. This notion follows on the work on tissue renin-angiotensin systems conducted for more than a decade at OCF by Drs Richard Re and Julia Cook. The prospect that disorder regulation of tissue renin-angiotensin systems could play an even greater role in cardiovascular pathobiology than previously appreciated is an exciting area for future research with important public health consequences.

In summary, these ''snapshots'' of research at OCF serve to illustrate both the spectrum and quality of biomedical science in the organization. In future reports we hope to highlight additional activities of potential interest to the readers of the *Journal*.