NIH AWARDS $1 MILLION TO SCRIPPS RESEARCHER

LA JOLLA, CALIF Aug. 7, 1992 -- The National Heart, Lung and Blood Institute of the National Institutes of Health has awarded $1 million to Nigel Mackman, Ph.D. of The Scripps Research Institute to study tissue factor gene regulation in circulating blood cells called monocytes.

The five-year grant, which totals $1,078,457, will focus on tissue factor, a cell-surface gene involved in blood coagulation. Although the research is still at the basic-science level, the future implications are for prevention and treatment of septic shock syndrome, stroke and heart attack.

"In a normal, healthy individual, tissue factor is expressed around blood vessels to limit bleeding in the event of vessel damage. This localized expression prevents inappropriate coagulation," Mackman says.

"Our research goal is to understand the role of tissue factor in disease situations, so that eventually we'll be able to intervene in the disease process," he notes. Mackman's research focuses on two main diseases -- septic shock and arteriosclerosis.
Septic shock is a complex, multisystem disease that is responsible for 80,000 deaths annually in the United States. This syndrome is associated with a wide variety of clinical disorders including bacterial sepsis and viral infection. Tissue factor expression within the vasculature is a major mediator of fatal bacteremic shock which leads to inappropriate blood coagulation, fibrin deposition and organ failure.

Mackman says recent studies have shown that inhibiting tissue factor activity with a monoclonal antibody protected against lethality in a baboon model of septic shock. In his research, Mackman will investigate the regulatory pathways that control the expression of tissue factor in septic shock.

The other disease that interests Mackman is arteriosclerosis, which includes a number of blood vessel diseases culminating in heart attacks and stroke.

"We believe that thrombotic complications associated with arteriosclerosis are probably due to circulating blood contacting tissue factor expressed in fat-laden monocytes within the plaque. Subsequent coagulation could occlude the artery, leading to heart attacks or stroke," Mackman explains.

"In our research, we're using the tissue factor gene as a model to understand regulation of gene expression in the monocyte," Mackman says. "Understanding the molecular events in the monocyte may allow us to intervene in the disease process at the level of gene expression."
Born in Rustington, England, Mackman received his doctorate in genetics at the University of Leicester, England, where he also was a postdoctoral fellow for two years. He came to The Scripps Research Institute in 1987 as a research fellow and in 1989 became an assistant member of the Department of Immunology.

Last winter, Mackman was named the first prize winner of the American Heart Association's Louis N. Katz Basic Science Research Prize for Young Investigators. The prestigious national award was given for his research on tissue factor.

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