SOUTHWESTERN NEWS

Media contact: Jennifer Haigh
214/648-3404
or email jhaigh@mednet.swmed.edu

NEONATOLOGY RESEARCH LEADS TO BETTER UNDERSTANDING OF HOW ESTROGEN PROTECTS AGAINST HEART DISEASE

DALLAS – February 1, 1999 – Scientists at UT Southwestern Medical Center at Dallas now have a better understanding of the protective role that estrogen plays in cardiovascular disease.

The new findings, published in the February issue of the *Journal of Clinical Investigation*, have profound implications for understanding how estrogen improves blood vessel function and provides the protection premenopausal women have against coronary artery disease.

"Premenopausal women have very little coronary heart disease compared to men, the incidence of the disease rises markedly after menopause, and hormone replacement therapy reduces the risks to premenopausal levels," said Dr. Philip Shaul, a professor of pediatrics whose research into nitric oxide's effects on newborns led to the findings regarding estrogen. "The benefits of estrogen in heart disease have to do with how estrogen causes the endothelial cells in blood vessels to make more of the compound, nitric oxide."

Shaul, a neonatologist, studies severe pulmonary hypertension in newborns: a condition in which the blood vessels in the lungs are constricted so tightly that they inhibit successful gas exchange. Specifically, his research is concerned with how endothelial cells produce the relaxing molecule, nitric oxide, so newborn infants' lungs can undergo increased blood flow and subsequently take over gas exchange from the placenta.

"Certain infants have problems with their lung circulation not opening up at birth," Shaul said. "There is very little blood flow to the lungs before birth, and that blood flow must increase several-fold in order for the lungs to take care of the job that the placenta previously held. This is one of the most dramatic examples of blood vessel relaxation throughout human development."

While studying infants who have this unsuccessful relaxation of lung blood vessels, Shaul has unlocked vital information on the cellular mechanisms of estrogen, which is applicable to understanding various causes of vascular disease.

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Previous studies have shown that estrogen stimulates the endothelial cells to produce nitric oxide. But until now, scientists have not understood the mechanism of how estrogen works on these blood vessel cells.

The researchers found that the response of endothelial cells to estrogen is completely different from the classical response that other body tissues have to estrogen. Most responses to estrogen come about from the hormone turning on a gene and usually initiating a slow response, Shaul said.

Instead, Shaul's team discovered that certain estrogen receptors have very rapid signaling effects in endothelial cells.

"The receptor has a totally new function in that it is sitting on the surface of the cell and is responsible for the very rapid effects of estrogen to cause cells to produce more nitric oxide," he said.

The results add to the growing understanding of how estrogen positively affects blood vessels. If this can be more fully elucidated, then scientists can work to refine estrogen replacement therapy for post-menopausal women; utilizing the hormone's positive effects while dampening down any pernicious effects. In addition, specific new therapies may be found to decrease the risk of vascular disease in men.

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