New Research Initiatives at Wright State Use Genetic Models to Understand Hypertension

by Mark Willis

Using genetic research techniques to study hypertension is not a simple process, according to Mariana Morris, Ph.D. Hypertension does not fit into a monogenetic model; many genes on different chromosomes influence how the body regulates blood pressure. "It's probably the interaction of those genes with the environment that results in hypertension," Dr. Morris says.

Mariana Morris, Ph.D., was appointed chair of the Department of Pharmacology and Toxicology at Wright State University School of Medicine in 1997. She came to Wright State from Wake Forest University School of Medicine in North Carolina, where she was professor of physiology and pharmacology and an associate in the Hypertension Center in the Department of Surgical Sciences. Hypertension and how the brain regulates blood pressure are the central themes of her research, which has had continuous support from the National Institutes of Health (NIH) throughout her career. The laboratory and research program that she has established in Dayton represents a major new initiative in cardiovascular research at Wright State.

Experimental studies now underway in her new lab include investigations of how salt intake and stress influence blood pressure and how blood pressure can be manipulated by genetic changes. A future collaboration is now being planned with toxicologists at Wright-Patterson Air Force Base to explore how stress impacts on the response to environmental chemicals.

The unifying theme to the research is blood pressure/brain relationships. Blood pressure is controlled by neural and hormonal outflow from the brain and most of the drugs used to treat hypertension act through the brain. Dr. Morris is especially interested in the role of angiotensin, a peptide hormone which is present in the brain and in the peripheral circulatory system. Dr. Morris says, "In the last few years developments in molecular genetics have produced models in which genes for the angiotensin system are turned on or off. These are important in the investigation of its function."

Dr. Morris's earlier research at Wake Forest used a transgenic animal model with increased brain levels of angiotensin. In this case, the rat contains multiple copies of a gene which controls angiotensin levels, the end result being a remarkable increase in blood pressure, with levels greater then 200 mmHg. Dr. Morris also found that these animals with high angiotensin levels were hypersensitive to intake of sodium chloride. "This is significant because it shows that an alteration in the brain system can alter a response to dietary manipulation," Dr. Morris says. "In humans it is known that societies that have high sodium intake have a greater incidence of hypertension," she continues. "There is some evidence that you can manipulate blood pressure with sodium control. The absolute amount of sodium that we need, and how great is the impact of sodium on blood pressure, is not known, but there definitely are people who are salt sensitive."

Since coming to Wright State, Dr. Morris has begun work on a new genetic model in mice. In this case, a gene for the angiotensin system has been removed or "knocked-out" rather than being added as in the transgenic model. The knock-out in this model is a gene that produces the receptor for angiotensin. Without this receptor, blood pressure is reduced. "Mice models are new for the study of the cardiovascular system," she explains. "It's much more difficult to study blood pressure in mice because they are so small, weighing 30-40 grams." However, Dr. Morris and her team have been successful in setting up a system to measure blood pressure chronically. They are just beginning studies to determine how the animals will respond to salt and stressful conditions, providing information on the role of a specific genetic change.

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