

Research Focuses on Genetic Epidemiology

By Robin Suits

Wright State University Boonshoft School of Medicine has become one of the top federally funded medical schools in the nation for research in the area of public health and preventive medicine. According to the National Institutes of Health, Wright State University ranks 17th in the nation among all medical schools for the amount of federal funding it receives for such research.

The Lifespan Health Research Center (LHRC) is one of the most important contributors to the university's growing reputation in this field. In the past five years alone, LHRC has won more than \$17 million in new grant support for its research on the health-related changes that occur in "normal" individuals throughout their life span. Home of the Fels Longitudinal Study, the world's largest and longest running study on human growth and body composition, the center's major emphases involve research into growth, maturation and aging, body composition, risk factors for cardiovascular disease, and general health status.

About half the research done at LHRC today is directly based on the rich treasure trove of anthropometric data gathered through the Fels Study since its founding in 1929, although that data often supports research that was unimaginable in the early years. For example, much of the focus in recent years has been on bringing the 21st Century techniques of genetic epidemiology—or the gene-based study of how and why diseases cluster in families and ethnic groups—to the mix. Here are some examples of LHRC's recent research:

Genetics of Infant Growth Rates: Infants who are small at birth and then grow rapidly during their first years of life are at increased risk for obesity, diabetes, and cardiovascular disease later in life. Until recently, little was known about how much growth rate was determined by genetic factors and how much was influenced by differences in infant feeding patterns. Using the unique longitudinal data on infant weight and length collected from more than 500 Fels Study participants, LHRC researchers have not only demonstrated that infant growth is highly influenced by genetics, but also have been able to identify which chromosomes are most likely involved. Knowledge of genetic determinants of growth may shed light on the mechanisms involved in the development of chronic disease later in life.

Genetic Epidemiology of Cardiovascular Disease Risk Factors: This is part of a collaborative effort to examine the role genetic factors play in cardiovascular disease (CVD) and to ultimately identify specific genes influencing the age-related progression of CVD risks. This study follows on the heels of an earlier examination of the genetic epidemiology of hypertension, and now seeks, in the

same families, to understand "the genetic architecture of age differences in cardiopulmonary function, vascular health, lipids, and hormone levels," according to Roger M. Siervogel, Ph.D., LHRC director and Fels professor of community health.

Genetics of Skeletal Maturation: During childhood, the skeletal age of a child can vary by two to three years from the child's chronological age. Specific genes influencing this variation have yet to be fully identified. LHRC researchers have been able to demonstrate a consistent genetic linkage between markers on a specific chromosome and the timing of skeletal maturation of children between the ages of 2 and 10, but the same linkage is not apparent in older children. Their work suggests that different genes may play a more important role in skeletal maturation after the age of 10. Such research could eventually provide clinicians with more effective ways of diagnosing and treating children with abnormal stature.

Genetics of Cortical Bone Mass During Childhood: The rate at which children acquire bone mass plays a major role in their bone health and risk of developing osteoporosis in adulthood. Using data from the Fels Study, LHRC researchers have discovered particular areas on a number of chromosomes that are linked to bone mass development in children. "Parallel research into the determinants of joint health across the life span also has demonstrated profound sex differences in cartilage thickness that is not explained by body mass alone," reports Dana Duren, Ph.D., LHRC assistant professor of community health.

Genetics of Craniofacial Morphology: Congenital anomalies of face and skull, such as cleft lip and palate, are among the most common birth defects. Despite great strides in identifying some of the genes that are responsible, the genetics of normal variation in craniofacial morphology have remained largely unknown. LHRC researchers have been able to use head radiographs from the vast Fels collection to identify particular areas of the genome involved in normal development of the face and skull. As it becomes increasingly possible to incorporate gene therapy and tissue engineering into the strategy for repairing craniofacial anomalies, a more comprehensive understanding of the genetics involved in these conditions is critical.

"There is no other study like the Fels Longitudinal Study, no other study in the world with data like this," says Ellen Demerath, Ph.D., LHRC associate director and associate professor of community health. "The important contribution we hope to make with our research here is to raise awareness about the importance of genetic and environmental factors in childhood in determining later health outcomes."