Researchers identify proteins that help develop mammalian hearts

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The absence of two proteins in mammalian embryos prevents the development of a healthy heart, a new study by researchers at the Medical College of Wisconsin, Milwaukee, has found.

The study, which appears in the May 15 issue of *Developmental Biology*, was led by Stephen Duncan, Ph.D., professor of cell biology, neurobiology and anatomy at the Medical College.

This is the first study that has successfully identified the factors responsible for the onset of heart formation in the mammalian embryo. Until now, no single mutation had been identified that was thought to be responsible for blocking proper development of the heart in mammalian embryos. The identification of these major developmental switches will allow researchers to unravel the fundamental mechanisms that define heart cell formation.

Understanding the molecular pathways that control the development of the heart has been the subject of much interest in the scientific community, as approximately 35,000 children are born in the United States each year with congenital heart defects. Many more die during gestation because of complications from improper heart development.

“Defining these molecular pathways has implications in the production of heart cells from stem cells,” said Dr. Duncan. “Our study suggests that mutations in GATA4 and GATA6 are likely contributors to the development of congenital heart disease in children. Indeed other

investigators at our Medical College, as well as elsewhere, have found mutations in one of the genes from our study in children born with heart abnormalities."

Dr. Duncan's lab found that either of two proteins, GATA4 and GATA6, controls the expression of genes that tell early embryonic cells to start making other proteins that eventually become beating heart cells.

"When either GATA4 or GATA6 were present, the stem cells were able to make most of the proteins that are required for heart function suggesting that they act in a redundant manner," Dr. Duncan said. "However, when both GATA4 and GATA6 genes were mutated, the embryonic stem cells were unable to form heart cells in the lab."

The study observed how the absence or mutation of GATA4 and GATA6 proteins impacted heart development in mice embryos. The embryos were cloned from GATA4 and GATA6 deficient stem cells.

"When embryos were cloned from normal stem cells, they made normal beating hearts," Dr. Duncan explained. "However, when embryos were cloned from the GATA4/GATA6 deficient stem cells, the embryos developed but were completely lacking all heart cells."

Source: Medical College of Wisconsin