# Researchers confirm prenatal heart defects in spinal muscular atrophy cases

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University of Missouri researchers believe they have found a critical piece of the puzzle for the treatment of Spinal Muscular Atrophy (SMA) - the leading genetic cause of infantile death in the world. Nearly one in 6,000 births has SMA, and it is estimated that nearly one in 30 to 40 people have the trait that leads to SMA.

In a new study in Human Molecular Genetics, Christian Lorson, professor in the Department of Veterinary Pathobiology and the Department of Molecular Microbiology and Immunology, has found prenatal cardiac defects in mice with SMA. Lorson believes this discovery has implications for eventual treatment as clinicians can no longer concentrate exclusively on the nervous system when treating SMA.

Lorson's research team, headed by Monir Shababi, research scientist, examined two animal models of SMA and discovered that cardiac defects are found throughout SMA development and include neonatal fibrosis in the heart, ventricle malformation, thinning of the cardiac wall and slower heart rates.

"It is likely that in severe cases of SMA, the disease is not limited to motor neurons; rather, it becomes a multisystem disease, and the cardiac contribution is just one of the systems," said Lorson, who works in the MU Bond Life Sciences Center. "These results are consistent with clinical reports of severe SMA cases that describe a number of cardiac defects. To fully address this disease, any new therapies or drugs must be

effective in every tissue, not just motor neurons. The more we understand the disease, the better off we will be in terms of developing therapeutics or better supportive care. What this conservatively means for humans is that therapies have to go beyond the nervous system in the most severe and most profound cases."

Spinal muscular atrophy is caused by loss of a gene known as SMN1. Humans have an additional gene called SMN2 which only makes a small amount of the normal SMN protein - the protein required to prevent SMA. SMN1 and SMN2 are greater than 99 percent identical, but a small difference between the two causes the dramatic difference in the amount of functional protein produced by SMN2.

Typically, the disease moves from the outlying limbs into the trunk of the body. Most deaths are caused by respiratory failure in the lungs. Researchers have been targeting SMN2 - what Lorson calls the "partially functioning backup copy" - because any increase in SMN2 means better results.

"SMN2 is like a light that's been dimmed, and we're trying anything to get it brighter. Even turning it up a little bit would likely help dramatically," Lorson said.

Provided by University of Missouri-Columbia