Gene mutation discovery sheds light on organ failure affecting babies

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A group of scientists and clinicians from the UK, the Netherlands, Italy and the U.S. have worked together and made an important discovery that explains an often fatal organ defect that affects unborn babies and

children.

Finding mutations of a key gene that controls how the urinary bladder grows before birth could be key to developing future treatments for this rare but devastating disease.

Research published today in the *Journal of Clinical Investigation* demonstrates why babies can have massively distended bladders that don't empty. This results in a back-up of urine that causes the kidneys to stop working.

Professor Adrian Woolf, a co-author of the paper and a kidney disease researcher in the Royal Manchester Children's Hospital and University of Manchester, said "Sadly most of the affected babies are terminated before birth due to the poor outlook. Although this condition is not common, it is one of the many hundreds of rare diseases that together affect one in seven of all of us. These diseases urgently need more research."

Dr. Esther Creemers, co-author at the Amsterdam UMC Research Centre said: "The gene at fault is called Myocardin and we show, for the first time, that it is essential for normal formation of muscle in the wall of the human bladder. When this goes wrong, the quality of the muscle is poor, and so the bladder can't empty.

"We found several families who carry critical changes in this gene" said Professor Bill Newman, from the Manchester Centre for Genomic Medicine. "The bladder disease is much worse in boys than in girls, but some affected people are also born with abnormal hearts, probably because the gene also control the growth of muscle in the heart or the large blood vessels nearby."

The newly published research is important in terms of developing

genetic counseling but also helps understand the mechanism of a congenital rare but fatal disease. This opens the way to consider more futuristic treatments such as gene therapy, and a similar strategy is being used to treat other serious inherited diseases in other organs.

More information: Arjan C. Houweling et al. Loss-of-function variants in myocardin cause congenital megabladder in humans and mice, *Journal of Clinical Investigation* (2019). DOI: 10.1172/JCI128545

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