Scientists identify gene linked to common birth defect in male genitalia

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King's College London, in collaboration with Radboud University Nijmegen Medical Centre in The Netherlands, has discovered a new gene associated with Hypospadias, the congenital malformation of the male genitalia. The research was published today in *Nature Genetics*.

It was previously known that genetics play a part in developing the condition, with five percent of patients having an affected male relative, but the genes involved were unknown. This study shows for the first time that a gene inherited from the mother is likely to be important in development of the condition.

Hypospadias is a common congenital condition which affects around 1 in 375 boys. In these infants the urethral opening is not located at the tip of the penis, but somewhere halfway, at the base of the penis, or in the scrotum. Children with the condition typically undergo surgery between six and 18 months of age, but the malformation may have medical, psychological and sexual consequences later in life.

Dr Jo Knight, based at the Comprehensive Biomedical Research Centre at King's, assisted in the analysis of a genome-wide association study on 436 boys with hypospadias and 494 without the condition, which was undertaken by Loes van der Zanden and colleagues at Radboud University Nijmegen Medical Centre in The Netherlands.

The study revealed a strong association between changes in the DGKK gene and hypospadias. A boy with a modified DGKK gene has 2.5 times

increased risk of being born with the condition compared to other boys. The DGKK gene is located on the X chromosome and is therefore inherited from the mother.

Dr Jo Knight said: 'Until now we knew very little about hypospadias and why some boys are born with the condition. We already knew that there was a greater chance of boys being born with hypospadias if a male relative has the condition, but this study shows that changes in the DGKK gene, found on the X chromosome and inherited from the mother, plays a major role in the development of the condition.

'But we still don't know exactly how this causes the condition, so there is more research to be done to look at other combinations of genes and environmental factors that might trigger the malformation.'

More information: *Nature Genetics* paper: 'Common variants in DGKK are strongly associated with risk of hypospadias'

Provided by King's College London