Polymorphisms of MAMLD1 gene in hypospadias

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Purpose: Mastermind-like domain containing 1 (MAMLD1) is a causative gene for the fetal development of male external genitalia. Almost 10% of patients with both severe and non-severe hypospadias exhibit mutations of MAMLD1. The aim of this work was to determine whether polymorphisms of MAMLD1 are a genetic risk factor for hypospadias. Material and methods: This study included 150 hypospadias with a range of severities and 150 controls. Direct sequencing of the MAMLD1 coding exons and their flanking splice sites was performed. In silico secondary and tertiary structure prediction and accessibility of changed amino acids were evaluated using JPred,

Netsurf and PHYRE software. Functional studies of the transactivation of haplotypes on Hes3 promoter were performed in vitro using cDNAs of missense variants of MAMLD1. Results: The p.P286S polymorphism was identified in 17/150 patients and 12/150 controls (11.3% vs. 8.0%, p = 0.32). The p.N589S polymorphism was identified in 22/150 patients a