

Tissue engineering in Mayer-Rokitansky-Küster-Hauser syndrome: state of the art and future perspectives

Paola PONTECORVI – *University of Rome La Sapienza*

Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is a rare and complex disease defined by congenital aplasia of the vagina and uterus in 46,XX women. The aetiopathogenesis of MRKH syndrome is still largely unknown. Recently, we performed array-CGH, MLPA assays, and molecular analyses on DNA and RNA samples from an Italian cohort of 36 unrelated MRKH patients. We identified copy number variations in 25% of them, including a novel heterozygous microduplication at Xp22.33, containing the PRKX gene, and a novel duplication of a specific SHOX enhancer. Through a network analysis for protein-coding genes, which we found in the altered genomic regions, we highlighted that PRKX is a central node (hub) of the MRKH-related network, where the most relevant biological connections are linked to the anatomical structure development. By using an *in vitro* approach, we proved that PRKX ectopic overexpression in a cell model of vaginal keratinocytes promotes cell motility through epithelial-mesenchymal transition activation, a fundamental process in urogenital tract morphogenesis. Moreover, our findings showed that PRKX upregulation can affect transcriptional levels of HOX genes implicated in urinary and genital tract development. Our study identified the dysregulation of PRKX expression as one of the possible molecular mechanisms underlying MRKH syndrome. As regard MRKH clinical management, the vaginal defect characterising the syndrome could be resolved with conservative or surgical approaches, by employing several types of autologous or xeno/allogenic grafts, which present pros and cons. Since 2006, in collaboration with the gynaecology team of Policlinico Umberto I of Rome, we have performed vaginoplasty using a modified Abbé–McIndoe technique with autologous *in vitro* cultured vaginal tissue in patients with MRKH syndrome. A 5-year follow-up study demonstrated satisfactory long-term sex life, improvement of psycho-emotional state, and quality of life in treated patients. Currently, we are characterising the microbiota of 20 MRKH patients, who successfully underwent vaginal reconstruction, and 20 healthy women to study through microfluidic systems the vaginal microenvironment and to develop pro/prebiotics-based strategies aimed at maintaining the correct balance of microorganisms for MRKH patients' long-term health benefits.