

Invited speakers

Comunicações por convite

CC-01**GENE-ENVIRONMENT INTERACTION IN CONGENITAL HEART DEFECTS***W.S. Kerstjens-Frederikse**Department of Genetics, University of Groningen, University Medical Center, the Netherlands**w.s.kerstjens@umcg.nl*

Each year one million children are born with a congenital heart defect (CHD) worldwide. Monogenic or chromosomal variations (partially) explain the CHD in some children, however, the etiology of most CHDs is complex and unclear. The interplay of genetic variants, regulating elements and environmental factors ultimately determine the development of the heart. The picture is far from complete, but some key players reported in the literature will be highlighted.

Fetal cholesterol biosynthesis is well known to affect cardiac development, as can be concluded from the occurrence of heart defects in 50% of patients with Smith-Lemli-Opitz syndrome, caused by mutations in the *DHCR7* gene. Maternal cholesterol, however, is hypothesized also to play a key role in early fetal cardiac development.¹ Maternal lifestyle factors may therefore affect the prevalence of congenital heart defects. The interaction of genetic variants in the folate pathway with maternal lifestyle factors is also associated with CHDs. Smoking of cigarettes and obesity in combination with specific polymorphisms are associated with CHD in the offspring.²

The serotonin pathway, and controversies about the association of maternal SSRI's with CHDs will be discussed.^{3,4,5} The role of placental transporters like P-glycoprotein might explain the differences in the reported teratogenic effects of several drugs.⁶

The report of *de novo* mutations in chromatin-modifying genes in patients with non-familial heart defects suggests that environmental factors might also perturb these pathways.⁷

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