W01-01 - FROM KARYOTYPE TO TARGETED MICROARRAY

I.Feenstra, B.W.Van Bon, D.A.Koolen, R.Pfundt, T.Kleefstra, N.De Leeuw

Department of Human Genetics, Radboud University Medical Centre, Nijmegen, The Netherlands

Introduction: Routine microscopic karyotyping is an important part of the diagnostic work-up in patients with multiple congenital anomalies (MCA) and/or intellectual disability (ID), allowing for the detection of microscopically visible chromosome aberrations. Smaller but clinically relevant deletions and duplications, however, remain unnoticed. Therefore high-resolution genome-wide technologies such as genomic microarrays are needed.
Objectives: To improve the genotype-phenotype relationship.
Aims: To elucidate causative copy number variations with microarray techniques.
Methods: The implementation of microarray technologiesed as a routine diagnostic setting to detect causative copy number variations (CNV) in MCA and/or ID patients.
Results: Patients with a chromosome aberration usually do not only display developmental delay, but can have behavioral disorders as well, like in the well-known microdeletion syndromes Velo-Cardio-Facial syndrome (22q11.2 deletion) and Smith-Magenis syndrome (17p11.2 deletion). New microdeletion and -duplication syndromes are frequently discovered with the implementation of new techniques and sometimes psychiatric problems are part of the phenotype too, including for example the 15q13.3 deletion and 16p11.2 deletion syndrome. A complicating factor in determining the phenotype however, is that these CNVs are detected as a de novo finding in children with autism spectrum disorders or schizophrenia, yet also in normal parents without a psychiatric disorder.
Conclusions: Improvement in molecular genetic techniques has resulted in promising results, in that the chance to find a causative etiology has increased from 5% to 15-20%. Collaborative and careful genotype-phenotype studies in these rare chromosome aberrations are needed to come to a good quality definition of the phenotypic spectrum, including psychiatric disorders.

https://doi.org/10.1016/S0924-9338(12)75668-7 Published online by Cambridge University Press