

**P48: Analysis of autosomal CNV profiles in patients and siblings in autism families**

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Copy number variants (CNVs) play a significant role in the etiology of Autism Spectrum Disorders (ASDs). Recurrent CNV risk variants are found in about 10-15% of patients with ASD and intellectual disability (ID). Moreover, the contribution of de novo CNVs is evidenced by unique causal CNVs in syndromic ASD and by the overrepresentation of de novo CNVs in ASD patients versus unaffected siblings in large scale studies. However little is known on the precise contribution of CNVs in patients with non-syndromic ASD.

In the current study deletions, duplications and multiplications are studied in relation to patient and family specific characteristics to identify CNV profiles that may be associated with ASD in subgroups of patients. The study sample contains 159 families ascertained through one or more clinically well characterized probands with non-syndromic ASD (55 multiplex, 104 simplex). In total 231 ASD patients (177 males, 54 females) and 99 siblings (34 males, 65 females) are included. The sample contains mainly patients with normal intelligence (89%). Genotyping for all family members was performed with Illumina Omni2.5-8v1 SNP array. After a statistical quality control, CNVs defined by less than 10 consecutive probes were excluded from the study. Thirteen variants with known clinical significance (CNV risk variants or causes of ASD) were also excluded. The remaining dataset consist of 21670 autosomal variants including 933 homozygous deletions, 11746 deletions, 8926 duplications and 65 multiplications.

Wilcoxon test statistics and 10000 permutation tests were used to compare de novo and inherited CNVs between ASD patients and unaffected siblings. The results show that ASD patients have significantly more de novo duplications than siblings ($p < 0.04$). In addition the gene content (average number of genes per de novo duplication) is higher in ASD patients ($p < 0.0006$). Analyses in multiplex families revealed an overrepresentation of inherited duplications and a higher gene content in patients versus siblings ($p < 0.003$) while this was not present in simplex families.

In conclusion, these family data support a role for duplications in the etiology of non-syndromic ASD. Further analysis and the relation with patient and family specific characteristics is subject of ongoing work. However a more distant aim is to unify our findings in existing family risk models and study the potential clinical significance.