Mark Gorman, Rebecca MacRae - *Whole Genome Sequencing and HLA typing in OMAS*

Abstract:

Background: Prior studies suggest a genetic contribution to opsoclonus-myoclonus ataxia syndrome (OMAS) but are limited.
Methods: We enrolled patients diagnosed with OMAS ≤ 18 years at a pediatric neuroimmunology clinic in Boston, USA, using the 2004 Genoa Criteria. WGS was conducted for the patients and their biological parents (when available), with one case including an unaffected twin. *De novo* germline variants (DNVs) in probands were identified and validated, and analyses of structural variants (SVs), recessive variants in neuroimmune-associated genes, and high-resolution HLA typing were performed.
Results: Our study included 42 probands, 23 of whom had neuroblastoma. We found 12 confirmed DNVs in protein-coding regions in nine (21.4%) probands. Ten patients (23.8%) had rare homozygous or compound heterozygous variants known to alter protein function, affecting 11 genes. However, no clearly disease-causing variants were identified. The *HLA-DRB1*01* allele was observed in 27 out of 84 (32.1%) alleles in the probands, significantly higher than that in the general population (Chi-square test, $p < 0.0001$). The *HLA-DOB*01:01* was very common (86%) and was compared to a prior study.
Conclusions: This first genome sequencing study reveals potential genetic contributors to OMAS, implicating polygenic predisposition with *HLA-DRB1*01:01* and *HLA-DOB*01:01* as possible genetic risk factors.