

Cameron Page, Michael Benson, Thayne Sweeten Ph.D., Anthony Torres M.D., *Utah State University*
Martin Kharrazi Ph.D., *California Department of Health*, Lisa Croen Ph.D., *Kaiser Permanente Division of Research*

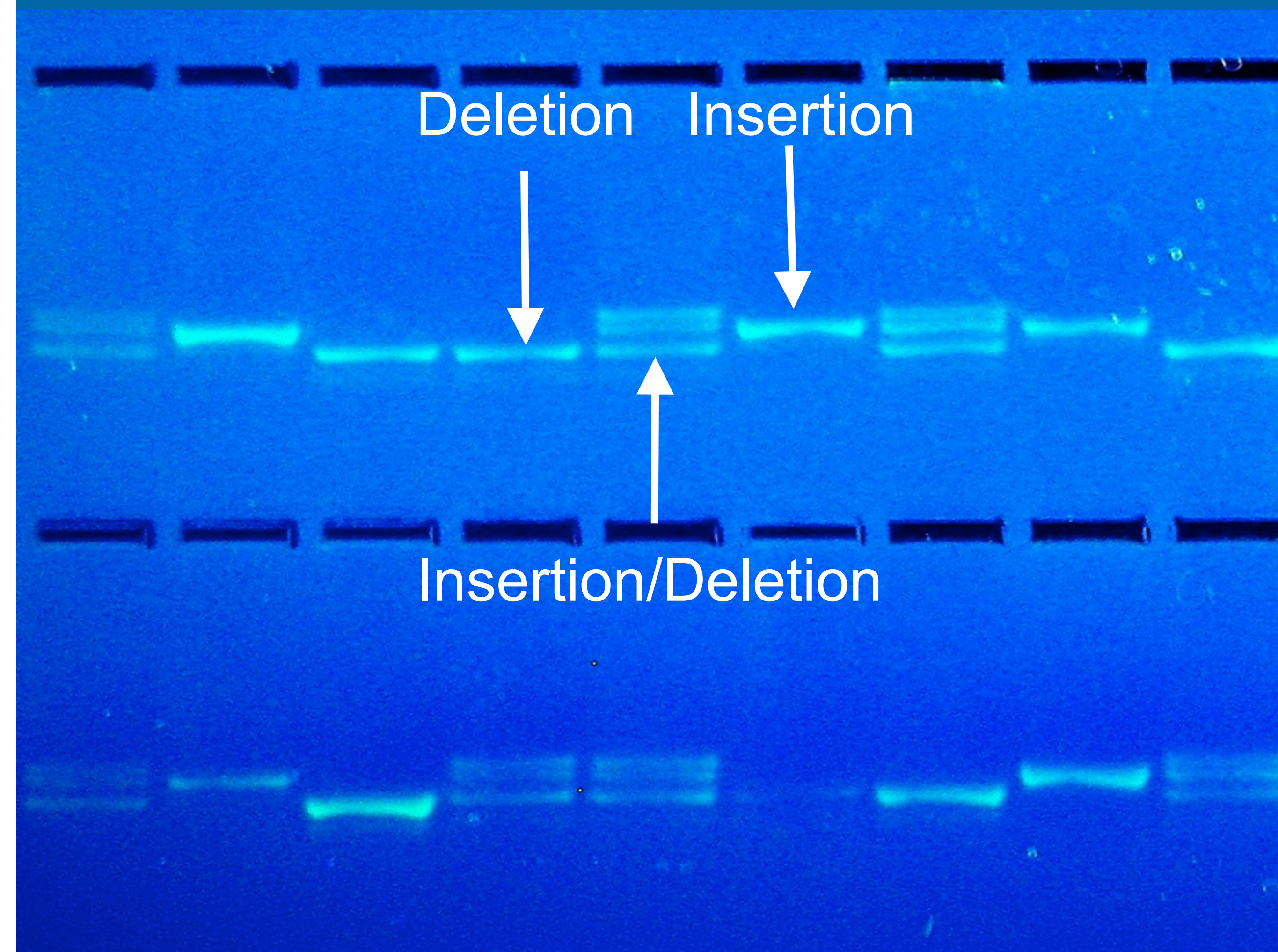
Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopment disorder characterized by deficits in communicative and social behaviors (Meltzer, 2017). As of 2012 the CDC reported that 1 of 68 children born in the U.S. have ASD (Christensen, 2016).

The immune systems of mother and child can be important in ASD. A signaling molecule, HLA-G, helps regulate maternal natural killer cell interaction with the fetus. A defect in HLA-G could increase NK cell activity, leading to abnormal neurodevelopment in the fetus (Carosella, 2008).

Our study focuses on a 14 base pair insertion/deletion found in the HLA-G gene of autistic subjects and their mothers, previously examined in an Italian population by Guerini (2014). We are also expanding to look at HLA-G and intellectual disability (ID) in ASD. HLA-DRB1, another gene in the HLA region of chromosome 6, has been linked to ASD and impaired ID (IQ<80, Wang, 2013).

Gel Electrophoresis



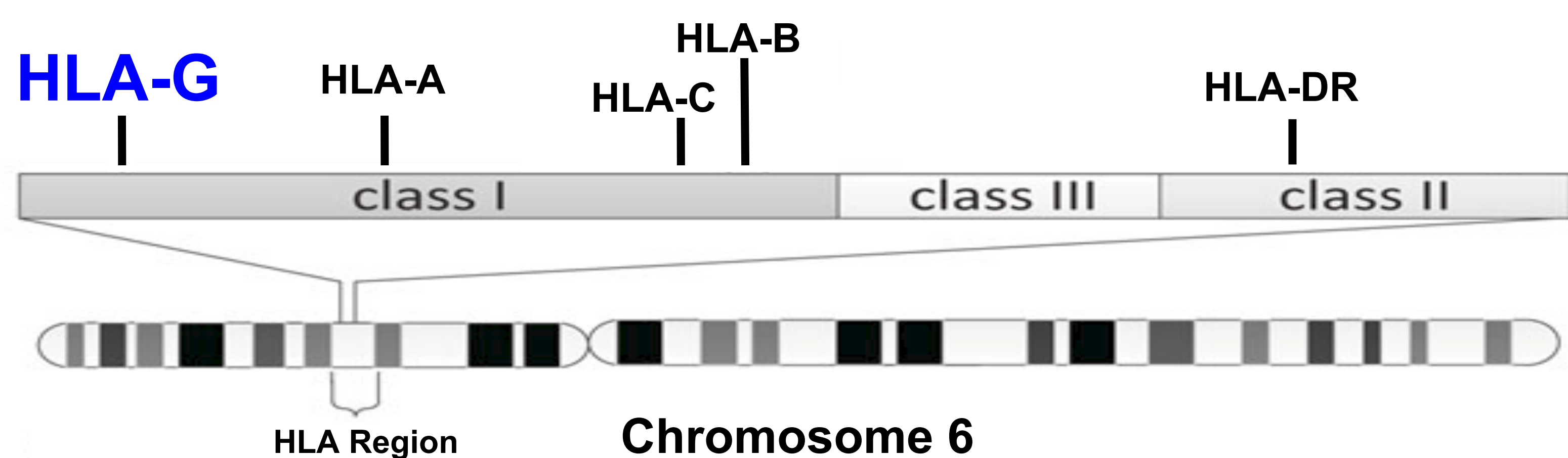
Methods

DNA from 259 subjects of the Early Markers for Autism (EMA) projects was genotyped for the HLA-G 14bp insertion/deletion.

Mothers of ASD with ID = 38
Mothers of ASD without ID = 52
Mothers of control subjects = 169

Genotyping was done by PCR and gel electrophoresis. A 14 base pair difference in PCR product size indicates a deletion or insertion in the DNA sequence

Autistic children are still in the process of being genotyped.



Conclusion

HLA-G 14bp insertion increased in mothers of ASD with ID compared to controls and ASD without ID.

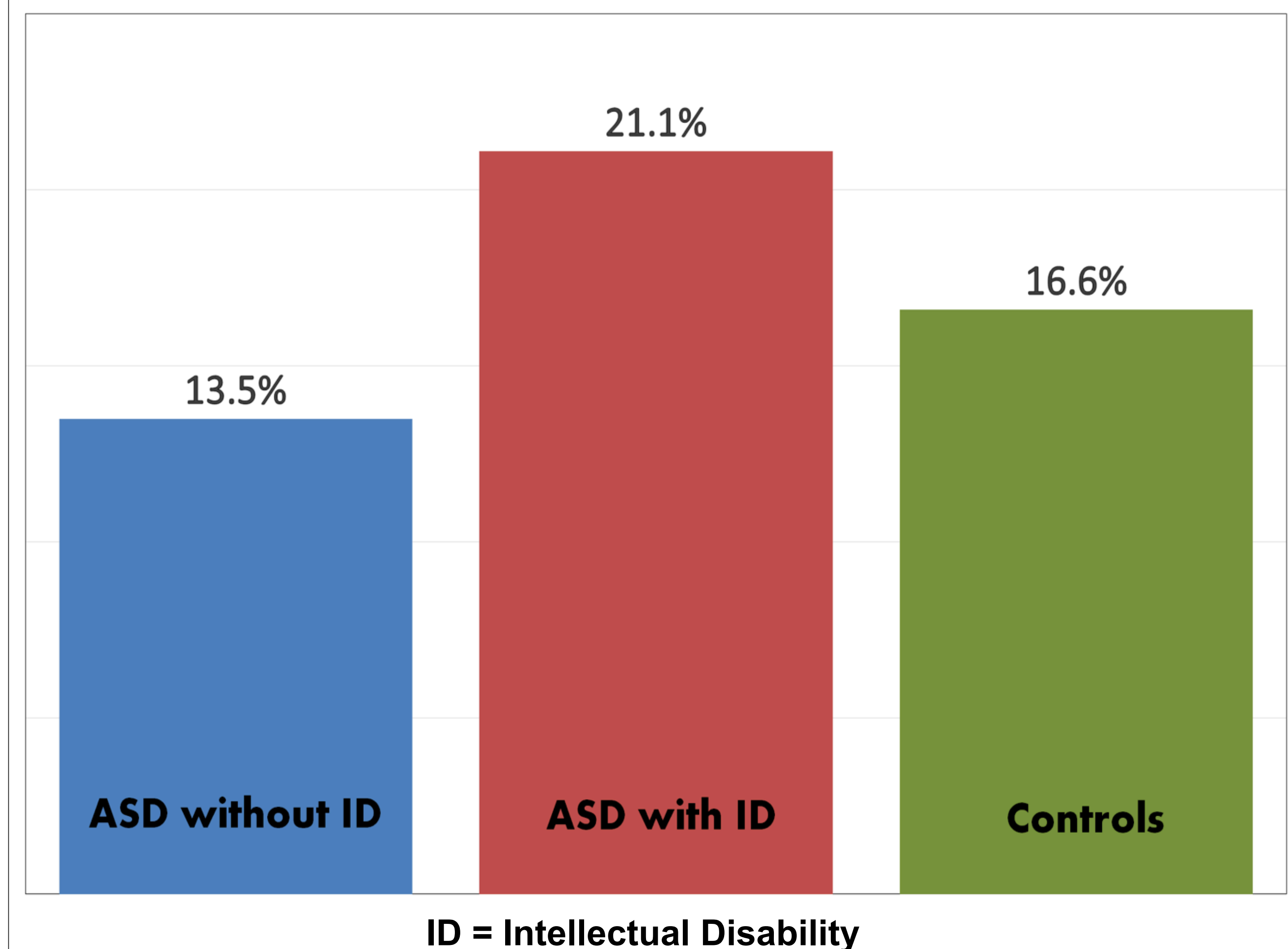
Although results for HLA-G genotyping in the mothers has not proven to be statistically significant, our population size is small.

Larger scale studies may be needed to show the significance of HLA-G polymorphisms and intellectual disability in autism.

We are still awaiting results for HLA-G genotyping in the autistic children.

Results

Frequency of mothers with HLA-G 14bp insertion



References

- Carosella, E.D., Favier, B., Rouas-Freiss, N., Moreau, P., LeMaout, J., 2008. Beyond the increasing complexity of the immunomodulatory HLA-G molecule. *Blood* 111, 4862–4870.
- Christensen DL, Baio J, Braun KV, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012. *MMWR Surveill Summ* 2016;65(No. SS-3)(No. SS-3):1–23.
- Guerini FR, Bolognesi E, Chiappedi M, Manca S, Ghezzi A, Agliardi C et al (2014). Activating KIR molecules and their cognate ligands prevail in children with a diagnosis of ASD and in their mothers. *Brain Behav Immun* 36: 54–60.
- Meltzer A, Van de Water J The role of the immune system in autism spectrum disorder. *Neuropsychopharmacology*. 2017;42:284–298.
- Wang HZ, Qin HD, Guo W, Samuels J, Shugart YY. New insights into the genetic mechanism of IQ in autism spectrum disorders. *Front Genet*. 2013 Oct; 18; 4:195.