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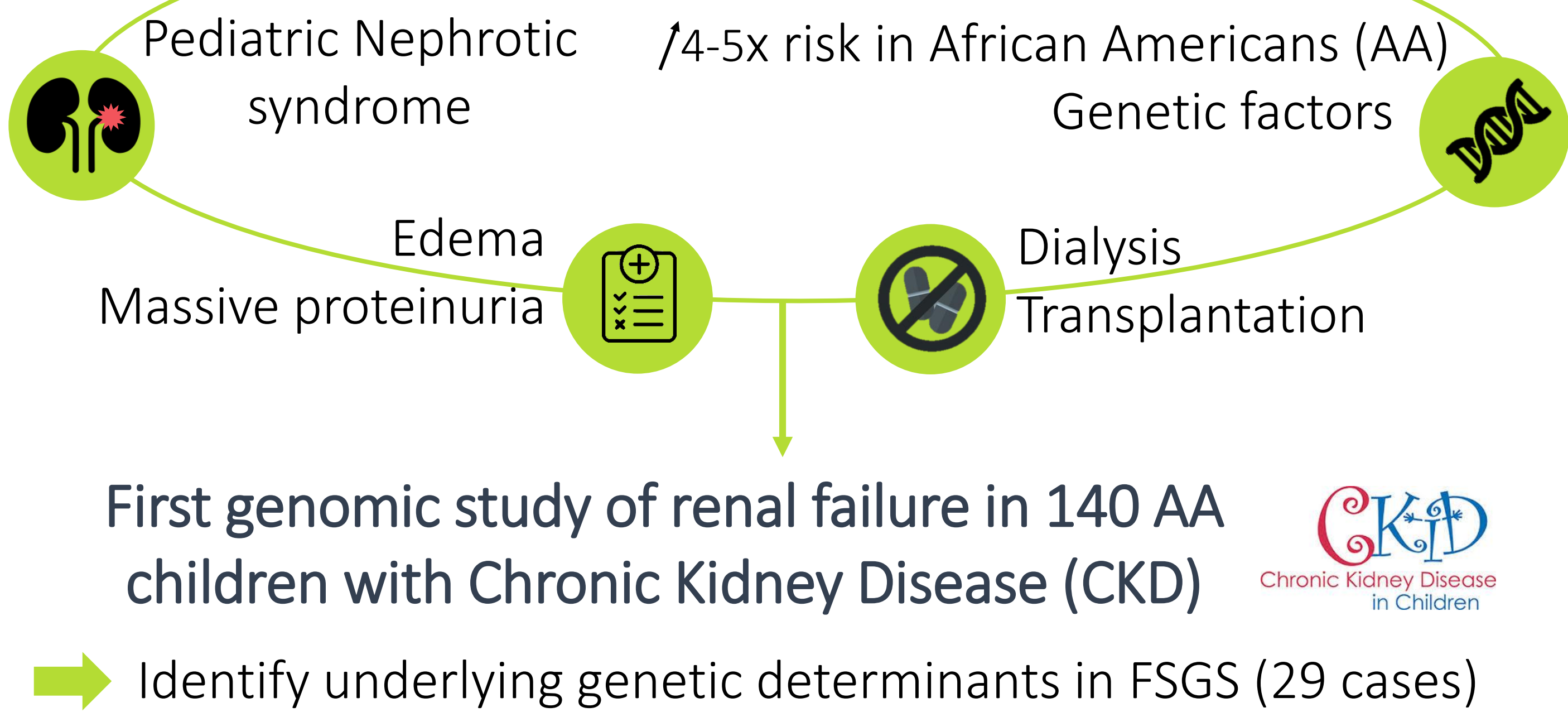
Statistical inference of immunogenetic parameters reveals *HLA-DRB1*11:01* allele associated with pediatric FSGS

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FOCAL SEGMENTAL GLOMERULOSCLEROSIS

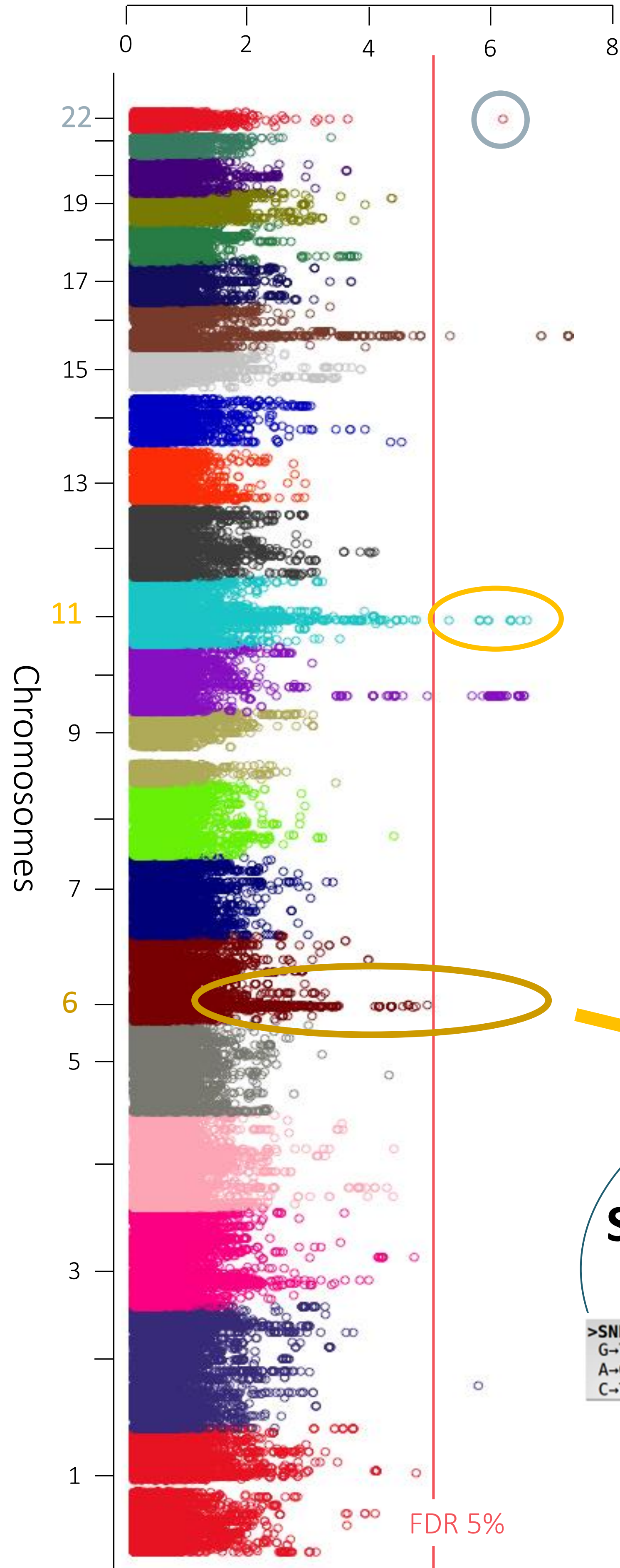
FSGS



METHODS

- ✓ **Genotyping arrays:** 254,000 SNPs on illumina[®] Exome Chips
- ✓ **Quality Control and HRC imputation:** 934,000 common SNPs with Minor Allele Frequency $\geq 0.3\%$ for statistical analysis
- ✓ **Association analysis with FSGS phenotype** using regression model
- ✓ **Gene-set enrichment analysis (GSEA)** using GSA-SNP2
- ✓ **Investigation of HLA:**
 - Imputation of 108 HLA alleles using HIBAG¹
 - Inference of immunogenetic parameters (e.g. HLA 5-gene haplotypes, amino-acids) using Easy-HLA²

$-\log_{10}$ (FSGS associated p-value)

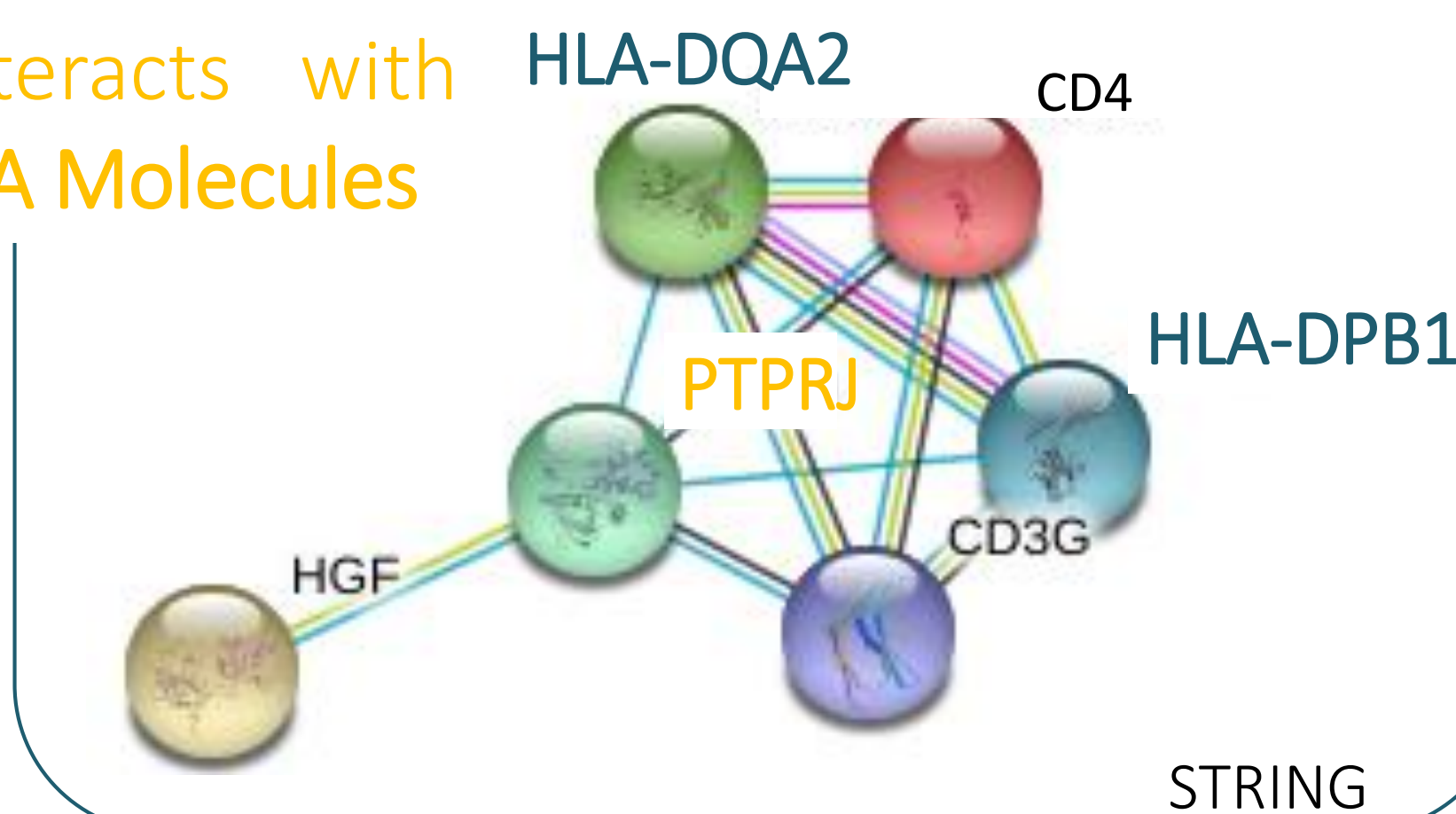


APOL1 - G1

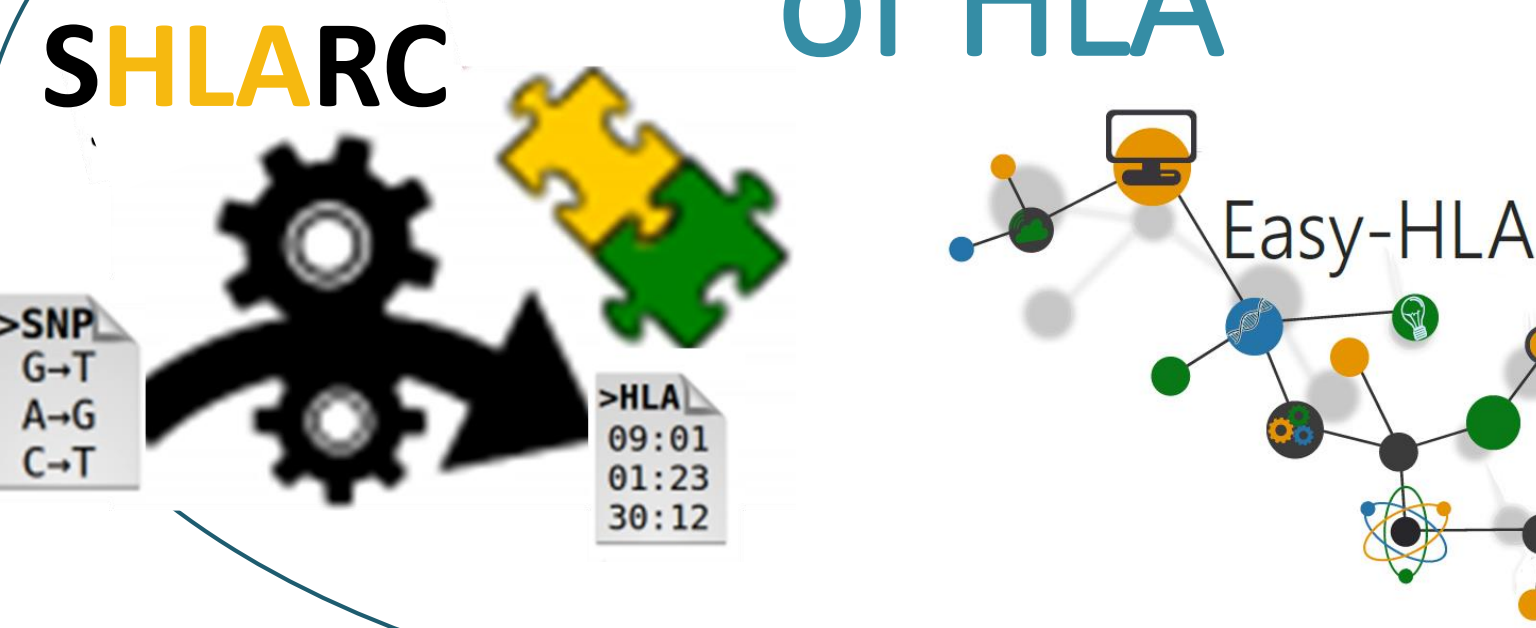
- ✓ Confirmation of previously major described signal in adult FSGS and CKD
- ✓ Validation of our analysis and cohort

PTPRJ

- 5 significant SNPs
- PTPRJ interacts with class II HLA Molecules

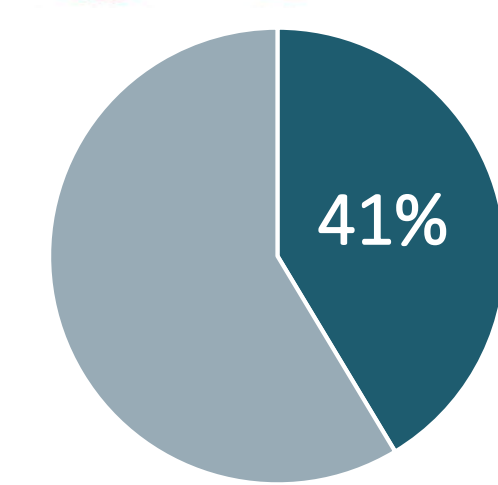


Further investigation of HLA



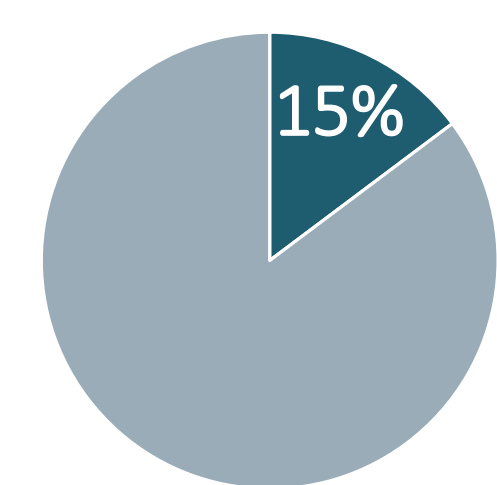
rs73885319

Kopp2011³



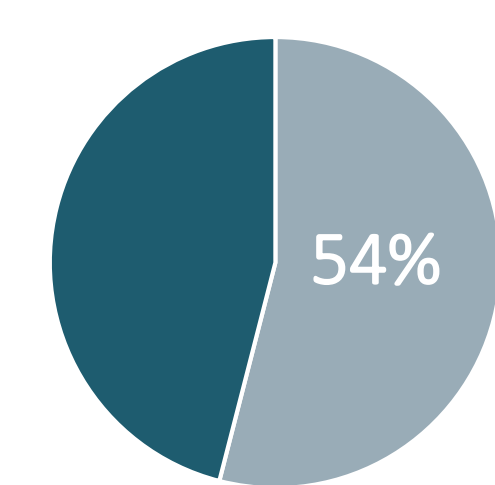
FSGS AA
kids
N=29

P = 10⁻⁷



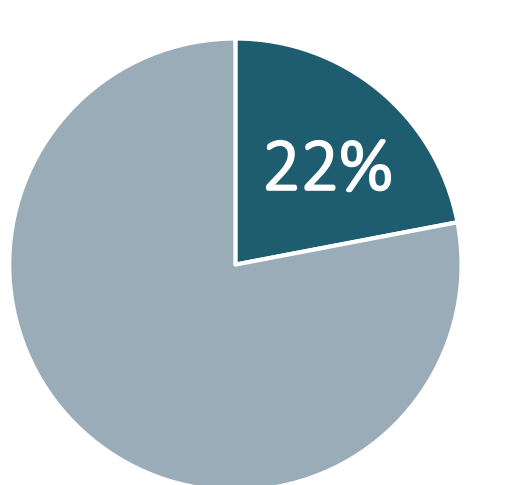
Non FSGS AA
kids
N=105

OR = 25.4



FSGS AA
adults
N=217

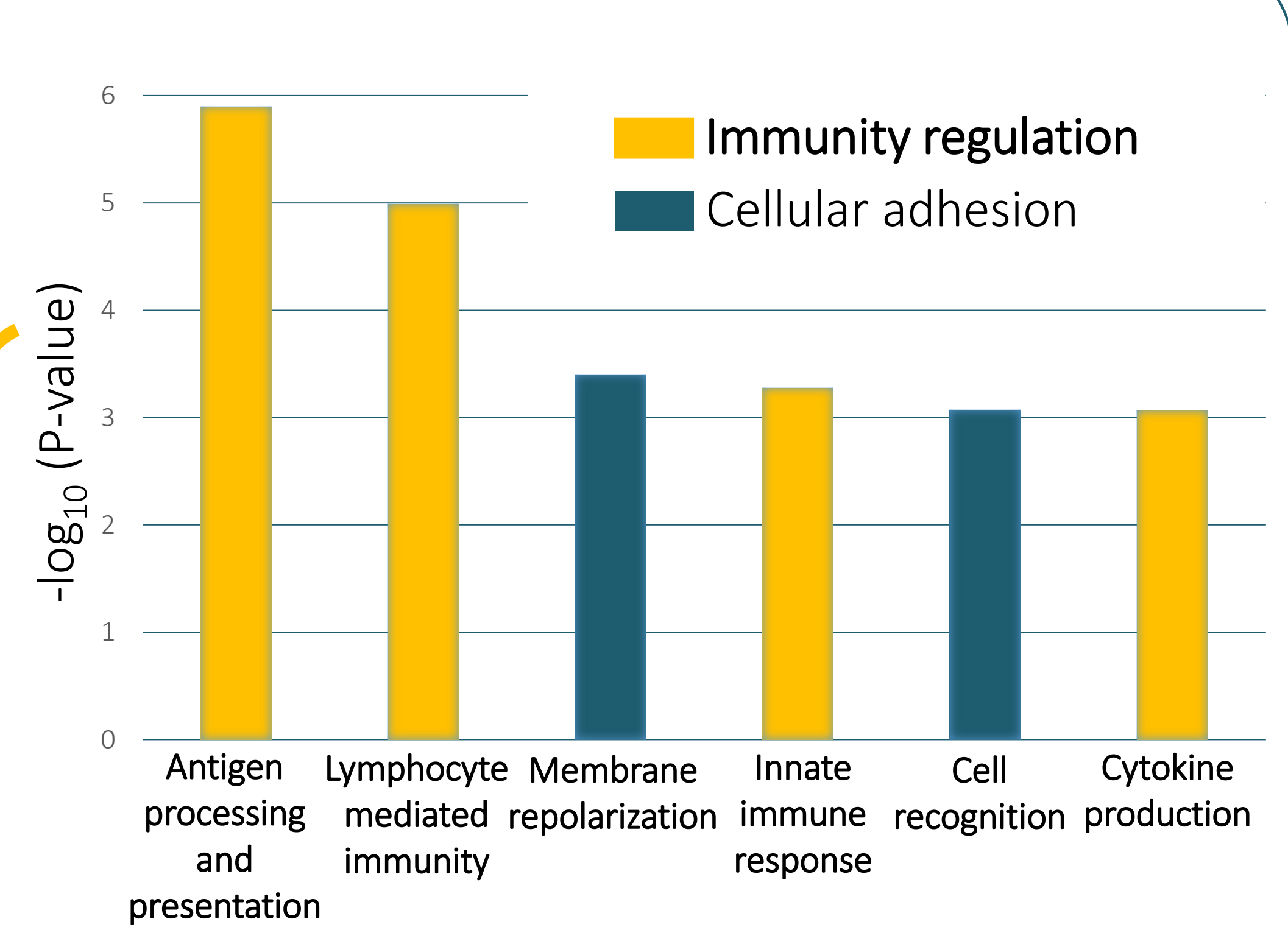
P = 10⁻⁸



Non FSGS AA
adults
N=383

OR = 17.4

GSEA with Gene Ontology



Importance of antigen processing and presentation pathways in pediatric FSGS

HLA ASSOCIATION WITH FSGS

- 108 HLA alleles (=80 Class I alleles + 28 Class II alleles)
- 714 HLA amino acids and 17 HLA 5-gene haplotypes

	P-value	OR
<i>HLA-DRB1*11:01</i> N = 13/29 FSGS kids	5.6x10 ⁻³	10.5
67F & 58E <i>HLA-DRB1</i> N= 9/29 FSGS kids	5.0x10 ⁻³	4.5

CONCLUSION

- ✓ Identification of 5 statistically significant and biologically-relevant loci with pediatric FSGS
- ✓ First demonstration of a role for class II HLA in FSGS
- ✓ Further genetic and functional analyses focusing on these loci will enhance our understanding of molecular pathogenicity mechanisms underlying pediatric FSGS.

¹ SHLARC, JOBIM 2019, Poster session Wednesday July 3rd, Poster n°41, Douillard et al.

² EasyMatch-R, JOBIM 2019, Demo session Wednesday July 3rd, Demo n°1, Geffard et al.

³ Kopp. JB et al, APOL1 genetics variant in FSGS and HIV-associated Nephropathy. JASN (2011) 22, 2129-37.