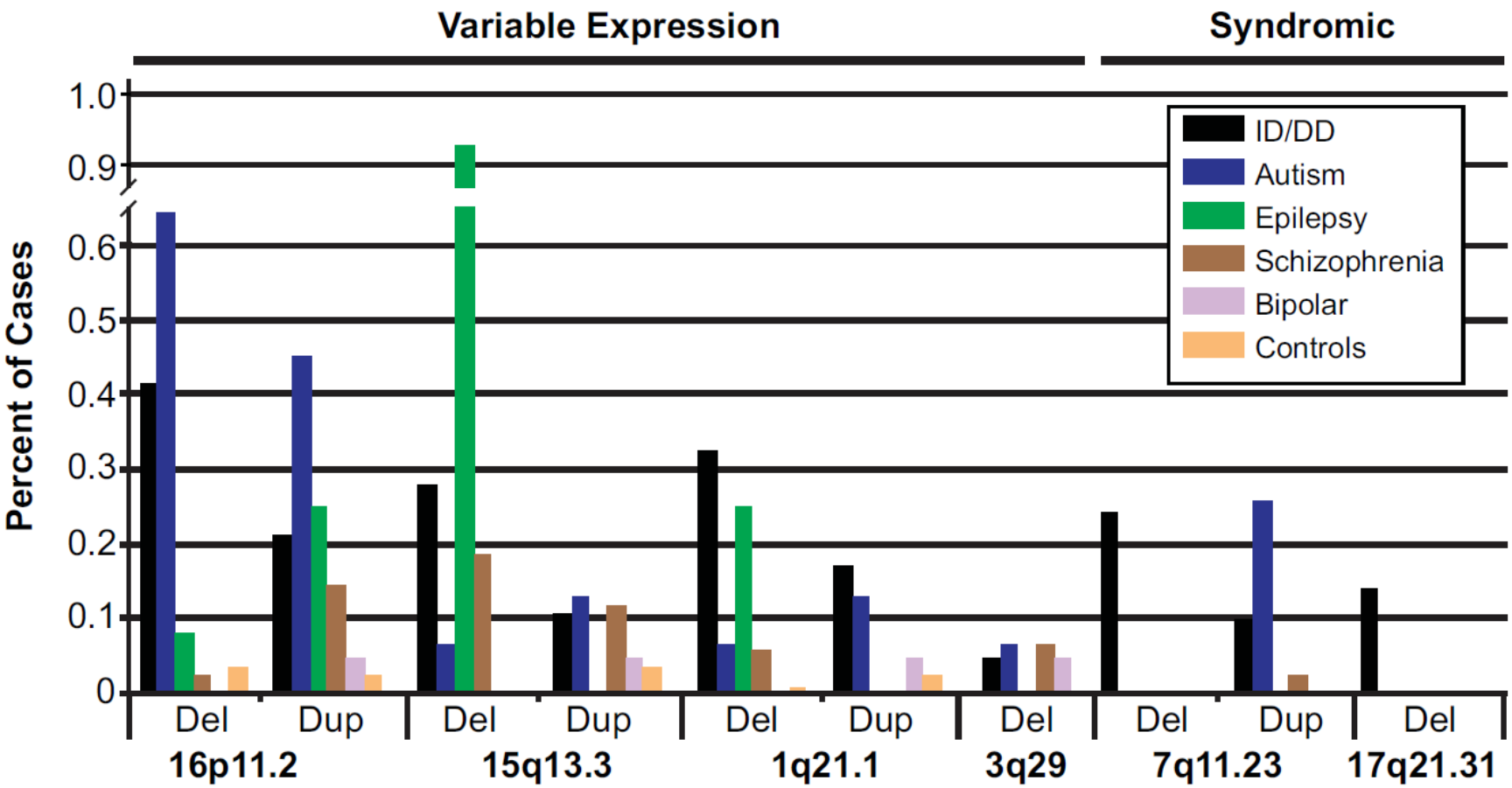
Variable expressivity of hotspot CNVs



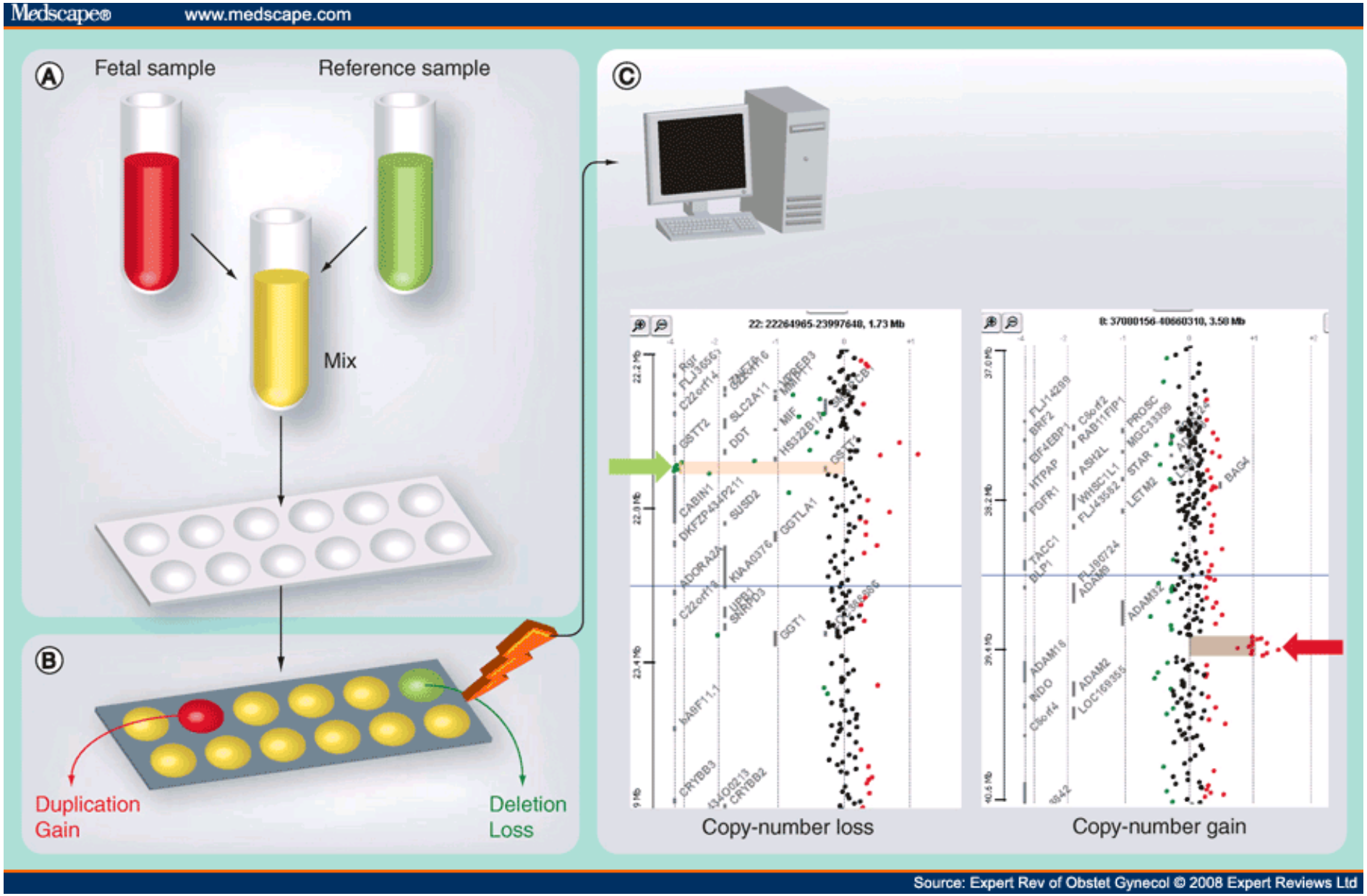
The frequency of CNV deletions and reciprocal duplications for six genomic hotspots associated with neurological disease are shown (ID/DD, autism, epilepsy, schizophrenia, and bipolar disorders).

Coe BP et al. Am J Med Genet C Semin Med Genet 2012;160C:118-29

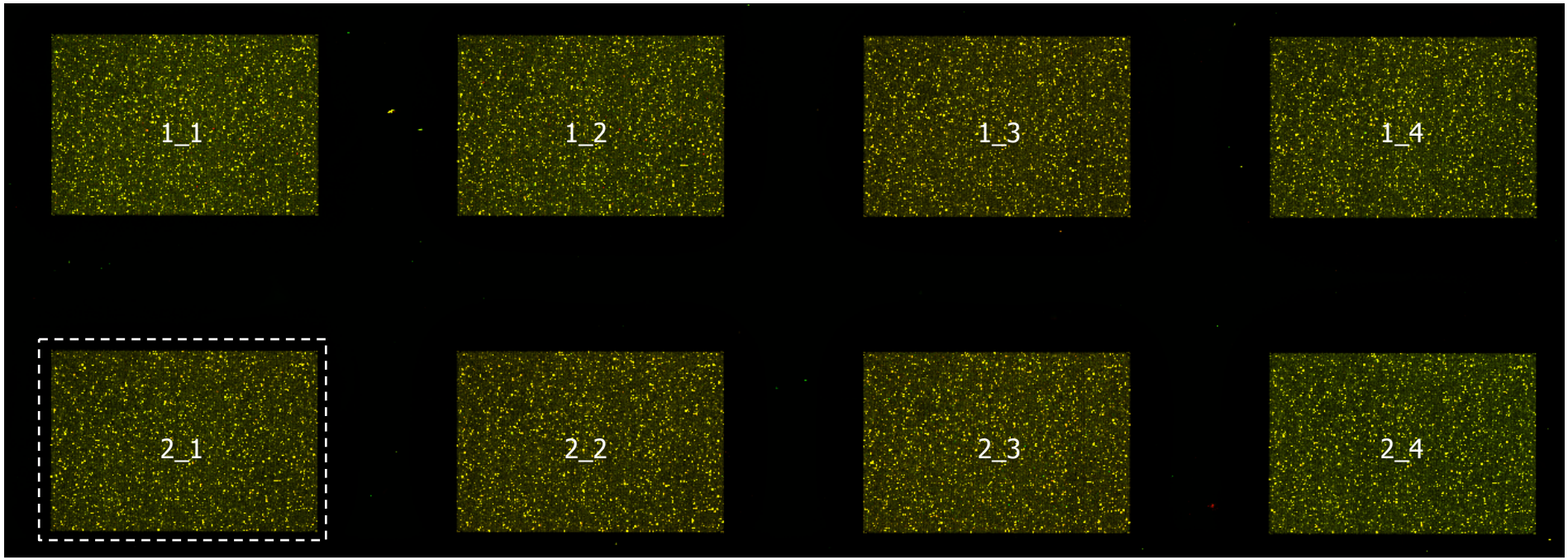
Cytogenomic array methodologies used to detect CNVs

Array Comparative Genomic Hybridization (Array CGH)	**SNP arrays**
Single-sequence oligonucleotides of ~60 bp	Two 20–60 bp oligonucleotides of different sequence
Two labeled DNAs (patient and control) per hybridization	Only patient DNA labeled and hybridized
Resolution down to size of oligonucleotides; exon by exon	Resolution limited by SNP distribution
No detection of UPD or consanguinity	Able to detect consanguinity and most UPD
Limited SNP addition possible recently	Detection of most known clinically relevant CNVs but not exon by exon

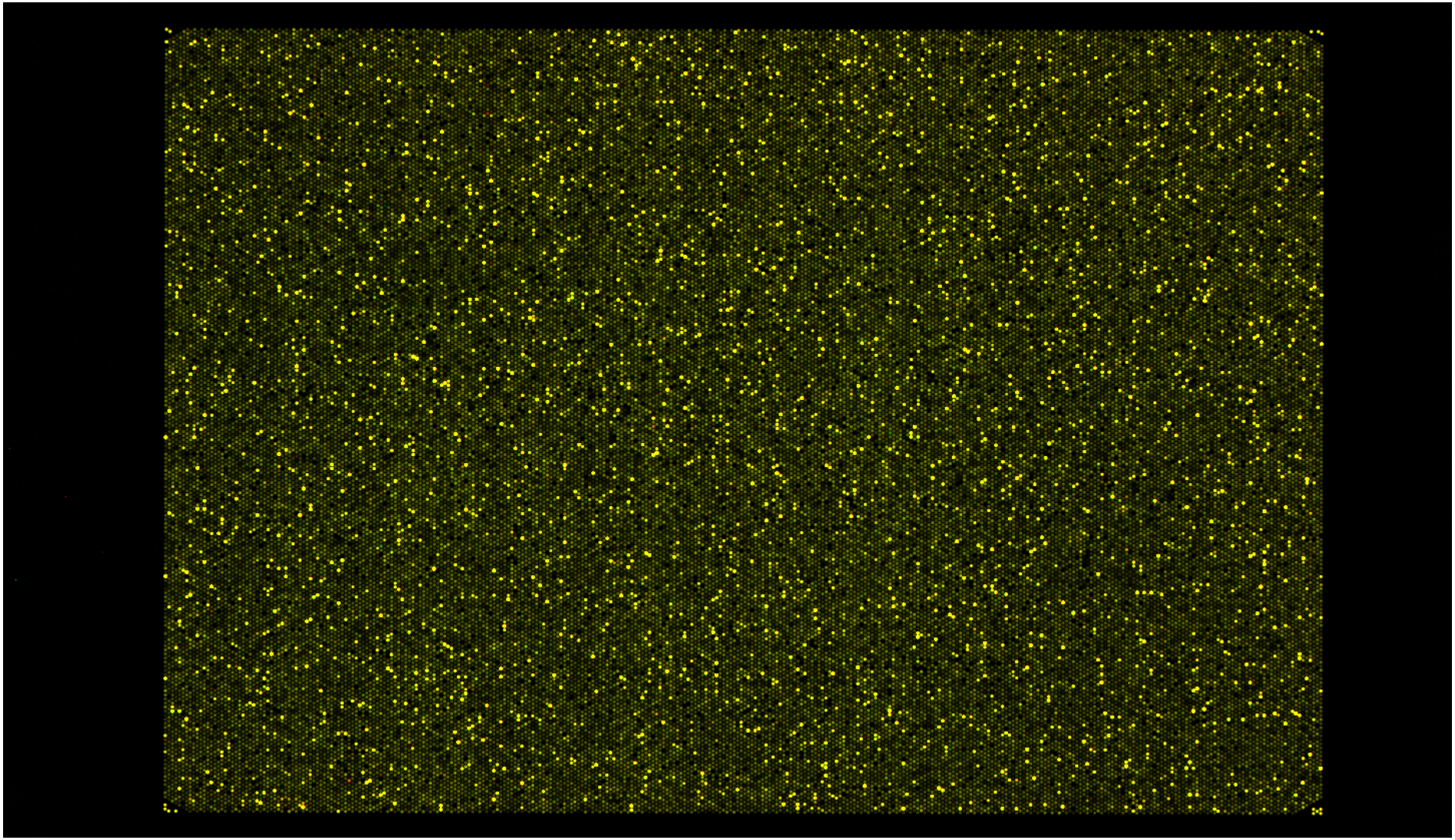
Array Comparative Genomic Hybridization (Array CGH)



Agilent 8x60k array



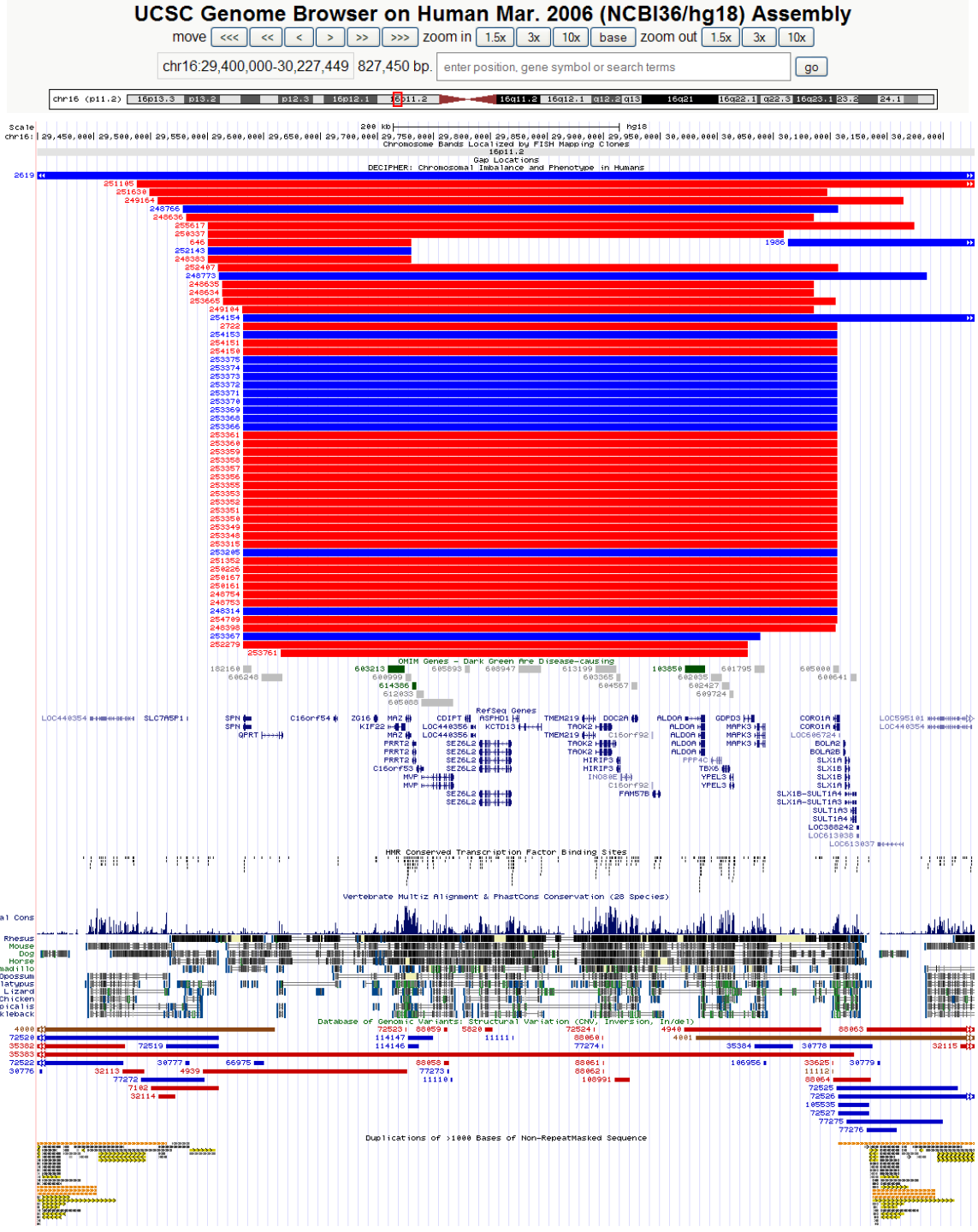
Agilent 8x60k array – subarray 2_1



CNV Databases

- Database of Genomic Variants: http://projects.tcag.ca
- USCS Genome Browser: http://www.genome.ucsc.edu/cgi-bin/hgGateway
- Ensembl Database: http://useast.ensembl.org/Homo_sapiens/Info/Index
- NCBI Map Viewer: http://www.ncbi.nlm.nih.gov/projects/mapview/
- DECIPHER Database: http://decipher.sanger.ac.uk/
- ISCA Consortium: https://www.iscaconsortium.org/

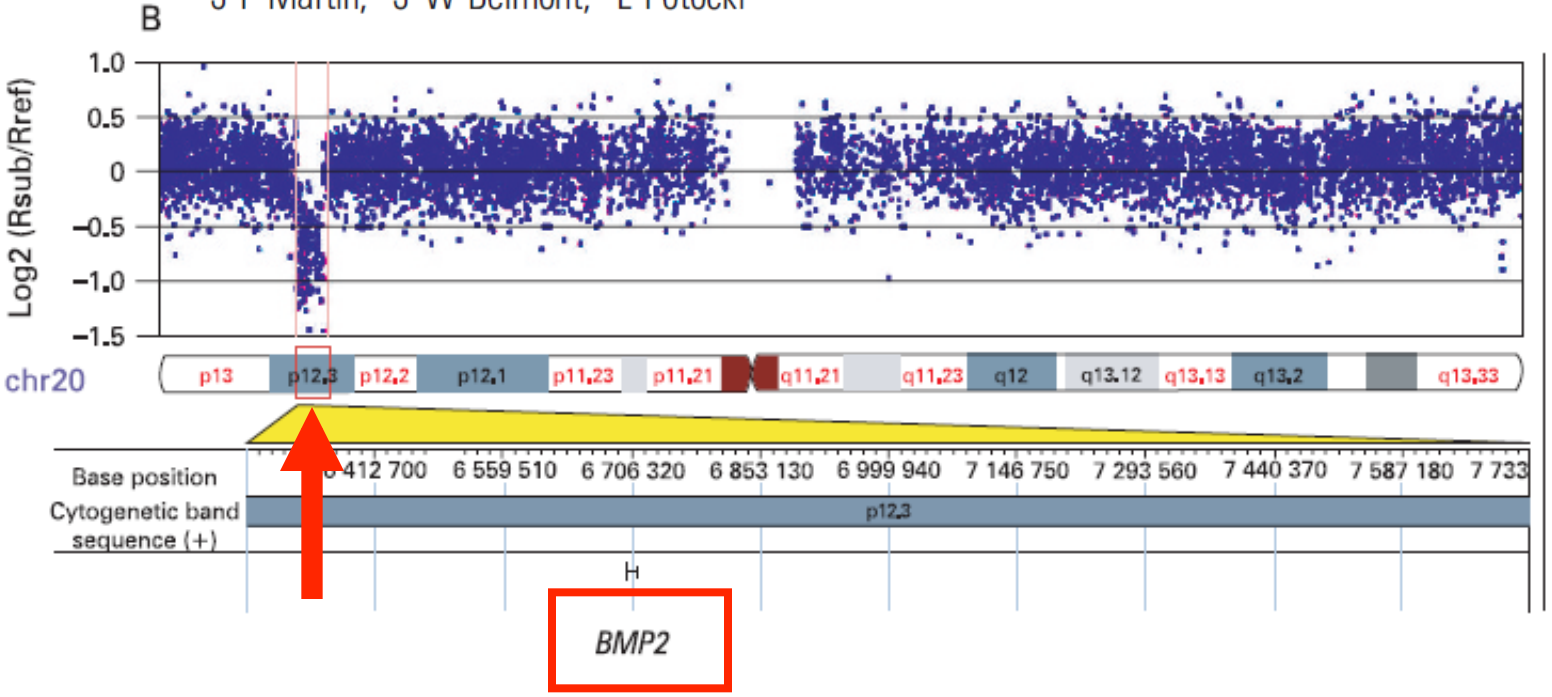
Recurrent CNVs at the 16p11.2 region



Gene Discovery via High Throughput SNP Genotyping

20p12.3 microdeletion predisposes to Wolff–Parkinson–White syndrome with variable neurocognitive deficits

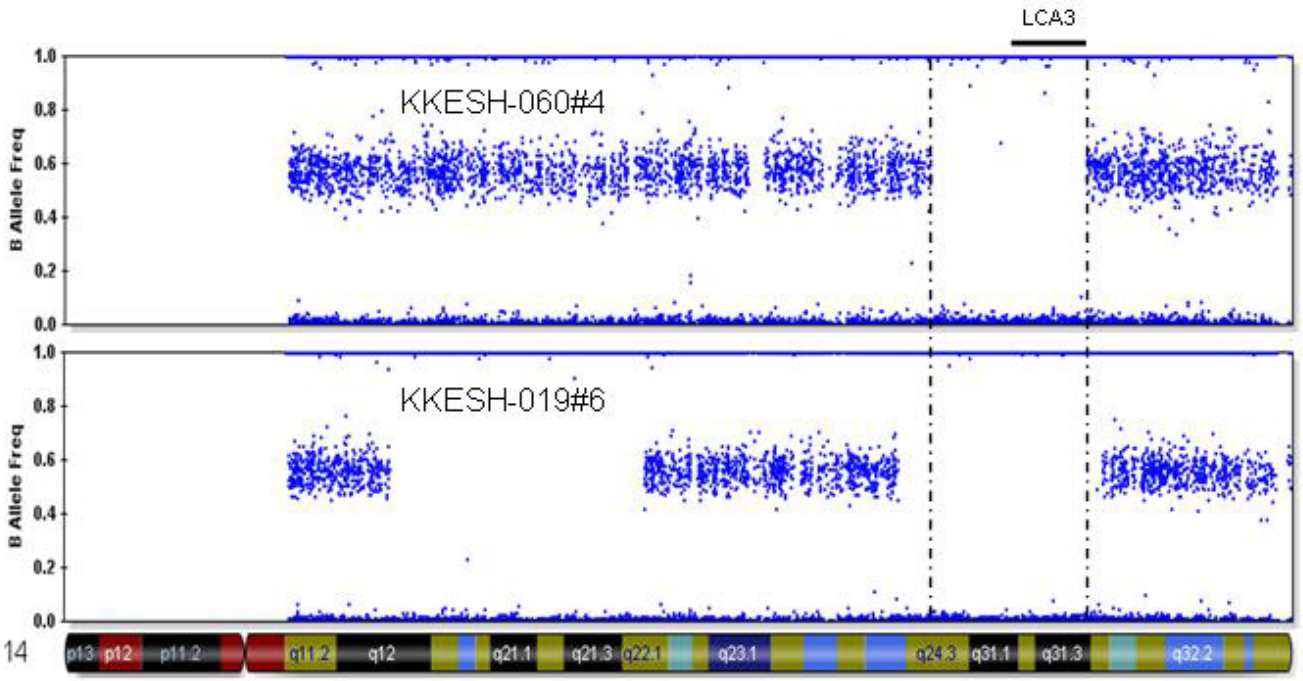
S R Lalani,[1] J V Thakuria,[2] G F Cox,[2] X Wang,[1] W Bi,[1] M S Bray,[1] C Shaw,[1] S W Cheung,[1] A C Chinault,[1] B A Boggs,[1] Z Ou,[1] E K Brundage,[1] J R Lupski,[1] J Gentile,[2] S Waisbren,[2] A Pursley,[1] L Ma,[3] M Khajavi,[1] G Zapata,[1] R Friedman,[4] J J Kim,[4] J A Towbin,[4] P Stankiewicz,[1] S Schnittger,[5] I Hansmann,[6] T Ai,[7] S Sood,[7] X H Wehrens,[7] J F Martin,[3] J W Belmont,[1] L Potocki[1]



ARTICLE

Mutations in *SPATA7* Cause Leber Congenital Amaurosis and Juvenile Retinitis Pigmentosa

Hui Wang,[1,7] Anneke I. den Hollander,[10,11] Yalda Moayedi,[3] Abuduaini Abulimiti,[1,7] Yumei Li,[1,7] Rob W.J. Collin,[10] Carel B. Hoyng,[11] Irma Lopez,[12] Molly Bray,[8] Richard Alan Lewis,[1,2,9] James R. Lupski,[1,5,9] Graeme Mardon,[1,2,3,4,6] Robert K. Koenekoop,[12] and Rui Chen[1,6,7,*]



Conclusions

- DNA sequence variation contributes to diversity of species.
- Types of DNA sequence variation include SNPs, insertion/deletions, microsatellites, and copy number variation.
- Many options for genotyping take advantage of natural DNA machinery.
- Mapping DNA sequence variation to human traits and disease is challenging but new technologies are advancing genomic science.