BRIGHAM AND WOMEN'S HOSPITAL

epiXchange

HARVARD MEDICAL SCHOOL
TEACHING AFFILIATE

EPISTOP molecular studies

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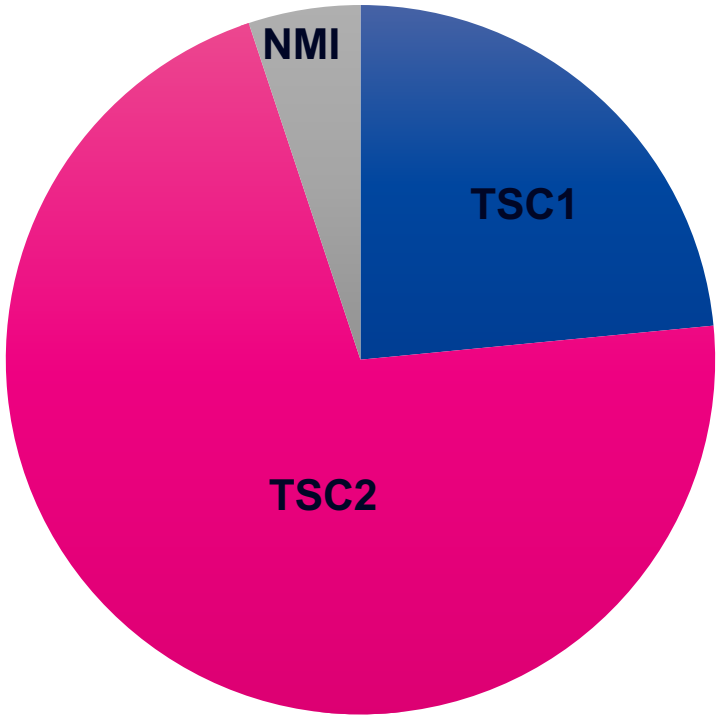
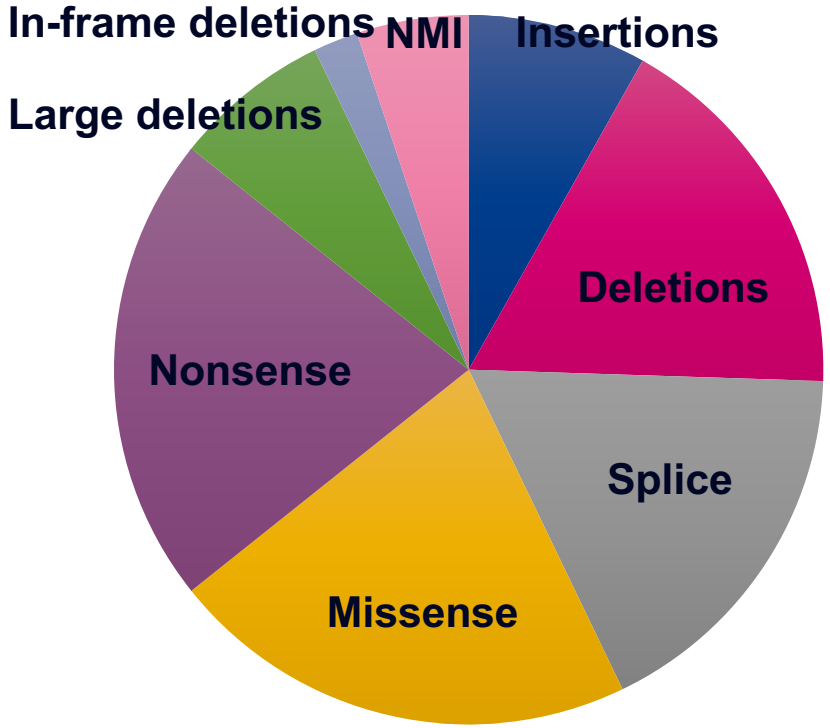
EPISTOP WP3: Identification of molecular biomarkers of epilepsy risk and epileptogenesis in TSC

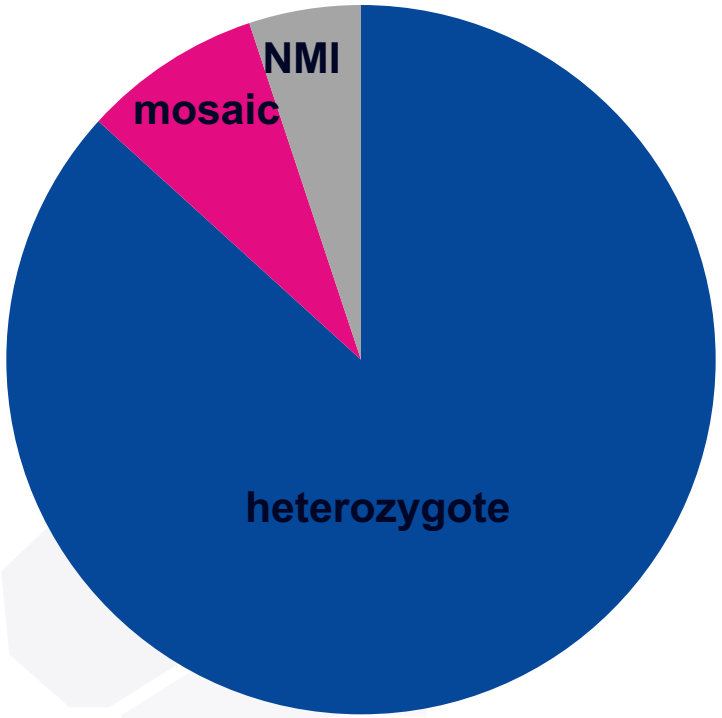
- Data sets are obtained for analysis at 3-4 time points per patient (subject entry, onset of epileptogenesis, onset of seizures, age 2 years)
  - RNA-Seq analysis of serial blood samples
  - Proteomic profiling of serial serum samples
  - miRNA profiling of serial plasma samples
  - Metabolomic profiling of serial serum samples
- Whole genome sequencing (WGS) on all subjects
- Comprehensive and deep TSC1/TSC2 mutation analysis

THESE TSC CHILDREN WILL BE SUBJECT TO THE MOST DETAILED MOLECULAR CHARACTERIZATION IN HUMAN HISTORY!

Comprehensive and deep TSC1/TSC2 mutation analysis

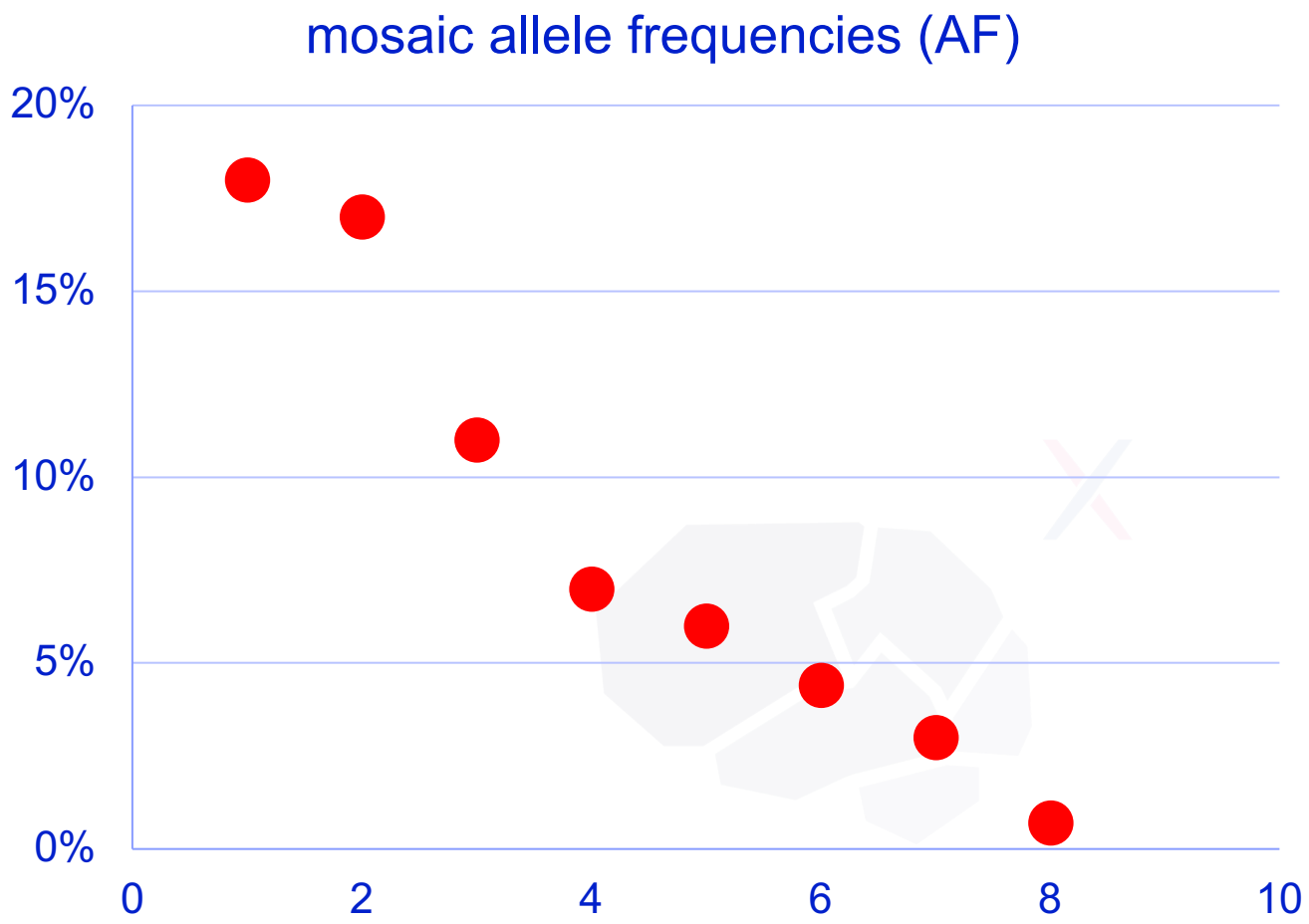




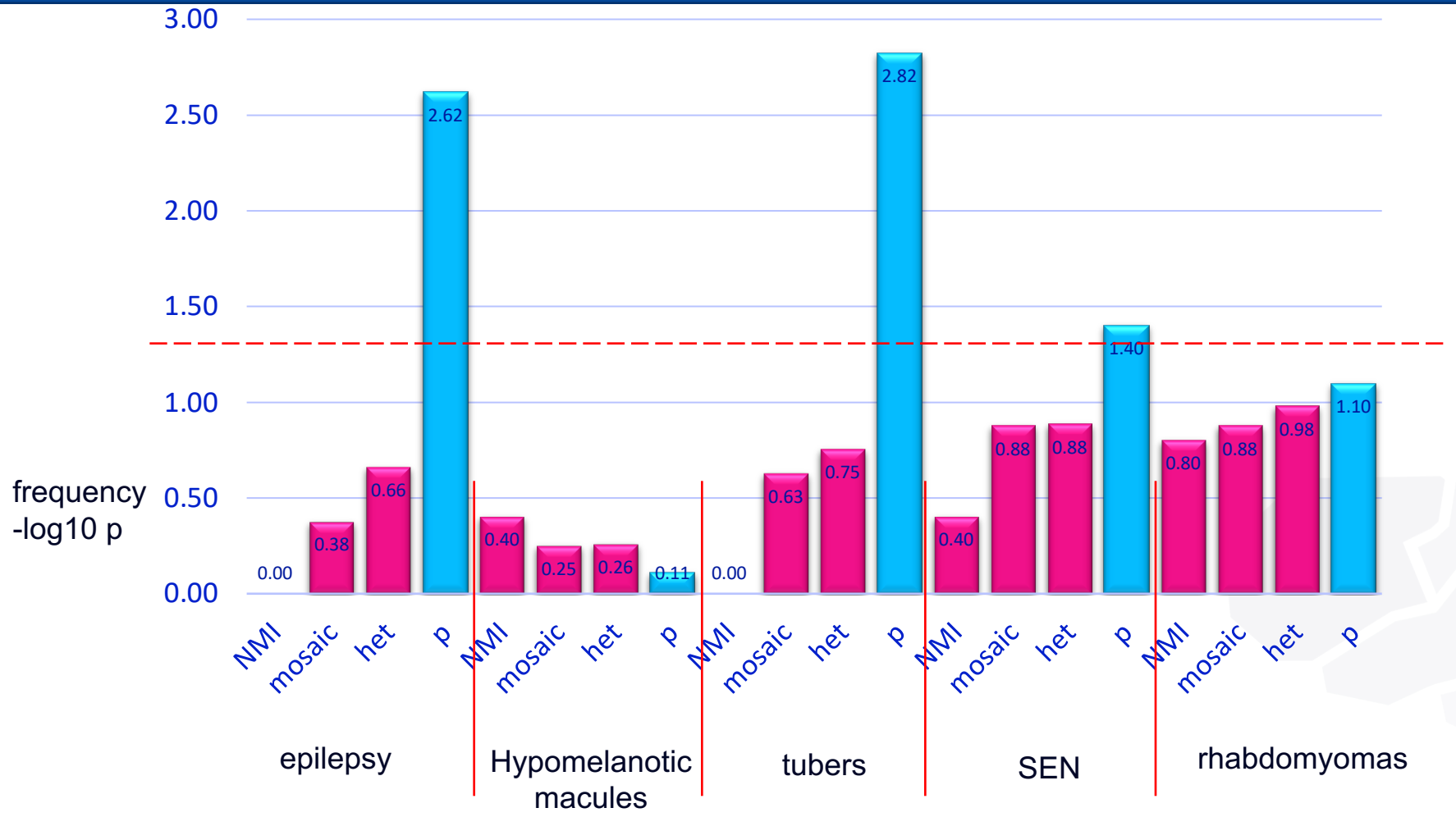


EPISTOP WP3: Identification of molecular biomarkers of epilepsy risk and epileptogenesis in TSC

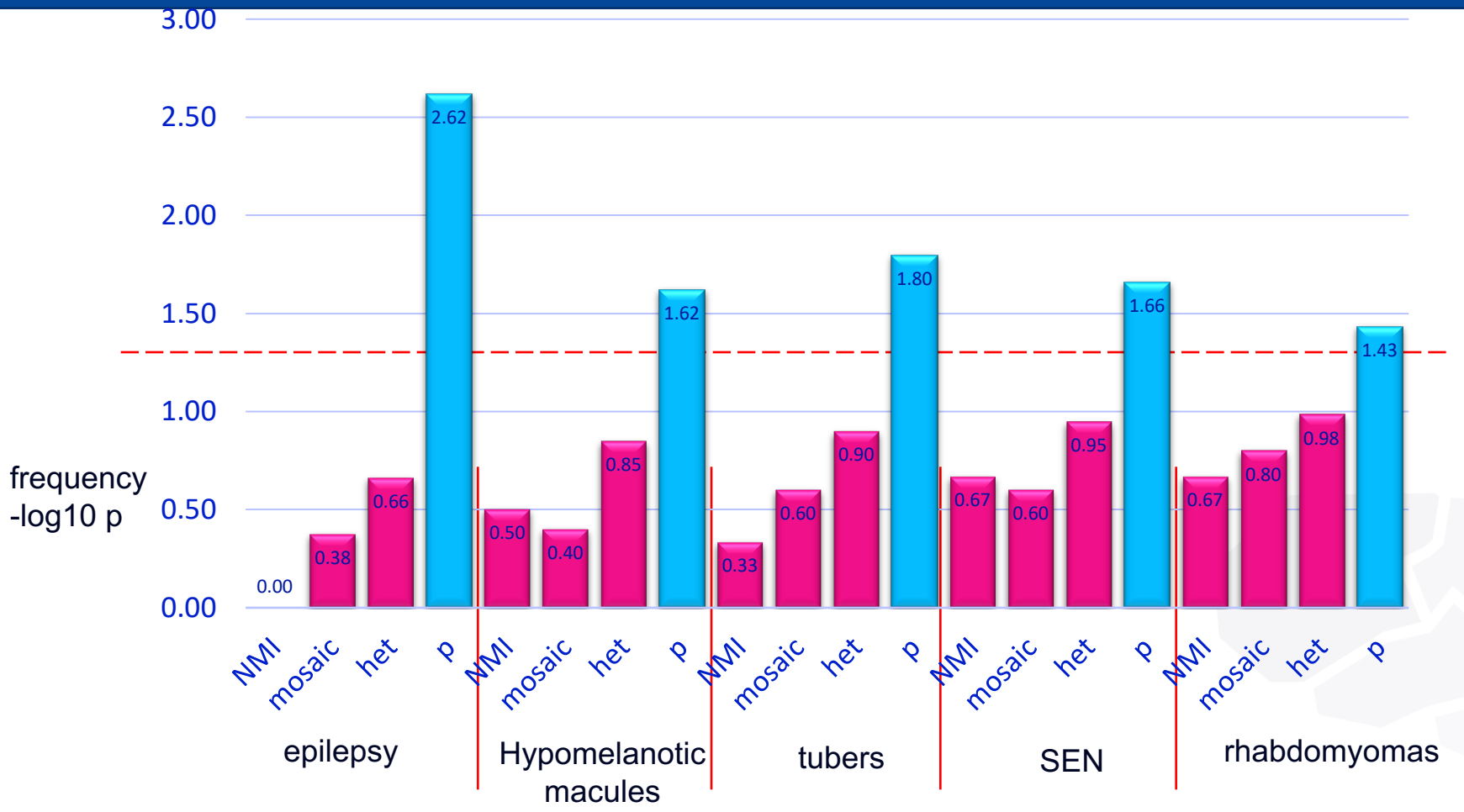
TSC2	c.3352C>T	p.Q1118*	nonsense	0.70%
TSC2	c.5024C>T	p.P1675L	missense	3%
TSC2	c.1748C>A	p.A583D	missense	4%
TSC2	c.1372C>T	p.R458*	nonsense	6%
TSC2	Exons 1-12		large del	7%
TSC2	Exons 39-41		large del	11%
TSC2	c.4324delG	p.E1442Rfs*34	del	17%
TSC2	c.3254delC	p.S1085Wfs*18	del	18%



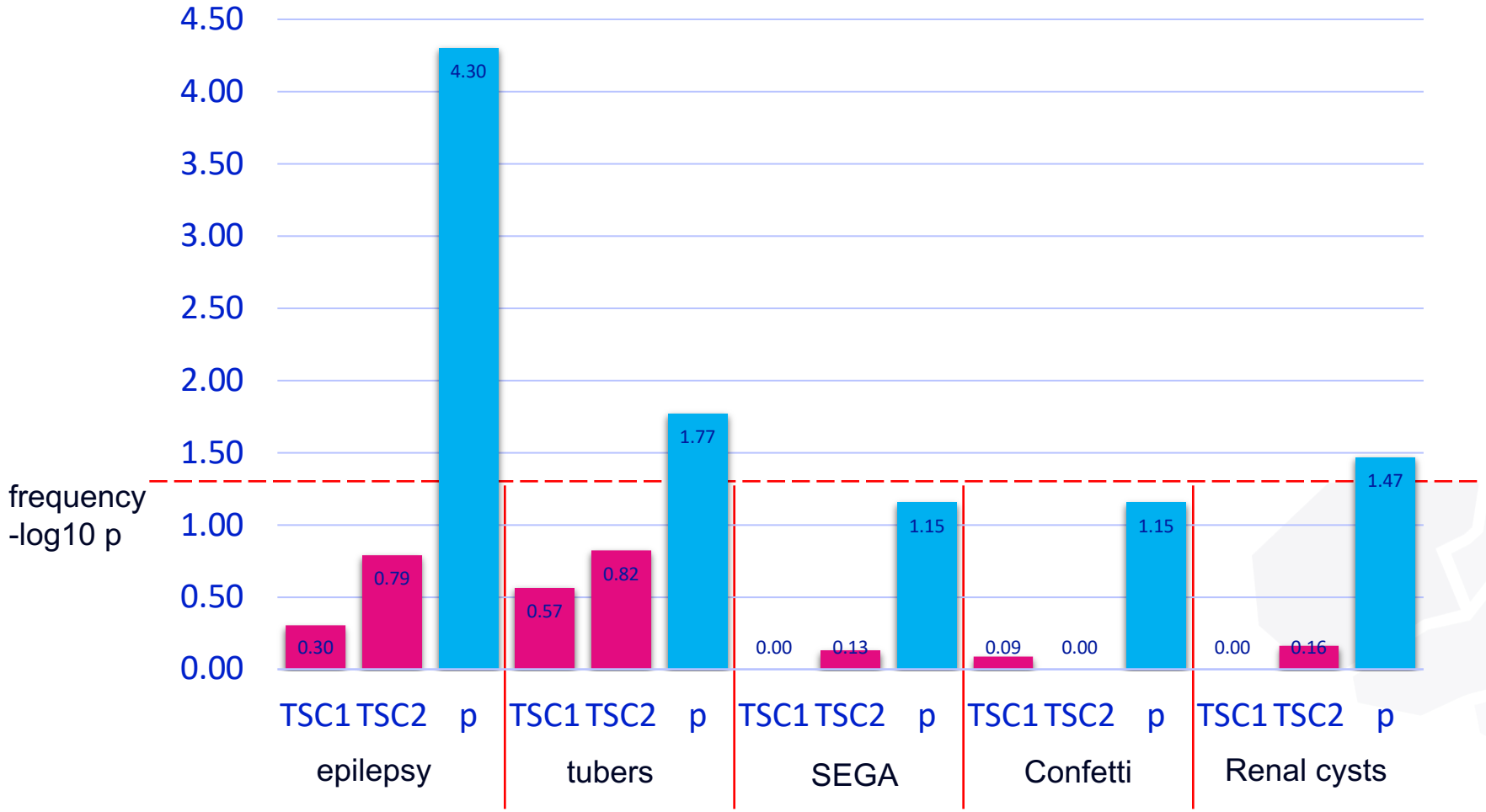
Comparison of TSC clinical features with mutation status at entry



Comparison of TSC clinical features with mutation status at age 24 months



Comparison of TSC clinical features with mutation status at entry



Epilepsy risk
30% for TSC1
79% for TSC2
P=0.00005

David Kwiatkowski on behalf of the EPISTOP work package 3 team

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