Supplementary Materials

Equivalent missense variant in the FOXP2 and FOXP1 transcription factors causes distinct neurodevelopmental disorders.

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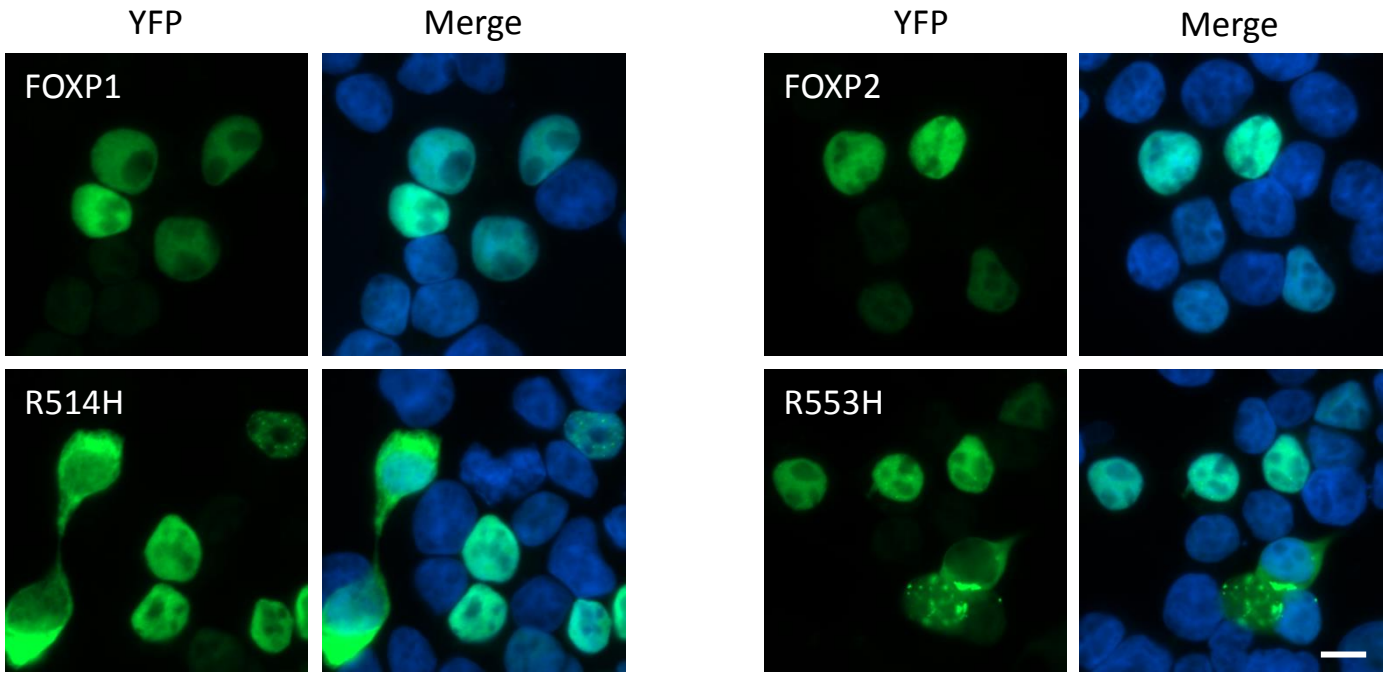
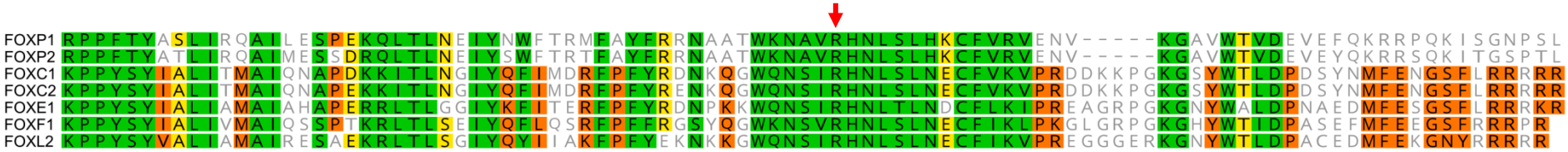


Supp. Figure S1. Aberrant subcellular localisation of the p.R514H FOXP1 and p.R553H FOXP2 variants in small epitope-tagged proteins. Immunofluorescence staining of HEK293 cells transfected with HisV5-tagged FOXP variants (green). Nuclei were stained with Hoechst 33342 (blue). Scale bar = 10 µm.



Supp. Figure S2. Protein sequence alignment of FOX domains from human FOX transcription factors. Red arrow indicates the arginine residue affected by the p.R553H FOXP2 and p.R514H FOXP1 variants. Pathogenic variants have been reported at the equivalent arginine residue in each of the FOX transcription factors shown here. UniProt accession numbers: FOXP1 (Q9H334), FOXP2 (O15409), FOXC1 (Q12948), FOXC2 (Q99958), FOXE1 (O00358), FOXF1 (Q12946), FOXL2 (P58012).

Supp. Table S1. Published pathogenic variants in FOXP1 and FOXP2. Missense, nonsense, frameshift and small indel variants are shown. FOXP2 = NM_014491.3; FOXP1 = NM_032682.5. Phenotypes: DD, developmental delay; ID, intellectual disability; ASD, autism spectrum disorder; PDD-NOS, pervasive developmental disorder nor otherwise specified; ADHD, attention deficit/hyperactivity disorder; CAS, childhood apraxia of speech.

Gene	Protein change	Reference	Phenotype
FOXP1	Initiation loss	Song et al (2015)	DD, ID, speech and language delay
FOXP1	p.P225T	Bekheirnia et al (2017)	DD
FOXP1	p.A339Sfs*4	O'Roak et al (2011)	DD, ID, speech and language delay, ASD
FOXP1	p.L414Dfs*46	Bekheirnia et al (2017)	DD
FOXP1	p.V283Pfs*11	Bekheirnia et al (2017)	DD, ID
FOXP1	p.V423Hfs*37	Lozano et al (2015)	DD, ID, speech and language delay, ASD
FOXP1	p.T431Gfs*29	Bekheirnia et al (2017)	DD, ID
FOXP1	p.Y439*	Sollis et al (2016)	DD, ID, speech and language delay, PDD-NOS
FOXP1	p.Q456*	Deciphering Developmental Disorders Study (2014)	Behavioural problems
FOXP1	p.R465G	Sollis et al (2016)	DD, ID, speech and language delay, autistic features
FOXP1	p.P466L	Deciphering Developmental Disorders Study (2014)	DD
FOXP1	p.R514C	Sollis et al (2016)	DD, ID, speech and language delay, PDD-NOS, ADHD
FOXP1	p.R514H	This study	DD, ID, speech and language delay
FOXP1	p.H515D	Bekheirnia et al (2017)	DD
FOXP1	p.R525Q	Bekheirnia et al (2017)	DD
FOXP1	p.R525*	Hamdan et al (2010)	DD, ID, speech and language delay, ASD
FOXP1	p. W534R	Srivastava et al (2014)	DD, ID
FOXP1	p.F541Lfs*5	Bekheirnia et al (2017)	DD, behavioural problems
FOXP2	p.Q17L	MacDermot et al (2005)	CAS
FOXP2	p.Q188_Q191dup	MacDermot et al (2005)	CAS
FOXP2	p.R328*	MacDermot et al (2005); Reuter et al (2017)	CAS, language impairment
FOXP2	p.Q390Vfs*7	Turner et al (2013)	CAS, language impairment
FOXP2	p.M406T	Roll et al (2010)	Language impairment, cognitive impairment
FOXP2	p.R478*	Reuter et al (2017)	Speech problems, language impairment
FOXP2	p.P505L	Reuter et al (2017)	Speech problems, language impairment
FOXP2	p.R536P	Reuter et al (2017)	Language impairment
FOXP2	p.F538Lfs*28	Reuter et al (2017)	Speech problems, language impairment
FOXP2	p.R553H	Lai et al (2001)	CAS, language impairment
FOXP2	p.R564*	Reuter et al (2017)	Language impairment
FOXP2	p.N597H	Laffin et al (2012)	CAS, language impairment