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Microglia in neurodegeneration

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Supplementary Table 1:

Trem2 variants associated with neurodegenerative diseases.

TREM2 Variants Associated with Neurodegenerative Diseases				
Variant	**Effect on protein**	**Functional change**	**Genotype**	**References**
Alzheimer's Disease				
97C→A	Q33X	Truncated, non-functional protein	Heterozygous	[1, 2]
140C → T	R47H	Impaired signaling ↓Lipoprotein binding ↓Lipoprotein uptake	Heterozygous	[3 2 4, 5]
185C → T	R62H	Impaired signaling ↓Lipoprotein binding ↓Lipoprotein uptake	Heterozygous	[2, 5]
295C → T	D87N	Enhanced signaling ↑ lipoprotein binding	ND	[6 5]
496C →T	H157Y	Enhanced signaling Increased shedding (sTREM2)	Heterozygous	[5, 7 8]
632C→T	L211P	Signaling equivalent to WT	Risk in African American	[5, 9]

Nasu-Hakola Disease				
40G →T	E14X	Truncated, non-functional protein	Homozygous	[10]
97C → A	Q33X	Truncated, non-functional protein	Homozygous	[1]
113A →G	Y38C	Misfolded protein, impaired glycosylation ↓ surface expression, ↓ phagocytosis	Homozygous	[11, 12, 13]
132G → A	W44X	Truncated, nonfunctional protein	Homozygous	[10]
197C → T	T66M	Misfolded protein, impaired glycosylation ↓ surface expression, ↓ phagocytosis	Homozygous	[5, 11, 12]
233G →A	W78X	Truncated, non-functional protein	Homozygous	[10]
377T →G	V126G	Impaired Glycosylation Impaired maturation ↓ surface expression	Homozygous	[1, 14]
401A→G	D134G	↓Surface expression	Homozygous	[1, 14]
267delG	Frameshift, premature stop	Non-functional protein	Homozygous	[1]

313delG	Frameshift, premature stop	Non-functional protein	Homozygous	[1]
482+2T→ C	Splice mutation (exon 3 missing)	Splice mutation nonfunctional protein	Homozygous	[15]
588G → A	K186N	No interaction with DAP12	Homozygous	[10, 14]
FTD/FTLD Disease				
42 + 3delAGG		Altered splicing ↓ protein	Homozygous	[16]
97C→A	Q33X	Truncated, non-functional protein	Homozygous	[17]
113A→ G	Y38C	Misfolded protein, ↓ surface expression, ↓ phagocytosis	Compound Heterozygous	[5, 11, 18]
197C→T	T66M	Misfolded protein, ↓ surface expression, ↓ phagocytosis	Homozygous (FTDL) Heterozygous (FTD)	[11, 12]
257A→T	D86V	Impaired Glycosylation ↓ surface expression	Compound heterozygous	[14, 19]
286C→A	T96K	↑ lipoprotein binding	ND	[5, 18]

		↑ signaling		
598G→A	W198X	Truncated protein	Homozygous	[20]
632C→T	L211P	Signaling equivalent to WT	ND	[5, 18]
Parkinson's Disease				
140C → T	R47H	Impaired signaling ↓Lipoprotein binding ↓Lipoprotein uptake	ND	(+) [21] (-) [22]
ALS				
140C → T	R47H	Impaired signaling ↓Lipoprotein binding ↓Lipoprotein uptake	*ND*	(+) [23]
Inconclusive Disease Association				
	R52H	↓surface expression ↓binding to some ligands		[5, 9, 24]
	R62C	↓surface expression ↓Activation by ligands		[5, 24]
	R136W			[24]
	R136Q			[24]
	E151K			[24]
	W191X	Stop-gain variant, predicted truncation		[9, 24]

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