

Table S2: Aminoacylation activity of mutated ARSs

Table S2a. Patient mutations and associated aminoacylation activity (% of wild type activity)

Gene	Mutation	Activity	Comment	Reference
AARS	p.Lys81Thr	± 54%	Steady-state yeast aminoacylation assays	31
	p.Arg751Gly	± 8%		
DARS	p.Asp367Tyr	“min. 3	Mutations in C-terminal domain; refers to (Cavarelli <i>et al.</i> , 1994) reduction”	41
	p.Ala274Val	fold		
	p.Met256Leu			
	p.Arg487Cys			
	p.Arg460His			
	p.Arg494Gly			
	p.Pro464Leu			
	p.Arg494Cys			
GARS	p.Ser635Leu	NA		48
	p.Arg596Gln	NA		
	p.Thr268Ile	NA		49
	p.Arg412Cys	NA		
HARS	p.Tyr454Ser	NA		42
IARS	p.Arg418*	“LoF” ±	Tet-Off yeast model: observed density (note: ≠ aminoacylation activity...)	36
		41%		
	p.Arg254*	“LoF” ±		
		39%		
	p.Asn992Asp	± 57%		
	p.Ile1174Asn	± 65%		
	p.Pro437Leu	± 58%		
	p.Val370Gly	± 86%		
p.Arg739Cys	“LoF”	Yeast complementation assay	37	
p.Phe556Ser	“Impaired”			

KARS	p.Tyr173His	NA		51
	p.Asp377Asn	NA		
	p.Arg438Trp	NA		52
	p.Glu525Lys	NA		
	p.Leu350His	NA		53
	p.Pro390Arg	NA		
LARS	p.Lys82Arg	NA		29,30
	p.Tyr373Cys	NA		
	p.Ala504Val	NA		
	p.Asn614Lys	NA		
MARS	p.Phe370Leu	± 18%	In HEK293 cells	33
	p.Ile523Thr	± 16%		
	p.Ser567Leu	± 40%	Aminoacylation activity in MARS yeast ortholog	34
	p.Ala393Thr	± 90% (NS)	Mes1 variants	
	p.Asp605Val	± 58%		
	p.Tyr344Cys	± 60%		
	p.Asp145Asn	NA		35
	p.Phe802Ser	NA		
RARS	p.Asp2Gly	NA		40
	Splice error (c.45+1G>T)	NA		
	p.Asp2Gly	NA		
	p.Cys32TrpfsX39	NA		
	p.Met1?	NA		
	p.Arg512Gln	NA		
SARS	p.Asp172Asn	49%	After 90 min.; GST-SARS in HEK293 cells	43
QARS	p.Tyr57His	± 72%	In lymphoblast cell lines with 1 mutant allele and 1	44
	p.Arg515Trp	± 63%	WT allele	

	p.Gly45Val	± 38%		
	p.Tyr57His	NA		45
	p.Lys496*	NA		
	p.Val476Ile	33%	In patient fibroblasts	46
VARS	p.Leu885Phe	NA		39
	p.Arg1058Gln	NA		
YARS	p.Pro213Leu	NA		38
	p.Gly525Arg	NA		

Table S2b. Aminoacylation activity in patients (when available; % of wild type activity)

Gene	Mutations	N	Allele 1	Allele 2	Activity	Comment	Reference
AARS	Compound heterozygous	2	p.Lys81Thr	p.Arg751Gly	± 31%	Steady-state yeast aminoacylation	31
	Homozygous	1	p.Arg751Gly	p.Arg751Gly	± 8%	assay	
IARS	Compound heterozygous	2	p.Trp435Cys	p.Asn1126fs	33%	In patient fibroblasts	<i>This article</i>
MARS	Compound heterozygous	1	p.Phe370Leu	p.Ile523Thr	± 17%	In HEK293 cells	33
	Homozygous	2	p.Ser567Leu	p.Ser567Leu	± 25%	Aminoacylation activity in MARS yeast ortholog Mes1	34
	Homozygous	6	& p.Ala393Thr	& p.Ala393Thr		variants	
SARS	Homozygous	4	p.Asp172Asn	p.Asp172Asn	49%	After 90 min; GST-SARS in HEK293 cells	43
QARS	Compound heterozygous	2	p.Gly45Val	p.Arg403Trp	± 35 %	In patient lymphoblast cell lines	44
	Compound heterozygous	2	p.Tyr57His	p.Arg515Trp	± 35 %		

Homozygous	3	p.Val476Ile	p.Val476Ile	33%	In patient fibroblasts	46
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