

Suppl. Table 1 to Plantier et al. “Functional mapping of the A2 domain from human factor VIII” (Thromb Haemost 2012; 107.2)

Res [*]	AA	Antigen [†]	Activity [‡]	Secretion [§]	Phenotype (Chronometric Activity %) [¶]	Comparison with HAMSTeR ^{**}
376	Lys	30.4±6.2	18.4±5.2			
377	Lys	72.5±2.8	88.9±11.6			
378	His	83.7±18.9	91.3±9.3			
379	Pro	68.8±3.1	87.1±13.2			
380	Lys	0.0	5±1.8	CRM-	Mild (10-15)	Identical
381	Thr	29±0.7	36.2±1.3			
382	Trp	18.7±2.4	8±2.8	CRM+	Severe (<1-7)	Identical
383	Val	49.0±0.9	57.0±5.4			
384	His	ND	ND		Severe (<1)	
385	Tyr	6.2±0.5	12.7±2.4	CRM-		
386	Ile	0.0	6.5±1.3	CRM-	Severe (<1-5)	Identical
387	ALA	WT	WT			
388	ALA	WT	WT			
389	Glu	ND	ND			
390	Glu	ND	ND		Severe (<1-4)	
391	Glu	78.8±6.6	119.8±6.2			
392	Asp	0.0	8.6±2.8	CRM-	Mild (29)	Identical
393	Trp	0.0	5.4±2.1	CRM-	Severe (<1)	Identical
394	Asp	ND	ND			
395	Tyr	ND	ND		Severe (<1)	
396	ALA	WT	WT		Moderate (2-5)	
397	Pro	0.5±0.4	11.4±2.4	CRM-		
398	Leu	71.4±1.8	100.5±10.8			
399	Val	53.3±7.6	80.2±14.7			
400	Leu	72.6±2.2	92.8±14.1			
401	ALA	WT	WT			
402	Pro	ND	ND			
403	Asp	48.4±1.0	82.7±10.1		Severe (<1)	Divergent
404	Asp	29.5±6.0	38.9±7.8			
405	Arg	65.8±6.2	72.9±5.4			
406	Ser	36.1±6.0	57.6±5.4			
407	Tyr	33.1±5.2	66.5±14.3			
408	Lys	50.8±8.6	60.2±9.3		Mild (7)	Similar
409	Ser	89.3±5.9	73.8±3.1			
410	Gln	30.3±3.8	60.4±10.7			
411	Tyr	ND	ND			
412	Leu	51.0±2.9	7.6±2.5	CRM+	Mild (5-7)	Identical
413	Asn	60.8±2.7	67.0±7.7			
414	Asn	55.6±3.2	82.2±1.7			
415	Gly	62.6±11.2	56.4±6.1			
416	Pro	43.7±6.2	53.0±3.2			
417	Gln	68.0±1.6	87.6±14.7			
418	Arg	25.0±0.4	48.3±9.9		Mild (<1-7)	Similar
419	Ile	0.0	7.6±2.5	CRM-		Identical
420	Gly	0.0	8.3±1.3	CRM-	Severe (<1-3)	Identical
421	Arg	44.2±9.6	75.2±4.7			
422	Lys	31.0±4.0	34.8±4.4			
423	Tyr	0.0	4.7±2.0	CRM-	Severe (<1)	Identical
424	Lys	0.0	5.5±1.6	CRM-		
425	Lys	0.0	5.7±3.2	CRM-	Severe (<1)	Identical
426	Val	44.6±5.0	28.2±4.7			
427	Arg	2.0±1.1	15.1±1.4	CRM-	Severe (<1)	Identical
428	Asn	0.0	6.6±1.6	CRM-		
429	Met	72.7±5.4	94.8±12.7			
430	Ala	WT	WT			
431	Tyr	0.0	12.6±1.0	CRM-	Moderate (4-7)	Similar
432	Thr	51.7±1.6	68.5±14.0			
433	Asp	ND	ND			
434	Glu	56.7±8.4	79.2±2.6			
435	Thr	20.2±0.1	34.8±8.5		Mild (10)	Similar
436	Phe	0.0	7.0±0.4	CRM-	Moderate (3)	Identical
437	Lys	53.5±4.8	76.8±11.6			
438	Thr	0.0	11.2±0.8	CRM-		
439	Arg	ND	ND		Mild	
440	Glu	65.7±2.3	50.8±5.6			
441	ALA	WT	WT			
442	Ile	87.1±0.5	90.3±16.3			
443	Gln	ND	ND			
444	His	78.5±4.6	78.9±7.7			
445	Glu	88.3±1.9	80.1±2.6			

446	Ser	ND	ND			
447	Gly	ND	ND		Severe (<1)	
448	Ile	0.0	10.4±2.4	CRM-		
449	Leu	84.7±2.3	99.0±1.8			
450	Gly	0.0	10.6±3.9	CRM-		
451	Pro	2.4±1.5	16.5±5.3	CRM-	Moderate (4-18)	Identical
452	Leu	76.5±5.5	71.6±6.0			
453	Leu	2.4±1.6	20.7±5.4			
454	Tyr	60.3±3.0	86.5±11.1			
455	Gly	53.0±5.4	66.4±3.0		Severe (<1)	Divergent
456	Glu	37.0±1.3	21.5±0.5		Moderate (3)	Similar
457	Val	31.5±0.2	36.8±5.9			
458	Gly	15.4±2.9	26.3±6.4		Moderate (2-5)	Similar
459	Asp	0.0	7.6±3.6	CRM-	Severe (2-14)	Identical
460	Thr	0.0	8.5±3.4	CRM-		
461	Leu	0.0	8.7±4.0	CRM-		
462	Leu	82.0±3.4	104.7±12.7			
463	Ile	0.0	10.4±4.5	CRM-		
464	Ile	34.1±3.6	63.0±14.7			
465	Phe	1.4±0.5	6.4±0.8	CRM-	Moderate (7)	Identical
466	Lys	16.5±1.9	22.7±3.5		Mild (27)	Identical
467	Asn	0.0	5.9±3.8	CRM-		
468	Gln	92.8±20.1	109.1±2.7			
469	ALA	WT	WT			
470	Ser	ND	ND			
471	Arg	4.4±1.8	11.4±2.6	CRM-	Mild (16)	Identical
472	Pro	3.7±1.0	15.0±2.3	CRM-		
473	Tyr	0.0	6.1±1.4	CRM-	Moderate (<1-3)	Identical
474	Asn	6.6±3.6	12.1±3.0	CRM-		
475	Ile	12.9±0.9	24.2±7.1		Mild (6-17)	Similar
476	Tyr	54.1±2.5	41.8±6.3			
477	Pro	23.7±2.7	35.4±11.1			
478	His	39.0±0.1	38.7±1.3			
479	Gly	0.0	5.5±1.7	CRM-	Moderate	Identical
480	Ile	ND	ND			
481	Thr	112.5±3.5	108.6±23.3			
482	Asp	0.0	5.9±4.0	CRM-		
483	Val	ND	ND		Mild	
484	Arg	ND	ND			
485	Pro	44.6±12.5	52.6±13.7			
486	Leu	81.6±3.0	93.7±17.2			
487	Tyr	88.7±0.8	39.7±11.8	CRM+		
488	Ser	59.6±9.1	115.8±13.1			
489	Arg	68.0±3.6	89.7±13.1			
490	Arg	74.3±10.8	88.0±18.0			
491	Leu	83.0±4.3	71.0±11.5			
492	Pro	50.0±2.0	60.4±11.8			
493	Lys	30.5±0.3	71.2±9.1			
494	Gly	81.3±2.9	76.3±12.9		Moderate (4)	Divergent
495	Val	57.4±6.3	91.8±13.8			
496	Lys	96.6±6.2	114.5±28.0			
497	His	82.8±5.2	81.8±26.9			
498	Leu	73.4±4.7	74.4±10.9			
499	Lys	56.4±14.9	66.1±9.9			
500	Asp	94.3±16.7	69.7±18.2			
501	Phe	34.9±1.7	59.5±9.0			
502	Pro	15.2±0.9	19.7±12.7			
503	Ile	17.4±1.6	19.1±6.0		Severe(<1)	Similar
504	Leu	16.8±0.4	22.9±4.5		Mild (7-14)	Similar
505	Pro	28.7±1.1	42.2±5.3			
506	Gly	20.6±0.2	36.0±8.2			
507	Glu	68.4±2.7	98.4±17.8			
508	Ile	39.6±8.9	60.6±17.4			
509	Phe	52.5±3.1	40.7±5.9			
510	Lys	ND	ND		Moderate (2)	
511	Tyr	28.9±0.9	33.3±5.3			
512	Lys	66.8±0.8	39.9±5.4			
513	Trp	ND	ND		Severe (<1)	
514	Thr	20.6±1.2	29.5±2.7			
515	Val	ND	ND		Mild	
516	Thr	ND	ND			
517	Val	58.8±1.1	52.2±5.0			
518	Glu	92.4±3.3	104.5±2.6			
519	Asp	42.4±3.9	50.7±6.8			
520	Gly	95.0±10.7	61.9±7.7		Mild (14)	Divergent
521	Pro	0.0	9.5±1.8	CRM-	Moderate (2-3)	Identical
522	Thr	33.8±3.5	27.3±4.4		Mild (8-40)	Identical
523	Lys	78.6±4.2	73.3±5.2			
524	Ser	92.8±1.2	101.1±9.9			
525	Asp	17.9±0.9	10.0±3.9		Moderate (6)	Identical
526	Pro	55.3±8.4	60.4±15.4			
527	Arg	0.0	8.7±3.5	CRM-	Mild (3-34)	Identical
528	Cys	0.0	12.1±7.2	CRM-	Severe (<1)	Identical
		44.6±2.5				
529	Leu		38.0 ±6.0			

530	Thr	68.7±4.6	87.6±12.0			
531	Arg	43.1±0.5	35.4±7.7		Mild (3-45)	Identical
532	Tyr	26.2±2.4	53.4±9.3			
533	Tyr	0.0	7.9±2.2	CRM-		
534	Ser	93.6±3.3	105.2±14.7		Severe (<1)	Divergent
535	Ser	0.0	12.8±4.6	CRM-	Moderate (3-15)	Identical
536	Phe	0.2±0.2	13.0±4.2	CRM-		
537	Val	14.8±1.0	26.5±3.8		Moderate (3)	Similar
538	Asn	0.5±0.4	16.4±5.7			
539	Met	99.7±9.0	77.2±18.9			
540	Glu	72.4±6.7	97.8±1.0			
541	Arg	0.0	9.0±2.1	CRM-	Mild (13-22)	Identical
542	Asp	2.7±1.5	11.9±4.1	CRM-	Severe (<1)	Identical
543	Leu	41.0±0.3	57.0±5.8			
544	Ala	WT	WT		Moderate (4)	
545	Ser	4.7±0.8	21.0±7.6			
546	Gly	0.0	21.2±6.1			
547	Leu	15.8±0.2	27.6±2.8		Severe (<1)	Similar
548	Ile	ND	ND		Mild (27)	
549	Gly	12.9±1.9	27.4±10.1		Severe (<1)	Similar
550	Pro	71.0±4.1	95.3±13.8			
551	Leu	22.0±0.4	33.9±5.7			
552	Leu	46.8±6.5	64.2±10.2			
553	Ile	ND	ND			
554	Cys	0.0	7.0±4.4	CRM-		
555	Tyr	ND	ND			
556	Lys	66.6±2.5	59.8±10.1			
557	Glu	ND	ND		Mild (16)	
558	Ser	32.9±1.3	18.2±5.2	CRM+	Mild (21)	Identical
559	Val	79.1±2.5	69.1±13.1		Mild (10)	Divergent
560	Asp	18.7±0.3	17.6±6.8		Mild (7)	Similar
561	Gln	66.5±0.6	44.7±9.7			
562	Arg	97.9±2.8	111.6±26.2			
563	Gly	68.1±1.7	12.7±3.4	CRM+		
564	Asn	ND	ND		Mild (19)	
565	Gln	ND	ND		Moderate	
566	Ile	19.4±0.5	12.7±8.3	CRM+	Moderate (1-4)	Identical
567	Met	101.5±0.2	94.1±5.9		Mild (17)	Divergent
568	Ser	74.5±2.7	101.8±27.8			
569	Asp	42.7±2.2	12.5±5.2	CRM+	Severe (<1)	Identical
570	Lys	ND	ND			
571	Arg	ND	ND			
572	Asn	ND	ND			
573	Val	75.5±5.4	31.9±13.2	CRM+		
574	Ile	22.4±8.8	43.7±6.7			
575	Leu	ND	ND		Mild (8)	
576	Phe	0.0	6.5±2.4	CRM-		
577	Ser	ND	ND			
578	Val	24.1±6.9	58.5±6.6			
579	Phe	0.0	7.4±3.4	CRM-		
580	Asp	0.0	9.3±3.6	CRM-	Severe (<1)	Identical
581	Glu	ND	ND			
582	Asn	ND	ND			
583	Arg	ND	ND		Mild (8-34)	
584	Ser	ND	ND		Severe (<1-8)	
585	Trp	0.0	4.5±4.2	CRM-	Severe (<1)	Identical
586	Tyr	0.0	4.5±2.0	CRM-	Severe (<1-8)	Identical
587	Leu	11.7±1.0	31.0±5.9			
588	Thr	57.7±4.4	102.6±16.6			
589	Glu	ND	ND			
590	Asn	ND	ND		Moderate (2-3)	
591	Ile	15.4±2.3	6.8±3.6	CRM+		
592	Gln	57.6±3.3	100.9±5.3			
593	Arg	ND	ND		Mild (2-38)	
594	Phe	4.5±2.8	18.0±4.8			
595	Leu	ND	ND			
596	Pro	65.8±0.3	107.5±11.8			
597	Asn	51.2±6.9	74.5±6.6			
598	Pro	ND	ND			
599	ALA	WT	WT			
600	Gly	75.3±1.7	106.9±8.8			
601	Val	50.4±1.3	80.0±13.0			
602	Gln	72.8±3.0	129.1±13.1			
603	Leu	19.5±2.4	46.2±8.9			
604	Glu	69.4±0.5	99.4±23.8			
605	Asp	16.7±2.4	35.6±1.5			
606	Pro	ND	ND			
607	Glu	48.7±7.0	74.2±5.1			
608	Phe	ND	ND			
609	Gln	ND	ND			
610	Ala	WT	WT			
611	Ser	57.0±1.1	84.6±13.6			

618	Asn	0.0	7.0±2.7		Severe (<1-31)	Identical
619	Gly	6.6±2.9	14.4±3.6	CRM-	Severe (<1)	Identical
620	Tyr	ND	ND			
621	Val	51.4±6.6	80.0±7.1		Moderate (3)	Divergent
622	Phe	0.7±0.5	9.3±2.5	CRM-		
623	Asp	41.2±6.3	72.1±3.7			
624	Ser	51.6±11.3	80.0±35.4			
625	Leu	0.0	10.9±2.0	CRM-	Mild (8-12)	Identical
626	Gln	ND	ND		Moderate (4)	
627	Leu	ND	ND			
628	Ser	63.5±3.9	103.3±24.5			
629	Val	59.2±7.1	85.2±14.3			
630	Cys	0.7±0.6	7.6±3.4	CRM-		
631	Leu	ND	4.8±0.8	CRM-	Mild (22)	Identical
632	His	43.3±8.4	72.3±17.9			
633	Glu	41.1±3.8	86.7±11.0			
634	Val	16.5±0.9	12.3±3.3		Severe (<1)	Identical
635	Ala	WT	WT			
636	Tyr	ND	ND		Moderate (2)	
637	Trp	0.0	5.6±0.8	CRM-		
638	Tyr	37.9±15.4	20.0±4.0			
639	Ile	ND	ND			
640	Leu	62.9±5.6	76.6±13.3		Severe	Divergent
641	Ser	ND	ND			
642	Ile	63.2±3.7	99.0±18.1			
643	Gly	0.4±0.4	4.7±1.5	CRM-	Severe (<1)	Identical
644	Ala	WT	WT		Moderate (14)	
645	Gln	ND	ND		Severe (<1)	
646	Thr	4.3±1.0	8.9±3.8	CRM-		
647	Asp	ND	ND			
648	Phe	64.4±5.0	143.1±2.1			
649	Leu	36.7±10.7	29.1±7.1			

* Residue number of the full-length FVIII sequence as found in the crystal structure (3CDZ, [23]). † Antigen level measured in % of wild type. ‡ Chromogenic FVIII activity measured in % of wild type. § CRM- : antigen<15% and activity<15%; CRM+: ratio activity/antigen<0.5. ¶ Phenotype reported in the HAMSTeRS database. Chronometric activity (% of wild-type plasma activity) between brackets when available. ND, not done. **Comparison of the phenotype severity with HAMSTeRS data: identical, when the same level of activity was retrieved; similar, when there is a decrease in activity but with different amplitude; divergent, when an activity is retrieved in contradiction to data from HAMSTeRS.
