

Supplemental material

Microdiversity of TEM β -lactamases: a network analysis of sequence-function relationships and exploration of sequence space

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Table S1 Sequences that were identical to at least one other sequence after removing the residues outside of the core region (24-280)

Representative variant			Identical variants		
ID	name	phenotype	ID	name	phenotype
64	TEM-34, TEM-97	2br	292	TEML-150	-
764	TEM-71	2be	666	TEM-188	2be
313	TEM-110	-	357	TEM-168	-
317	TEM-171	-	15	TEML-267	-
111	TEM-181	-	412	TEML-48	-
396	TEM-122	2br	668	TEM-163	-
818	TEM-1	2b	62	TEML-273	-
			112	TEM-214	-
			138	TEML-285	-
			295	TEML-308	-
			451	TEML-318	-
			479	TEM-206	2b
			480	TEML-254	-
			482	TEML-324	-
			538	TEML-132	-
			569	TEML-335	-
			573	TEML-265	-
			626	TEML-212	-
			672	TEML-349	-
			702	TEML-352	-
			737	TEML-225	-
			744	TEML-357	-
			769	TEML-362	-
			132	TEM-98	-
923	TEM-65	2br	84	TEM-67	2br
63	TEM-47	2be	507	TEM-48	2be
779	TEM-52	2be	229	TEM-92	2be
910	TEM-32	2br	492	TEM-159	2br
10	TEM-29	2be	535	TEM-115	2be
286	TEM-19	2be	604	TEM-120	2be
256	TEM-20	2be	625	TEML-344	-
197	TEM-30, TEM-99	2br	261	TEML-303	-
			557	TEML-151	-

Table S1 continued

Representative variant			Identical variants		
ID	name	phenotype	ID	name	phenotype
783	TEM-116	2b	161	TEML-47	-
			267	TEML-304	-
			273	TEML-81	-
			328	TEML-41	-
			476	TEML-322	-
			517	TEML-72	-
			553	TEML-51	-
			673	TEML-350	-
			715	TEML-354	-
			763	TEML-361	-
			123	TEML-46	-
			785	TEML-367	-
			812	TEML-369	-
300	TEM-57	2b	718	TEML-149	-
610	TEM-43	2be	929	TEM-161	-

Table S2 Nodes that were isolated from the main network (m: sequence is of the right length, but the mutations differ, f: sequence is missing too many residues, l: the sequence is too long).

ID	Name	Mutations	Reason	Lowest identity
206	TEM-87	Q6K, E104K, D163H, R164C, M182T	m	2
565	TEML-93	N-8, V84I, A184V, K192R, G236E, I282R, C-6	m	2
512	TEML-202	I5V, V31L, G54N, V84A, G87K	m	4
368	TEML-224	N-10, I13K, P14A, F16C, A18K, G283V, A284P, C-6	m	2
220	TEML-235	M272T, D273E	m	2
611	TEML-341	N-23, W165Y, E166Y, P167G, M182T	m	2
31	TEML-270	N-24, 41--CRTSHR--42, G41P, A42C, V84I, E104K, A184V, E240R, Q269R, A270K, T271K, M272T, 290-- GLEQKLISEEDLNSAVDHHHHHH	m	14
578	TEM-151	M69V, R164H, N276D, A284G	m	2
695	TEM-89	Q39K, E104K, S130G, G238S, C-8	m/f	3
350	TEML-74	N-8, K34R, V84I, A184V, S243P, C-6	m	2
199	TEML-135	V84I, A184V, M211L, E212L	m	2
649	TEML-347	N-11, M69I, M182T, C-11	m/f	2
139	TEM-205	V84I, E104K, R164S, M182T, A184V	m	2
327	TEM-194	Q99R, L137I, G156R, N175H, A185P, M186V, K192T, G196V, Q205P, Q206R, L220I	m	9
202	TEML-145	P226L, R244L, A248E	m	2
145	TEML-134	P183L, A184Y	m	2
140	TEM-60	Q39K, L51P, E104K, R164S, A187R, S223C, F230L	m	4
772	TEML-364	N-13, I282K, C-8	m	2
754	TEML-359	N-23, A150D, H153R, N154Q, M155I, H158K, V159E, W165I, E168D, A172G, I173K, P174L, N175G, E177L, M182T, A184K, M186I, T188S	m	16
159	TEML-87	N-8, V84I, L102M, E121G, A184V, G218E, C-6	m	3

Table S2 continued

ID	Name	Mutations	Reason	Lowest identity
21	TEML-243	N-23, P62S, V80I, V84I, E147G, M182T, A184V, L201P, I208M, A224V, I247V, R275L	m	9
723	TEML-97	N-1, L21F, E104K, R164S, M182T, I282E, C-8	m/f	3
244	TEML-91	N-8, V84I, H96R, A184V, A248T, G255S, C-6	m	2
647	TEM-123	Q6K, E104K, G238S, A248-, R275A	m	2
334	TEML-139	E104D, Y105A	m	2
201	TEML-292	W165-, E166G, P167T	m	3
379	TEM-152	M69V, R164H, E240K, N276D	m	2
189	TEM-193	N136H, L138F, R164C, E166G, E168K, N170T, N175H, M186V, T188N, L220I	m	8
91	TEML-80	N-8, V84I, T133A, R178H, A184V, C-6	m	2
214	TEML-84	N-8, K73R, V84I, L113P, A184V, C-7	m	3
508	TEM-195	Q99R, R164C, N175H, M186V	m	3
558	TEML-44	S4D, I5P, L21F, R164S, T265M, C-9	m	3
41	TEM-59	Q39K, S130G, C-9	m	3
688	TEML-158	G283E, A284K, S285Q, 286--KC--287, I287T, K288D, C-2	m	2
260	TEML-302	N-23, M68L, M69T	m	2
116	TEML-76	N-8, R65H, V84I, A184V, E240K, C-6	m	2
616	TEML-343	N-23, S70G, W165Y, E166Y, P167G	m	2
381	TEM-178	A42S, R43T, V44S, P145S, K146Q, R178A, E212-, G238R	m	8
544	TEML-82	N-8, V33A, K34N, V84I, A184V, I260F, C-6	m	3
605	TEML-191	Q6S, N276M, R277S, A280V, E281D, I282M, A284G	m	5
42	TEM-211	Q6K, E104K, S130T, M182T, G238S, R275L	m	2
6	TEML-147	F60L, V84I, T140A, A184V, P219S	m	2
694	TEML-143	V84I, I173K, A184V, K234T	m	2
456	TEML-319	N-13, M182T, C-10	f	2
439	TEML-88	N-8, M69V, C77R, V84I, A184V, C-6	m	2

Table S2 continued

ID	Name	Mutations	Reason	Lowest identity
546	TEM-124	Q6K, E104K, M182T, A248-, R275A	m	2
407	TEML-239	P257S, R259H	m	2
775	TEML-365	N-23, V84I, E104Y, Y105N	m	2
243	TEML-96	N-8, F16S, V84I, N175I, A184V, L193P, C-6	m	2
551	TEM-164	L40V, I279T	m	2
148	TEML-102	N-8, C77R, V84I, A184V, V262I, C-10	m	3
700	TEML-204	N-19, V23A, V84I, A184V, K192E, I246V, C-4	m	2
157	TEML-85	N-8, F60L, V84I, P107S, A184V, C-6	m	2
432	TEML-317	V84I, A184V, P257X, S258X, R259X, I260X, V261X, V262X, I263X, Y264X, T265X, 266--YRSYLHDGE--267, T266S, S268N, Q269Y, A270G, C-20	m	25
284	TEML-79	N-8, V31A, V84I, A184V, V262A, C-6	m	2
933	TEM-173	A213V, R244S, N276K	m	2
204	TEM-108	S4D, I5P, V80E, G196S, N276S	m	2
401	TEM-182	M69I, W165L, R275L	m	2
918	TEM-50	M69L, E104K, G238S, N276D	m	2
677	TEML-140	A25V, H26R, A184V, L250V	m	2
147	TEML-156	G78D, A79T, V80L, V84I, R178S, A184V, A187P, P257R	m	4
268	TEML-98	N-8, V84I, I95T, N136D, T140A, A184V, W210R, C-6	m	3
531	TEML-330	N-2, I5M, F16L, A17R, A18H, C20A, L21F, P22-, V23L, A25C, H26S, E28R, T29N, L30A, V31G, K32E, T71A, V84I, A184V	m	6
191	TEML-291	N-23, W165Y, E166Y, P167G, L201P	m	2
223	TEML-205	N-28, V31M	m	5
238	TEML-296	D115E, M117K, L162X	m	3
542	TEML-201	N-11, S53X, M182T, C-11	m	2
561	TEML-334	N-16, M69X, W165X, N276X	m	3

Table S2 continued

ID	Name	Mutations	Reason	Lowest identity
336	TEML-253	M129I, S130A, A184V, 290-- VTVRPSLLIYTLD	l	2
533	TEML-40	R204W, M211V, C-2	m	2
414	TEM-187	L21F, R164H, A184V, T265M, C-1	m	2
663	TEML-92	N-8, F15S, E37G, E63K, V84I, A184V, C-6	m	2
304	TEML-104	N-8, E58G, V84I, Y97C, A184V, A202T, C- 9	m	4
712	TEML-99	N-8, H26L, D101G, R164H, A184V, P252L, C-6	m	4
406	TEML-255	E48X, E281X, I282X, G283X, A284X	m	5
766	TEML-83	N-8, S70G, F72L, V84I, A184V, L190M, C- 6	m	2
19	TEML-221	N-15, H153X, C-11	m	3
659	TEML-42	P145X, T181X, A184V, I263X, T265P, I287D, C-3	m	4
575	TEML-337	N-23, V84I, E104A, Y105A	m	2
75	TEM-42	N-3, Q39K, A42V, G238S, E240K, T265M, C-2	m	2
387	TEM-101	Q39K, G238S, E240K, A280V	m	2
219	TEML-153	P27F, E28D, T29L, K32F, A36C, S82F, V84I, A184V	m	6
13	TEML-94	N-8, V84I, D179G, A184V, R222C, F230L, C-6	m	3
782	TEM-130	D35P, Q39K, E104K, R164S, A237T	m	2
3	TEML-89	N-8, A11G, S82F, V84I, T141A, E177G, A184V, C-6	m	3
34	TEML-78	N-8, V84I, A184V, G228S, C-7	m/f	2
539	TEM-162	E28K, D38N, E64K, V84I, N100S, L102V, A184V	m	4

Table S3 Nodes that were identified in the clustering process. The order of their removal is given in the column "order of removal".

Order of removal	ID	Variant	Mutations	Relative betweenness
1	818	TEM-1 (N-23)		207,81
2	783	TEM-116	V84I, A184V	66,92
3	640	TEM-12	R164S	31,94
4	416	TEM-2	Q39K	35,98
5	386	TEM-33	M69L	29,59
6	568	TEM-135	M182T	39,41
7	393	TEM-63	L21F, E104K, R164S, M182T	48,85
8	313	TEM-110	L21F, T265M	31,51
9	65	TEM-15	E104K, G238S	28,02
10	779	TEM-52	E104K, M182T, G238S	28,60
11	526	TEM-35	M69L, N276D	13,15
12	152	TEM-129	Q39K, E104K, R164S	12,82
13	10	TEM-29	R164H	13,42
14	358	TEM-16	Q39K, E104K, R164H	17,25
15	441	TEM-85	L21F, R164S, E240K, T265M	21,09
16	911	TEM-36	M69V, N276D	11,81
17	509	TEM-84	N276D	13,20
18	376	TEM-3	Q39K, E104K, G238S	11,10
19	286	TEM-19	G238S	8,28
20	455	TEM-10	R164S, E240K	8,17
21	9	TEM-155	Q39K, R164S, E240K	9,16
22	63	TEM-47	G238S, E240K, T265M	6,92
23	197	TEM-30, TEM-99	R244S	6,71
24	111	TEM-181	A184V	6,55
25	914	TEM-39	M69L, W165R, N276D	5,45
26	371	TEM-17	E104K	5,38
27	909	TEM-31	R244C	5,09
28	64	TEM-34, TEM-97	M69V	4,91
29	690	TEM-28	R164H, E240K	4,89
30	195	TEM-6	E104K, R164H	4,22
31	232	TEM-24	Q39K, E104K, R164S, A237T, E240K	4,00
32	658	TEM-4	L21F, E104K, G238S, T265M	3,00
33	901	TEM-5	R164S, A237T, E240K	2,40
34	919	TEM-51	R244H	2,33
35	670	TEM-154	M69L, R164S	1,60

Table S3 continued

Order of removal	ID	Variant	Mutations	Relative betweenness
36	681	TEM-93	M182T, G238S, E240K	1,50
37	128	TEM-45	M69L, R275Q	1,33
38	14	TEML-124	V84I, A184V, A284L	1,00
39	60	TEM-169	M69L, W165G	1,00
40	156	TEML-199	A184X	1,00
41	345	TEML-95	N-8, F19S, F24L, V84I, S106P, A184V, C-6	1,00
42	440	TEM-106	E104K, M182T	1,00
43	69	TEML-275	A184V, E240G, W290L	0,67
44	515	TEM-144	R164C, E240K	0,67
45	566	TEM-215	H153R	0,67
46	576	TEM-40	M69I	0,67
47	713	TEM-11	Q39K, R164H	0,67
48	903	TEM-9	L21F, E104K, R164S, T265M	0,67
49	920	TEM-56	Q39K, E104K, H153R	0,67
50	396	TEM-122	R275Q	0,25
51	913	TEM-38	M69V, R275L	0,67

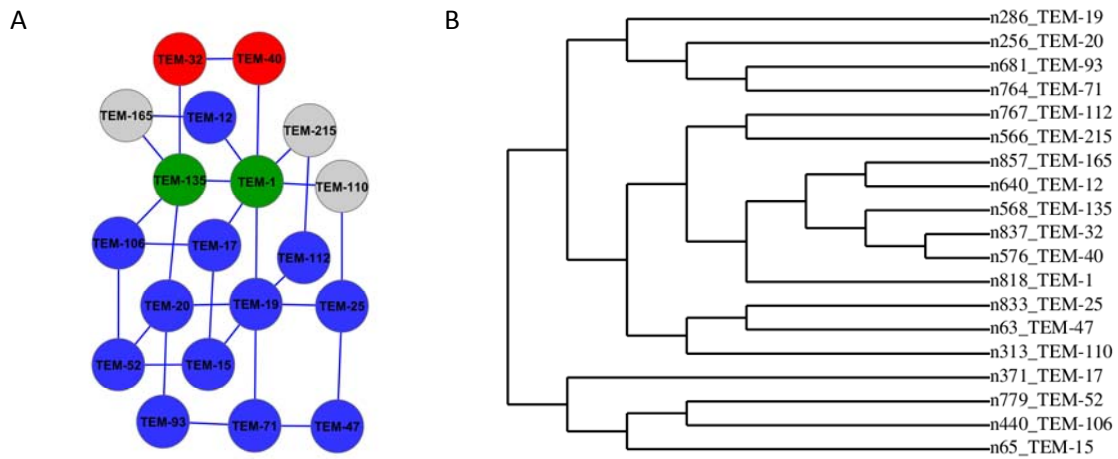


Figure S1 Comparison between representations of a set of TEM variants as phylogenetic tree and as a network. Tree was created on www.phylogeny.fr [1]

- [1] **Dereeper A, Audic S, Claverie J-M, Blanc G.** 2010. BLAST-EXPLORER helps you building datasets for phylogenetic analysis. *BMC Evol. Biol.* **10**:8