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Supplementary information

Identification of broadly tumour-reactive γδ TCRs from multiple myeloma

In the format provided by the authors and unedited

Supplementary Table 1. MM patient information for samples used

* Algonquin (ALQ) data cut-off: 28-Oct-25

Cohort	Sample_ID	Sex	Disease Status	Age at collection	Prior LOT	ISS Stage Dx	Date of Dx	Age at Dx	Cytogenetics	Light Chain	Heavy Chain	Status	ALQ - Cohort	ALQ - Response Group	ALQ - Best Response	ALQ - Response at C2D1	ALQ - Progression (event)	ALQ - PFS
ALGONQUIN	ALQ-02-012	Female	Relapse	68	2	Unknown	Unknown	Unknown	Unknown	Lambda	IgA	Dead	2a	Responder	VGPR	VGPR	1	9.8226
ALGONQUIN	ALQ-02-013	Female	Relapse	68	3	Unknown	Unknown	Unknown	Unknown	Kappa	IgA	Unknown	2a	Responder	sCR	VGPR	1	24.7372
ALGONQUIN	ALQ-02-015	Male	Relapse	76	3	Stage II	Unknown	Unknown	Unknown	Lambda	IgA	Unknown	2a	Responder	CR	SD	0	48.0289
ALGONQUIN	ALQ-02-018	Female	Relapse	53	2	Unknown	Unknown	Unknown	Unknown	Kappa	Kappa	Unknown	2a	Responder	sCR	VGPR	0	46.452
ALGONQUIN	ALQ-02-020	Female	Relapse	79	4	Unknown	Unknown	Unknown	Unknown	Kappa	IgG	Unknown	2a	Responder	VGPR	PR	1	24.5401
ALGONQUIN	ALQ-08-019	Male	Relapse	59	3	Stage II	Unknown	Unknown	Standard	Kappa	IgG	Unknown	2a	Responder	PR	SD	1	26.0512
ALGONQUIN	ALQ-08-021	Male	Relapse	55	2	Stage III	Unknown	Unknown	del1p, amp1q	Lambda	IgG	Dead	2a	Non-Responder	PD	PD	1	0.657
ALGONQUIN	ALQ-08-022	Female	Relapse	61	4	Unknown	Unknown	Unknown	Unknown	Lambda	Lambda	Unknown	2a	Responder	sCR	PR	0	45.7622
ALGONQUIN	ALQ-08-023	Female	Relapse	43	2	Stage III	Unknown	Unknown	Standard	Kappa	IgG	Unknown	2b	Responder	PR	PR	1	6.3732
ALGONQUIN	ALQ-08-024	Male	Relapse	54	3	Unknown	Unknown	Unknown	Not done	Lambda	IgG	Dead	2b	Responder	PR	PR	1	1.7411
ALGONQUIN	ALQ-08-026	Male	Relapse	63	3	Stage I	Unknown	Unknown	NA	Kappa	IgG	Unknown	2b	Responder	sCR	VGPR	0	25.2957
ALGONQUIN	ALQ-12-012	Male	Relapse	85	4	Stage I	Unknown	Unknown	Unknown	NA	IgG	Unknown	2a	Responder	VGPR	SD	0	14.7175
ALGONQUIN	ALQ-12-013	Male	Relapse	73	2	Unknown	Unknown	Unknown	Unknown	Kappa	IgG	Dead	2a	Responder	CR	PR	1	38.8305
ALGONQUIN	ALQ-12-014	Male	Relapse	78	3	Stage III	Unknown	Unknown	Standard	Unknown	Unknown	Dead	2a	Non-Responder	ND	ND	1	1.1498
ALGONQUIN	ALQ-12-015	Male	Relapse	67	2	Stage II	Unknown	Unknown	Unknown	Lambda	IgG	Dead	2a	Responder	sCR	SD	1	26.3141
ALGONQUIN	ALQ-12-016	Male	Relapse	78	2	Stage II	Unknown	Unknown	NA	Lambda	IgA	Dead	2a	Non-Responder	SD	SD	1	1.8397
ALGONQUIN	ALQ-12-017	Female	Relapse	76	2	Stage III	Unknown	Unknown	Unknown	Kappa	Kappa	Unknown	2a	Responder	CR	CR	0	41.1629
ALGONQUIN	ALQ-12-018	Male	Relapse	63	2	Stage I	Unknown	Unknown	Not done	Lambda	Lambda	Dead	2b	Responder	CR	VGPR	1	12.1879
ALGONQUIN	ALQ-12-019	Male	Relapse	53	4	Stage I	Unknown	Unknown	Not done	NA	Lambda	Unknown	2b	Non-Responder	SD	SD	1	2.3325
ALGONQUIN	ALQ-12-020	Male	Relapse	79	2	Stage II	Unknown	Unknown	NA	Kappa	IgG	Dead	2b	Responder	VGPR	PR	1	14.6518
ALGONQUIN	ALQ-12-021	Female	Relapse	56	2	Stage I	Unknown	Unknown	NA	NA	IgG	Unknown	2b	Responder	PR	SD	0	36.5637
ALGONQUIN	ALQ-13-019	Male	Relapse	53	4	Stage III	Unknown	Unknown	del1p, amp1q	Lambda	Lambda	Dead	2a	Responder	VGPR	PR	1	4.2378
ALGONQUIN	ALQ-13-021	Female	Relapse	70	2	Stage II	Unknown	Unknown	Standard	Kappa	Kappa	Unknown	2a	Responder	PR	SD	1	42.5427
ALGONQUIN	ALQ-13-022	Male	Relapse	82	2	Unknown	Unknown	Unknown	High risk	Kappa	IgG	Dead	2b	Responder	VGPR	PR	1	20.4336
ALGONQUIN	ALQ-14-005	Male	Relapse	38	2	Stage II	Unknown	Unknown	High risk	Kappa	IgA	Unknown	2a	Responder	VGPR	PR	1	31.636
ALGONQUIN	ALQ-17-009	Female	Relapse	72	3	Stage III	Unknown	Unknown	t(11;14)	Lambda	IgG	Unknown	2a	Responder	PR	SD	0	48.3246
ALGONQUIN	ALQ-17-010	Male	Relapse	71	3	Stage III	Unknown	Unknown	Standard	Lambda	IgG	Unknown	2a	Responder	VGPR	SD	1	22.7332
ALGONQUIN	ALQ-17-011	Male	Relapse	74	4	Stage III	Unknown	Unknown	Standard	Kappa	IgG	Unknown	2a	Responder	CR	PR	1	41.82
ALGONQUIN	ALQ-17-012	Female	Relapse	69	2	Stage III	Unknown	Unknown	Standard	Kappa	IgA	Unknown	2a	Non-Responder	SD	SD	1	5.5519
ALGONQUIN	ALQ-17-013	Male	Relapse	69	2	Stage II	Unknown	Unknown	del17p, gain 11q13	Lambda	IgA	Dead	2b	Responder	VGPR	SD	1	8.3771
ALGONQUIN	ALQ-17-014	Female	Relapse	66	3	Stage II	Unknown	Unknown	Standard	Kappa	IgG	Unknown	2b	Responder	VGPR	SD	0	38.3706
ALGONQUIN	ALQ-19-015	Male	Relapse	71	2	Stage II	Unknown	Unknown	del1p, amp1q	Lambda	Lambda	Dead	2a	Responder	CR	CR	1	18.1012
ALGONQUIN	ALQ-19-016	Female	Relapse	72	2	Stage II	Unknown	Unknown	Standard	Lambda	IgG	Unknown	2a	Responder	CR	VGPR	1	39.4218
ALGONQUIN	ALQ-19-017	Male	Relapse	79	3	Stage I	Unknown	Unknown	Unknown	NA	IgG	Dead	2a	Non-Responder	SD	SD	1	30.979
ALGONQUIN	ALQ-19-019	Male	Relapse	77	6	Stage III	Unknown	Unknown	Standard	Kappa	Kappa	Dead	2a	Non-Responder	SD	SD	1	1.8068
ALGONQUIN	ALQ-19-020	Female	Relapse	69	3	Stage II	Unknown	Unknown	Standard	Lambda	Lambda	Unknown	2b	Responder	VGPR	VGPR	0	10.2168
ALGONQUIN	ALQ-19-021	Male	Relapse	69	2	Stage II	Unknown	Unknown	Standard	NA	IgG	Unknown	2b	Responder	VGPR	PR	0	35.3811
PreGame	MM01	Male	Relapse	49	5	Stage II	2007	35	Unknown	Kappa	IgG	Alive	NA	NA	NA	NA	NA	NA
PreGame	MM02	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM03	Male	Diagnosis	74	0	Stage II	2020	74	amp1q	Kappa	IgA	Alive	NA	NA	NA	NA	NA	NA
PreGame	MM04	Female	Relapse	79	3	Stage II	2013	71	del13	Kappa	IgG	Dead	NA	NA	NA	NA	NA	NA
PreGame	MM05	Female	Relapse	66	5	Unknown	2013	58	Unknown	Kappa	FLC	Alive	NA	NA	NA	NA	NA	NA
PreGame	MM06	Female	Diagnosis	57	0	Unknown	2022	57	Unknown	Unknown	Unknown	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM07	Male	Relapse	72	3	Unknown	2007	65	Unknown	Unknown	Unknown	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM08	Male	Diagnosis	60	0	Unknown	2008	60	Unknown	Lambda	IgA	Dead	NA	NA	NA	NA	NA	NA
PreGame	MM09	Male	Diagnosis	74	0	Stage II	2022	74	Unknown	Kappa	IgA	Alive	NA	NA	NA	NA	NA	NA
PreGame	MM10	Female	Relapse	66	4	Unknown	1995	47	Unknown	Kappa	IgG	Dead	NA	NA	NA	NA	NA	NA
PreGame	MM11	Female	Relapse	58	2	Unknown	2010	55	Unknown	Kappa	FLC	Dead	NA	NA	NA	NA	NA	NA
PreGame	MM12	Female	Relapse	58	3	Unknown	2010	55	Unknown	Kappa	FLC	Dead	NA	NA	NA	NA	NA	NA
PreGame	MM13	Male	Diagnosis	63	0	Unknown	2023	63	Unknown	Unknown	Unknown	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM14	Male	Diagnosis	77	0	Unknown	2010	77	Unknown	Lambda	IgG	Dead	NA	NA	NA	NA	NA	NA
PreGame	MM15	Female	Relapse	49	5	Stage II	Unknown	47	Unknown	Lambda	IgG	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM16	Female	Relapse	81	3	Unknown	2019	Unknown	Unknown	Unknown	Unknown	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM17	Female	Diagnosis	73	0	Stage I	Unknown	73	t(11;14)	Lambda	FLC	Alive	NA	NA	NA	NA	NA	NA
PreGame	MM18	Female	Relapse	58	4	Unknown	2015	53	Unknown	Lambda	IgG	Dead	NA	NA	NA	NA	NA	NA
PreGame	MM19	Male	Diagnosis	59	0	Unknown	2023	59	t(IGH/14q32)	Lambda	Unknown	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM20	Male	Diagnosis	67	0	Unknown	2018	67	Unknown	Kappa	IgG	Alive	NA	NA	NA	NA	NA	NA
PreGame	MM21	Male	Diagnosis	87	0	Stage III	2022	87	Unknown	Unknown	Unknown	Unknown	NA	NA	NA	NA	NA	NA
PreGame	MM22	Female	Diagnosis	62	0	Unknown	2021	62	Unknown	Unknown	Unknown	Unknown	NA	NA	NA	NA	NA	NA

Supplementary Table 2. Sequences of Guide RNAs used for gene knockout with CRISPR Cas9.

Gene	sgRNA Sequence
TRAC_1	AGAGUCUCUCAGCUGGUACA
TRAC_2	UGUGCUAGACAUGAGGUCUA
BTN3A1_1	ACCAUCAGAAGUUCCCUCCU
BTN3A1_2	GGCACUUACGAGAUGCAUAC
B2M_1	GAGUAGCGCGAGCACAGCUA
B2M_2	GGCCACGCUGGAUAGCCUCC
HLA_A_1	CCAGUCACAGACUGACCGAG
HLA_A_2	CGUCCUGCCGGUACCCGCGG
HLA_A_3	GGAUGUGAAGAAAUACCUCA
HLA_B_1	GAGCAUGUACGGCUGCGACG
HLA_B_2	GCUGUCGAACCUCACGAACU
HLA_B_3	AGACUGACCGAGAGAGCCUG
HLA_C_1	AGCGACGCCGCGAGUCCGAG
HLA_C_2	GGCGGUGUCGAAAUACCUCA
HLA_C_3	AGGCUGACCGAGUGAGCCUG
Scrambled	GCACUACCAGAGCUAACUCA

Supplementary Table 3. CDR3 sequences of validated tumor-reactive gamma delta TCRs

TCR_name	V_delta_gene	CDR3_aa
TCR1	TRDV1	TRD:CALGNLPTRLYWGIRFSLSYTDKLIF;TRG:CALWEVEVDYYKKLF
TCR2	TRDV1	TRD:CALGNLPTRLYWGIRFSLSYTDKLIF;TRG:CATWDINYYKKLF
TCR6	TRDV1	TRD:CALGVSLVSYLLLGDRSTLTAQLFF;TRG:CATWDRLYKKLF
TCR10	TRDV1	TRD:CALGKAFLRGVGDRTDKLIF;TRG:CATWDSGDWIKTF
TCR11	TRDV2	TRD:CACDTVGGRTYSWDTRQMFF;TRG:CALWEANQELGKKIKVF
TCR18	TRDV1	TRD:CALGELGPYWGIRMYTDKLIF;TRG:CALWVIKHGDYKKLF
TCR20	TRDV1	TRD:CALGDSPRPPYWGIAAYTDKLIF;TRG:CATWDRPGYKKLF
TCR21	TRDV1	TRD:CALGEPPVFLRPTGMYTDKLIF;TRG:CATWGYTTGWFKIF
TCR22	TRDV1	TRD:CALGELLGPTTLLGVYRSWDTRQMFF;TRG:CATWDRQNYYKKLF
TCR24	TRDV1	TRD:CALGAFLRGYPTYTDKLIF;TRG:CATWDGLTGNYYKKLF
TCR26	TRDV1	TRD:CALGGGVGRIRILTDYTDKLIF;TRG:CATWRFHFPSGYKKLF
TCR28	TRDV1	TRD:CALGGYIPTFRTYWGILRTRGADKLIF;TRG:CATWDRCYKKLF
TCR29	TRDV1	TRD:CALGELIPNFLRLTLLGDMGKYTDKLIF;TRG:CATWDQGWKKLF
TCR33	TRDV3	TRD:CAFIQFGLLGYWDDGATDKLIF;TRG:CATWDRPFSSDWIKTF
TCR36	TRDV1	TRD:CALGEGSFFLPVLGDTIDKLIF;TRG:CATWDGYYKKLF
TCR38	TRDV1	TRD:CALGELDRPTYWGKDTDKLIF;TRG:CATWDRLPYKKLF
TCR40	TRDV3	TRD:CALRPSYWGAYTDKLIF;TRG:CALWEAGYYYKKLF
TCR43	TRDV1	TRD:CALGETISAFLPRGFSHSVKLIF;TRG:CATWDRYYKKLF
TCR45	TRDV1	TRD:CALGELRGLPLSYWGTYTDKLIF;TRG:CATWGINYKKLF
TCR59	TRDV2	TRD:CACDTLTGGYFSWDTRQMFF;TRG:CATWDDYYKKLF
TCR62	TRDV1	TRD:CALGELFPHILGDSETDKLIF;TRG:CATWTHYYKKLF
TCR65	TRDV3	TRD:CALRPSYWGAYTDKLIF;TRG:CALWEVTPRNYYKKLF
TCR67	TRDV1	TRD:CALGELNPTGEYTDKLIF;TRG:CATWDKVGYKKLF
TCR70	TRDV1	TRD:CALGASLPPMLPGLYTDKLIF;TRG:CATWDGYYYKKLF
TCR75	TRDV1	TRD:CALGELAWVGLFGGYYEEDRSLIF;TRG:CATWDGDYKKLF
TCR77	TRDV1	TRD:CALGDRRRPTYWGRDTDKLIF;TRG:CALWEAPRYYKKLF
TCR78	TRDV1	TRD:CALGGSAFLQGVGTGGFYNGKLIF;TRG:CATWDSPLRKKLF
TCR79	TRDV1	TRD:CALGEVLPFSFLCWGTDIKYTDKLIF;TRG:CALWENYYKKLF
TCR82	TRDV1	TRD:CALGELLRWGCSAKLIF;TRG:CATWEMCYSSDWIKTF
TCR83	TRDV1	TRD:CALGEPPGGYAWTEYTDKLIF;TRG:CATWDMEGYKKLF
TCR84	TRDV1	TRD:CALGERHSYLGVTYWGHTLVSGKLIF;TRG:CALWEVRYYKKLF
TCR95	TRDV1	TRD:CALGELREHTDKLIF;TRG:CATWDHTTGWFKIF
TCR100	TRDV1	TRD:CALGDPAFLQPLLGDSDKLIF;TRG:CATWDGLWDKKLF
TCR101	TRDV1	TRD:CALGSYSPPSPRLKRTYTDKLIF;TRG:CATWEGLNYYKKLF
TCR104	TRDV1	TRD:CALGELGFRILGTDKLIF;TRG:CATWDGLGIRYKKLF
TCR108	TRDV1	TRD:CALGELGLPIGPYTDKLIF;TRG:CALWEDYYKKLF
TCRv1	TRDV1	TRD:CALGELFLTYWGIRATDKLIF;TRG:CATWDAPSRLNYYKKLF
TCRv2	TRDV1	TRD:CALGELGIFLPLLGDPGAYTDKLIF;TRG:CATWDSSLNYYKKLF
TCRv3	TRDV1	TRD:CALGSTMGLPRILGYWGRDLTAQLFF;TRG:CATWSSDWIKTF
TCRv4	TRDV1	TRD:CALGEGFSYSWGPHTDKLIF;TRG:CATWDGWGNYKKLF
TCRv5	TRDV1	TRD:CALGELRSLFRAWGMRVDKLIF;TRG:CALWELYYYKKLF
TCRv6	TRDV1	TRD:CALGELVFLVWGIEGADKLIF;TRG:CATWDGPIGYKKLF
TCRv8	TRDV1	TRD:CALGDKFLPYLITGGYLRYGTDKLIF;TRG:CATWDPLYYKKLF
TCRv9	TRDV1	TRD:CALGERNYIWGIWCDTDKLIF;TRG:CATWDTHGWFKIF
TCRv10	TRDV1	TRD:CALGEPPLELIF;TRG:CAFPVGYKKLF
TCRv11	TRDV1	TRD:CALGELGYFLPTGYWGIRGELYTDKLIF;TRG:CATWDSYYKKLF
TCRv12	TRDV1	TRD:CALRLHPSPLVWNWGIQPDKLIF;TRG:CATWEVSYYKKLF
TCRv13	TRDV1	TRD:CALGLGGSYTDKLIF;TRG:CATWVIWWIKTF
TCRv14	TRDV1	TRD:CALGELSLPMITTGGWSVLVYTDKLIF;TRG:CATWDVYYKKLF
TCRv15	TRDV1	TRD:CALGEKSPPAFFLFTGGYADSTDKLIF;TRG:CATWDGPSYYKKLF
TCRv16	TRDV1	TRD:CALGELGLPRFTGGLLSTDKLIF;TRG:CATWAYYKKLF
TCRv17	TRDV1	TRD:CALGEPEGYPDKLIF;TRG:CATWLSTGWFKIF
TCRv18	TRDV1	TRD:CALGEDLLYWGIRPPTDKLIF;TRG:CATWVPIGYYKKLF
TCRv19	TRDV1	TRD:CALGDALVFSYRVLGAPLFGTDKLIF;TRG:CATWVYYKKLF
TCRv22	TRDV1	TRD:CALGELTGWEPYTDKLIF;TRG:CATWDGPNWLPTDYYKKLF
TCRv23	TRDV1	TRD:CALGESLPTVKLIF;TRG:CATWDGPNWLPTDYYKKLF
TCRv24	TRDV1	TRD:CALGSWAFLWLRTDKLIF;TRG:CALWEFHYYKKLF
TCRv27	TRDV1	TRD:CALGFLGYWGIGRIRGDTDKLIF;TRG:CATWDKYWGKKLF
TCRv28	TRDV1	TRD:CALGASFFLGLRGGATDKLIF;TRG:CATWDIPLNYYKKLF
TCRv29	TRDV1	TRD:CALAVSPWGWYTDKLIF;TRG:CATWDRYYKKLF
TCRv30	TRDV3	TRD:CAFHTGYWGIRGTDKLIF;TRG:CALWEHYKKLF
TCRv31	TRDV3	TRD:CAFHTGYWGIRGTDKLIF;TRG:CALWEVRYKKLF
TCRv32	TRDV1	TRD:CALGEYRGLPSPYWGYTLKGVSYTDKLIF;TRG:CATWDGRNYYKKLF

Supplementary Table 4. Gamma delta TCR sequences obtained from PreGame cohort MM patients

Sample_ID	No. Unique paired gd TCR seqs	Total gd T cells
MM01	14	54
MM02	31	105
MM03	26	66
MM04	37	234
MM05	16	16
MM06	7	45
MM07	14	60
MM08	6	8
MM09	3	3
MM10	77	317
MM11	14	31
MM12	6	25
MM13	8	21
MM14	32	300
MM15	223	6879
MM16	25	207
MM17	14	101
MM18	57	230
MM19	67	379
MM20	39	190
MM21	17	169
MM22	33	134