

## Supplementary Materials

**Table S1.** The purity of BR109 with various accelerated treatment conditions was verified by SEC.

Sample	Multimer peak (%)	Main peak (%)	Fragment peak (%)
BR109	0.1	99.9	0
BR109-HT	0.1	96.9	2.9
BR109-low pH	0.5	99.3	0.2
BR109-moderate pH	0	96.9	3.1
BR109-high pH	0.3	95.7	4.0

**Table S2.** Expression levels of GPRC5D in different MM cell lines were detected by flow cytometry assay.

Cell line	Concentration of BR109 (µg/mL)			
	0	0.02	1	50
MM.1R	0.5% <sup>1</sup>	98.7%	100%	97.9%
MM.1S	0.3%	68.6%	98.4%	98.5%
NCI-H929	0.3%	42.8%	82.2%	97.4%
RPMI8226	0.4%	19.0%	64.7%	96.9%

<sup>1</sup> This value is the percentage of cells in the same fluorescence channel boundary (gate) to the total cells under the same experimental conditions.

**Table S3.** The efficacy results at the end of the dosing at day 18.

Group	Antibody	Administration (mg/kg)	TV (mean±SEM <sup>1</sup> ) mm <sup>3</sup>	T/C (%)	TGI (%)	pValue
1	PBS	1.0	3303.18 ± 166.65	-	-	-
2	BR109	1.0	85.62 ± 49.21	2.59	97.41	<0.001
3	BM03	1.0	2429.01 ± 264.07	73.54	26.46	0.087

<sup>1</sup> SEM: Standard Error of the Mean

**Table S4.** The tolerance of mice at the end of the dosing.

Group	Antibody	Number of mice Day0/Day18	Day 0 Body Weight (mean±SEM) g	Day 18 Body Weight (mean±SEM) g	Body Weight Change (mean±SEM)
1	PBS	5/5	24.58 ± 0.65	25.78 ± 1.26	-0.27%
2	BR109	5/5	25.37 ± 0.52	25.97 ± 0.77	-1.71%
3	BM03	5/5	27.07 ± 0.6	30.05 ± 0.56	-2.26%

**Table S5.** The efficacy results at the end of the experiment at day 21.

Group	Antibody	Administration (mg/kg)	TV (mean±SEM) mm <sup>3</sup>	T/C (%)	TGI (%)	pValue
1	IsotypeCD3 (i.v.)	0.8	2416.58 ± 155.28	-	-	-
2	BR109 (i.v.)	0.05	59.45 ± 42.78	2.46	97.54	<0.001

3	BR109 (i.v.)	0.2	0 ± 0	0.00	100.00	<0.001
4	BR109 (i.v.)	0.8	0 ± 0	0.00	100.00	<0.001
5	Talquetamab analog (i.v.)	0.05	1240.41 ± 150.36	51.33	48.67	0.177
6	Talquetamab analog (i.v.)	0.2	99.29 ± 80.79	4.11	95.89	<0.001
7	BR109 (s.c.)	0.2	0 ± 0	0.00	100.00	<0.001

**Table S6.** The tolerance of mice at the end of the experiment.

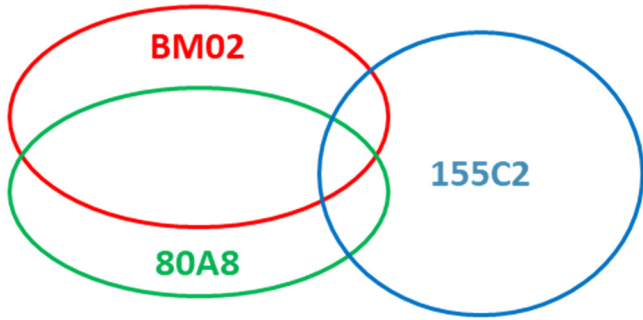
Group	Antibody	Number of mice Day0/Day18	Day 0 Body Weight (mean±SEM) g	Day 21 Body Weight (mean±SEM) g	Body Weight Change (mean±SEM)
1	IsotypeCD3 (i.v.)	5/5	24.8 ±0.50	27.8±0.54	12.34%
2	BR109 (i.v.)	5/5	24.7 ±0.54	26.0±0.86	5.25%
3	BR109 (i.v.)	5/5	24.0 ±0.51	24.1±0.57	0.58%
4	BR109 (i.v.)	5/5	24.7 ±0.67	24.5±1.28	-0.86%
5	Talquetamab analog (i.v.)	5/5	24.3 ±0.79	24.4±1.47	1.18%
6	Talquetamab analog (i.v.)	5/5	24.4 ±0.46	24.7±1.28	1.13%
7	BR109 (s.c.)	5/5	24.5 ±0.55	25.7±0.80	4.90%

**Table S7.** The binding activities of BR109 to HEK293T\_hGPCR5D/cynoGPCR5D/mGPCR5D were determined by flow cytometry assay.

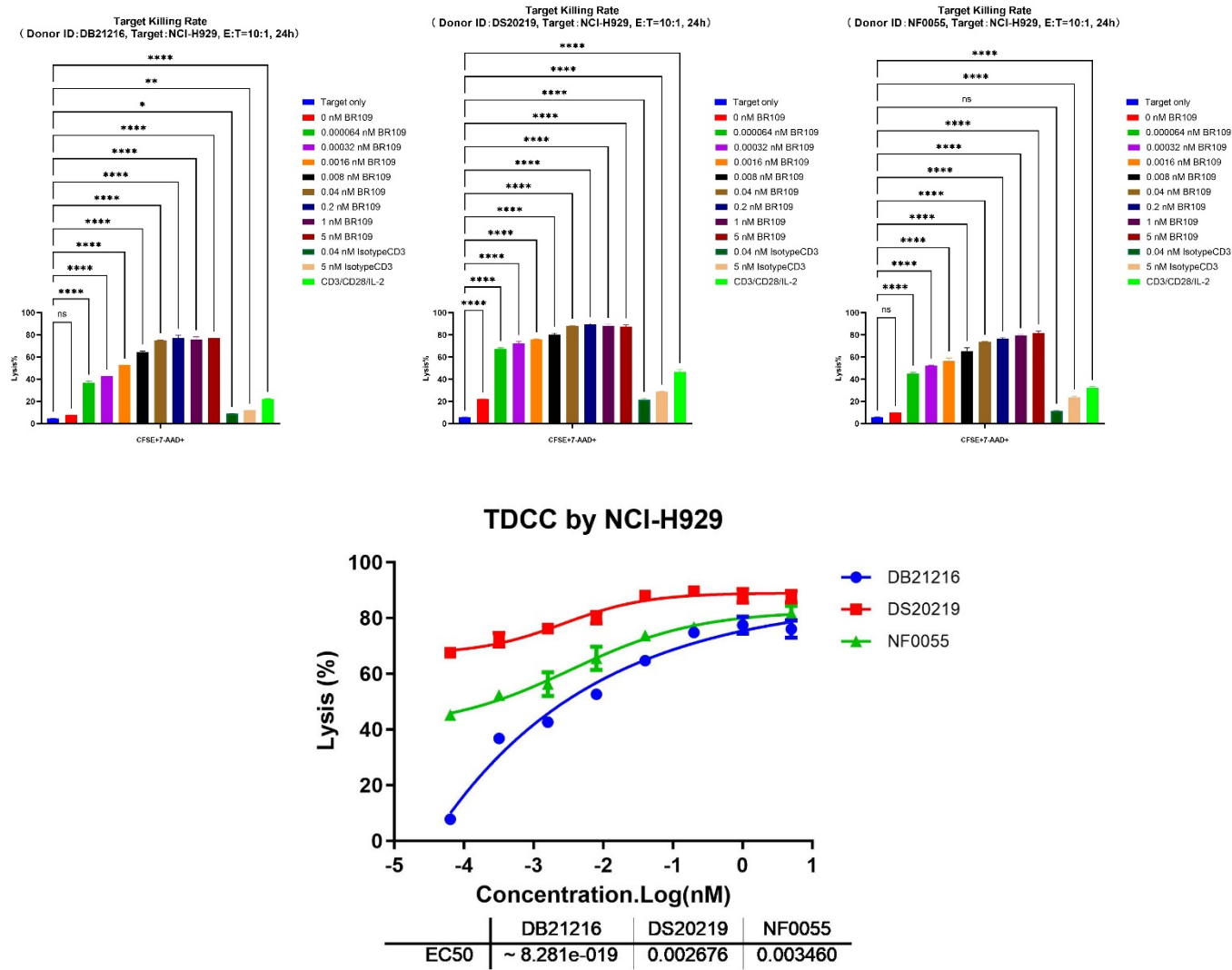
EC <sub>50</sub> (nM)	HEK293T_hGPCR5D	HEK293T_cynoGPCR5D	HEK293T_mGPCR5D
BR109	1.97 <sup>1</sup>	38.15	389.8
	1.99	30.62	324.1

<sup>1</sup> The experiment was performed twice in duplicate.

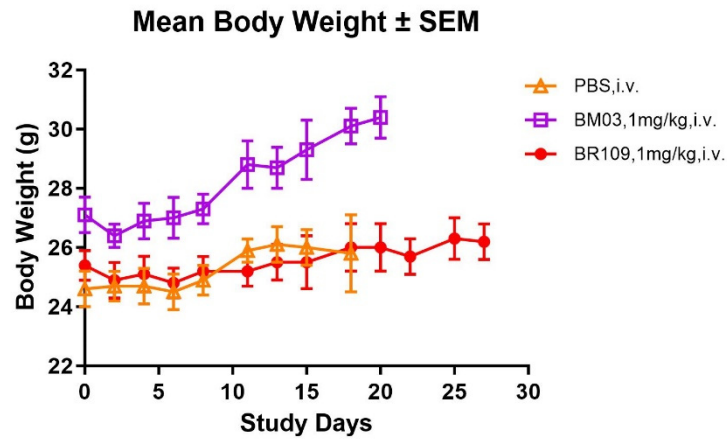
	BM02 -Alexa488	80A8 -Alexa488	155C2 -Alexa488
BM02	83%	57%	35%
80A8	100%	99%	29%
155C2	89%	73%	94%



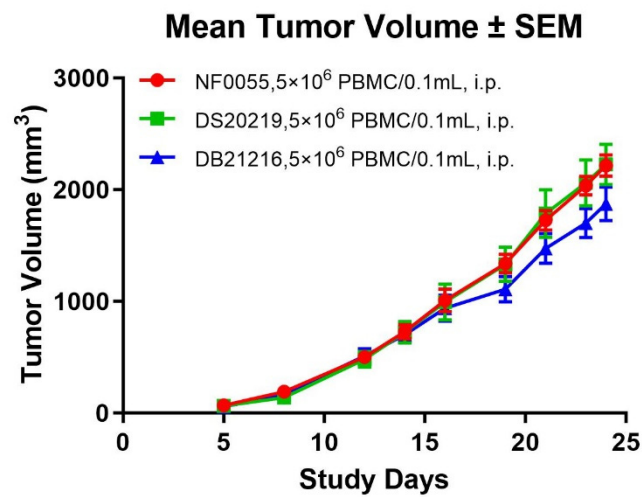
**Figure S1.** The epitope binning of anti-GPRC5D antibodies.



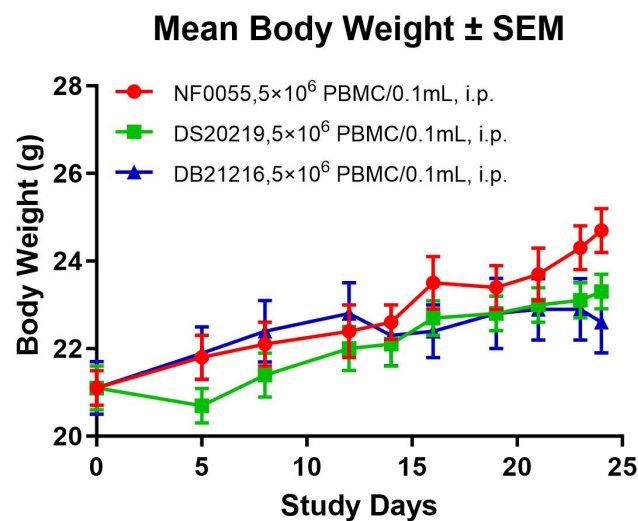
**Figure S2.** Cytotoxicity of GPRC5D×CD3 TCB BR109 when coculturing multiple myeloma cell line NCI-H929 with human PBMCs from three different donors.



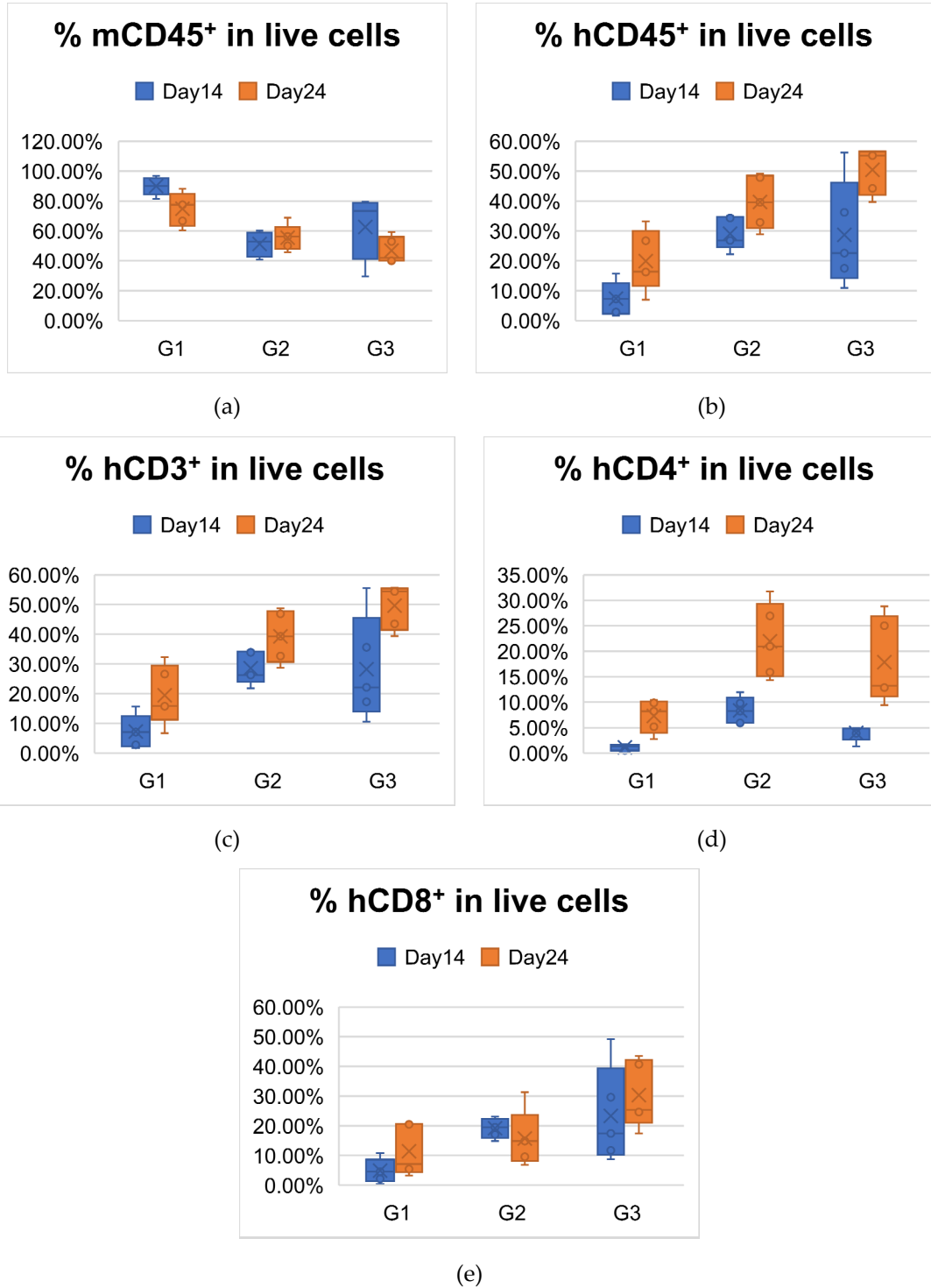
**Figure S3.** Body weights of NCI-H929 xenograft NPG mice with human immune cells (donor ID: DZ211314) treated with BR109 or BM03.



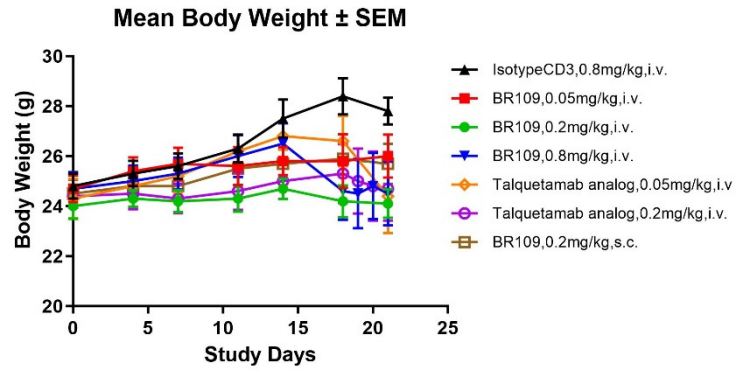
**Figure S4.** Tumor volumes of NCI-H929 xenograft NPG mice with human immune cells from three different donors (donor ID: NF0055, DS20219, DB21216). No drug was administered in this experiment.



**Figure S5.** Body weights of NCI-H929 xenograft NPG mice with human immune cells from three different donors (donor ID: NF0055, DS20219, DB21216). No drug was administered in this experiment.



**Figure S6.** The reconstruction of human immune cells from three different donors, (a) mouse CD45<sup>+</sup> cell populations, (b) human CD45<sup>+</sup> cell populations, (c) human CD3<sup>+</sup> cell populations, (d) human CD4<sup>+</sup> cell populations, and (e) human CD8<sup>+</sup> cell populations in the NCI-H929 xenograft NPG mice models. G1: NF0055; G2: DS20219; G3: DB21216.



**Figure S7.** Body weights of NCI-H929 xenograft NPG mice with human immune cells (donor ID:DB21216) treated with BR109 or Talquetamab analog.