

Self-Assembling Multi-Antigen T Cell Hybridizers (MATCH) for Precision Immunotherapy in Multiple Myeloma

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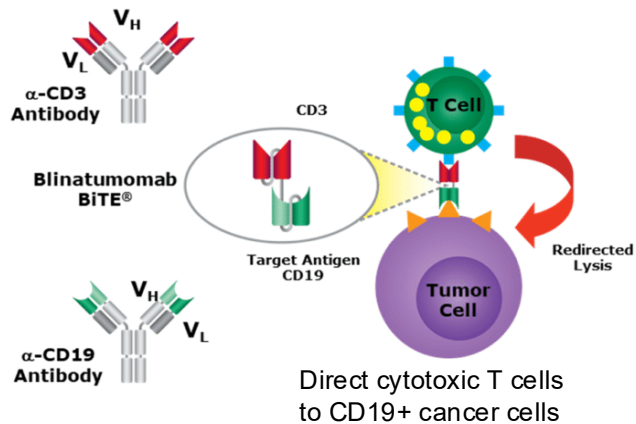
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07/15/2025

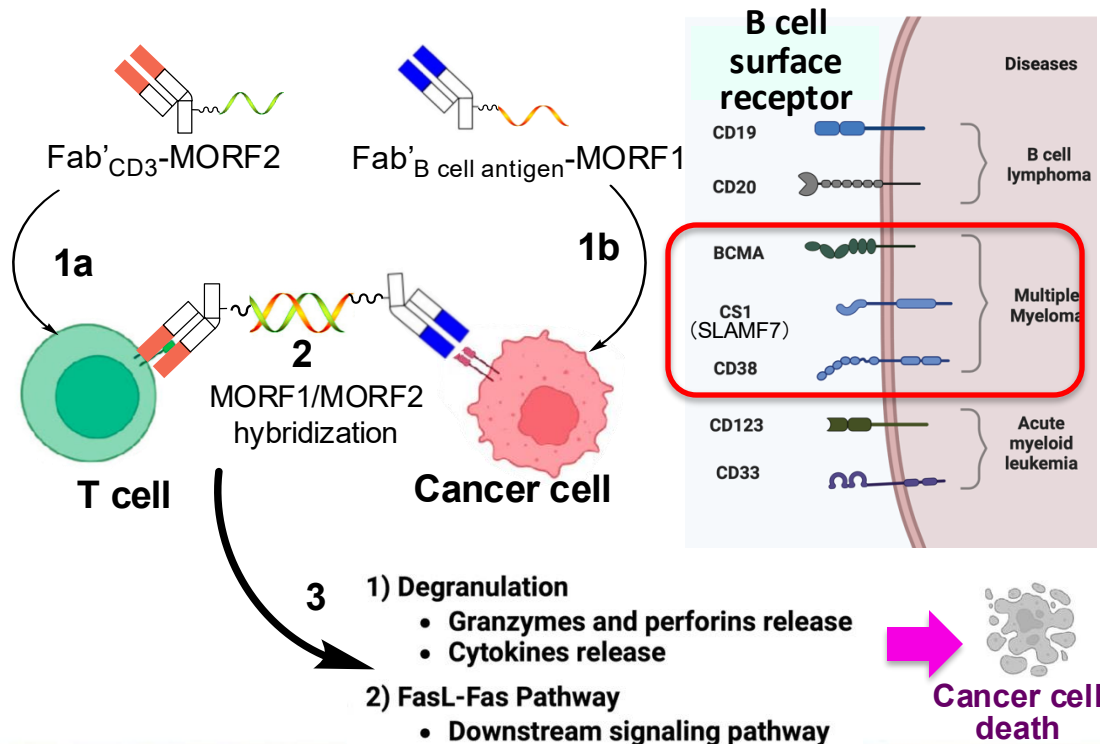
Bispecific T-cell engager (BiTE)

Blinatumumab

Mechanism



Multi-Antigen T Cell Hybridizers (MATCH)



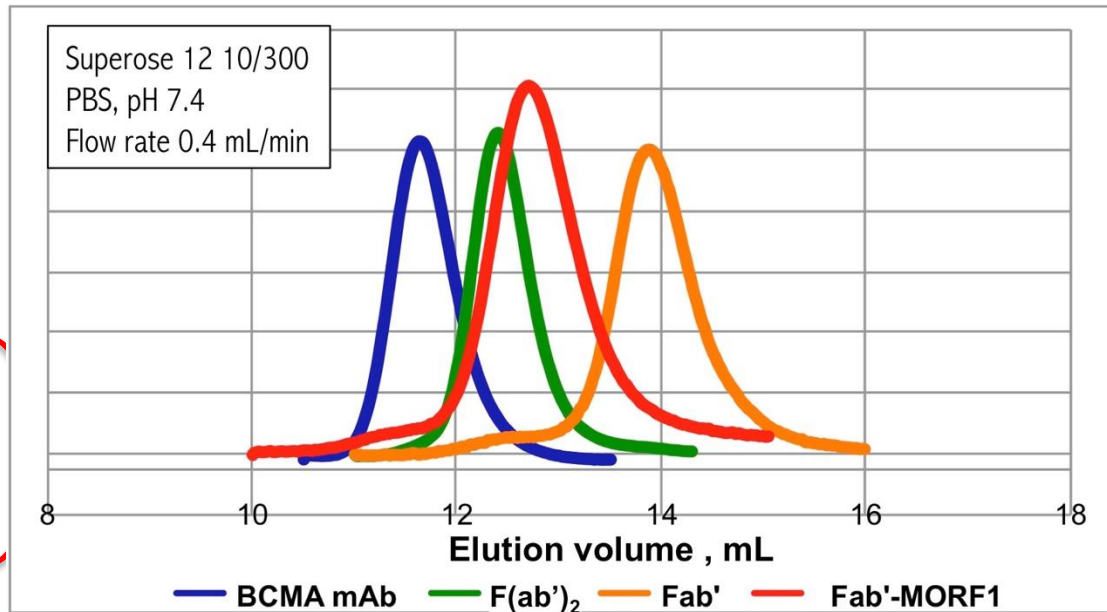
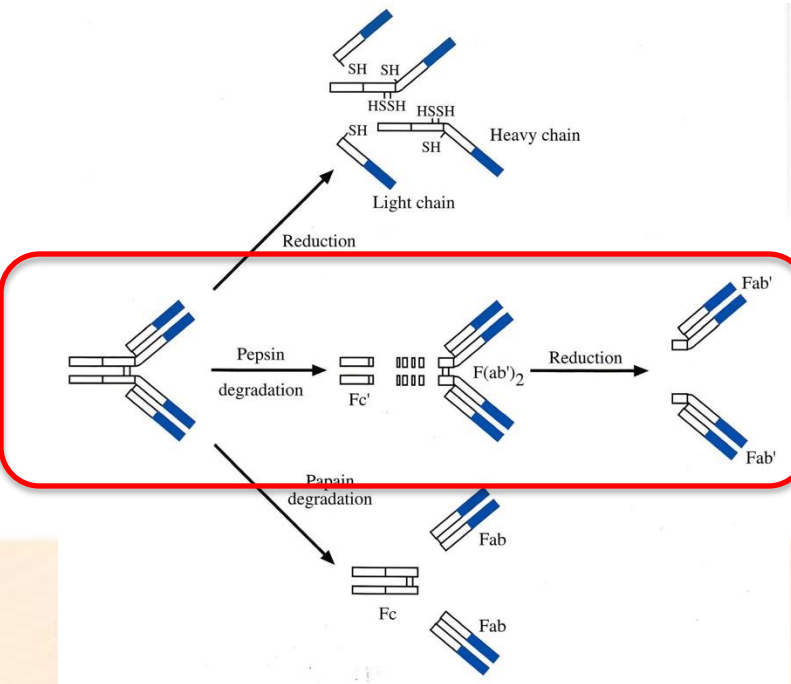
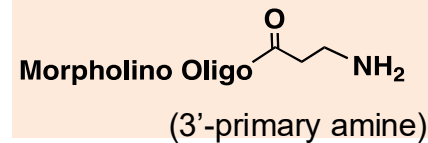
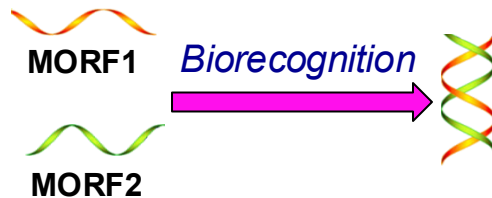
Challenges:

- Antigen loss/heterogeneity → resistance
- Cytokine release syndrome (CRS), neurotoxicity
- Lack of tumor-specific antigens → off-tumor toxicity

The Rapid, High-fidelity Heterodimerization of Two-Components in MATCH

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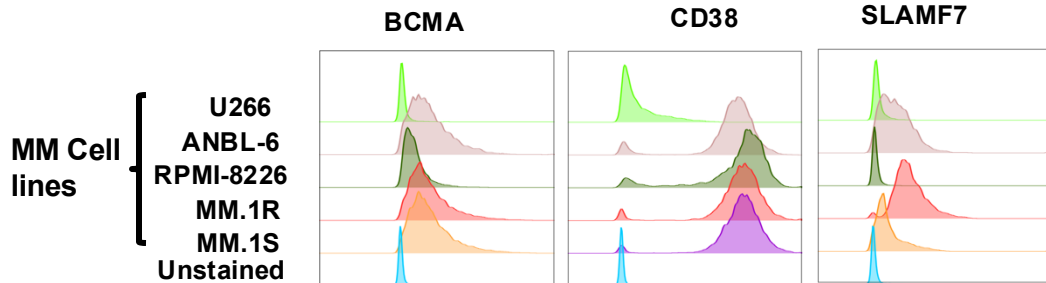
MM cell targets	BCMA	Fab' _{BCMA} -MORF1
	SLAMF7	Fab' _{SLAMF7} -MORF1
	CD38	Fab' _{CD38} -MORF1
T cell targets	CD3	Fab' _{CD3} -MORF2



**NEXT-GENERATION
DELIVERY INNOVATIONS**

MATCH Opens A New Avenue to Personalized Medicine for MM

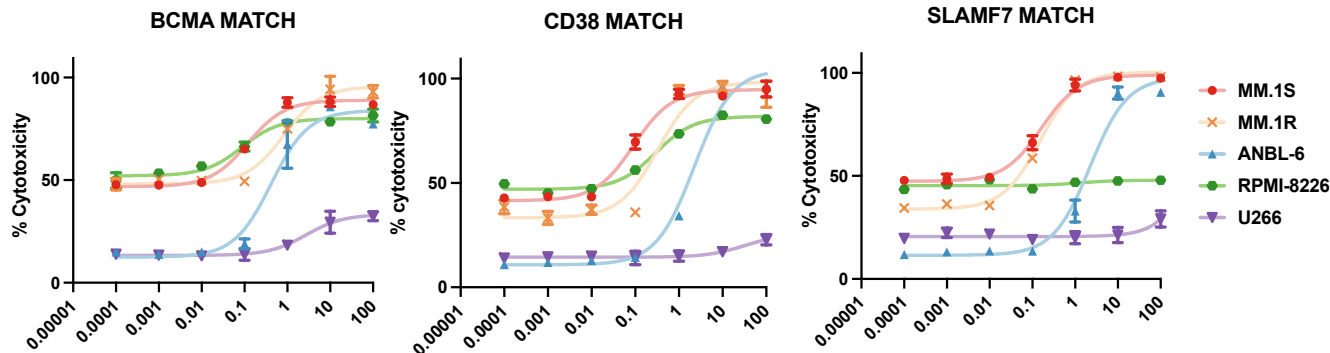
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EC ₅₀	BCMA	CD38	SLAMF7
MM.1R	0.83 nM	0.33 nM	0.15 nM
MM.1S	0.11 nM	0.10 nM	0.16 nM
RPMI-8226	0.08 nM	0.29 nM	-
U266	-	-	-
ANBL-6	0.42 nM	2.2 nM	2.2 nM

EC₅₀ values are in single digit nM range!

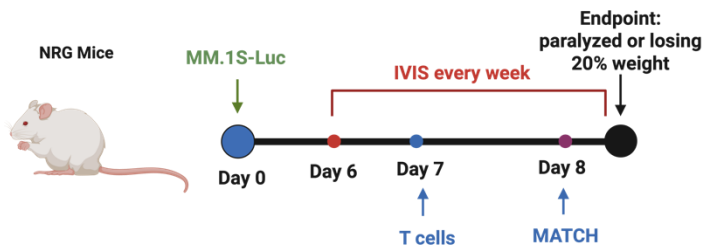
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T cell targets	CD3	Fab' _{CD3} -MORF2



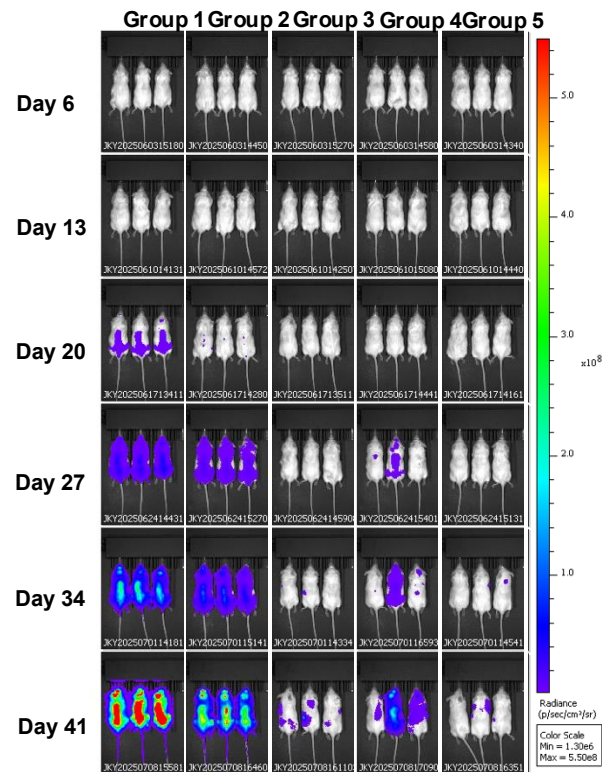
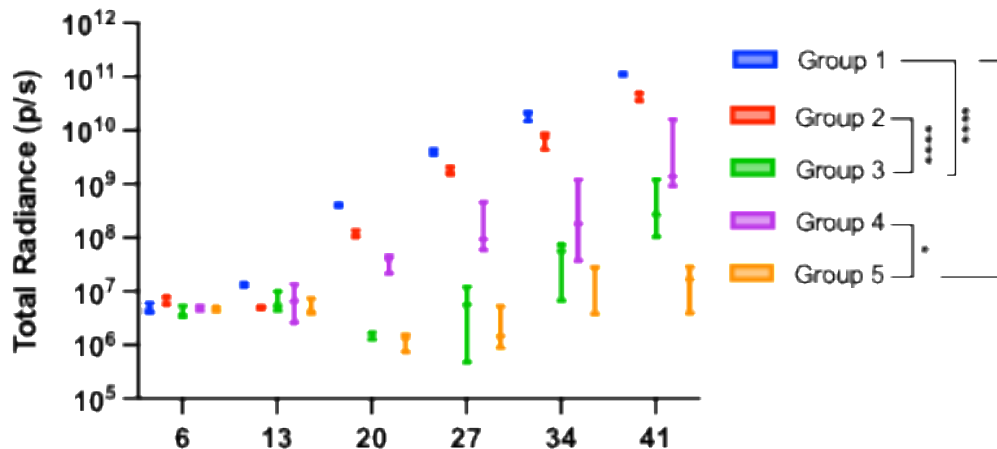
MATCH-mediated cytotoxicity on variable MM Cells (T:B 1:1, 24 h)

Evaluate the Efficacy and Safety of MATCH in A Preclinical Model

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	T cells	Treatment
Group 1	-	-
Group 2	1×10^6 T cells	-
Group 3	1×10^6 T cells	0.5 nmol BCMA MATCH
Group 4	3×10^6 T cells	-
Group 5	3×10^6 T cells	0.5 nmol BCMA MATCH



Explore the Translational Potential of MATCH Therapy

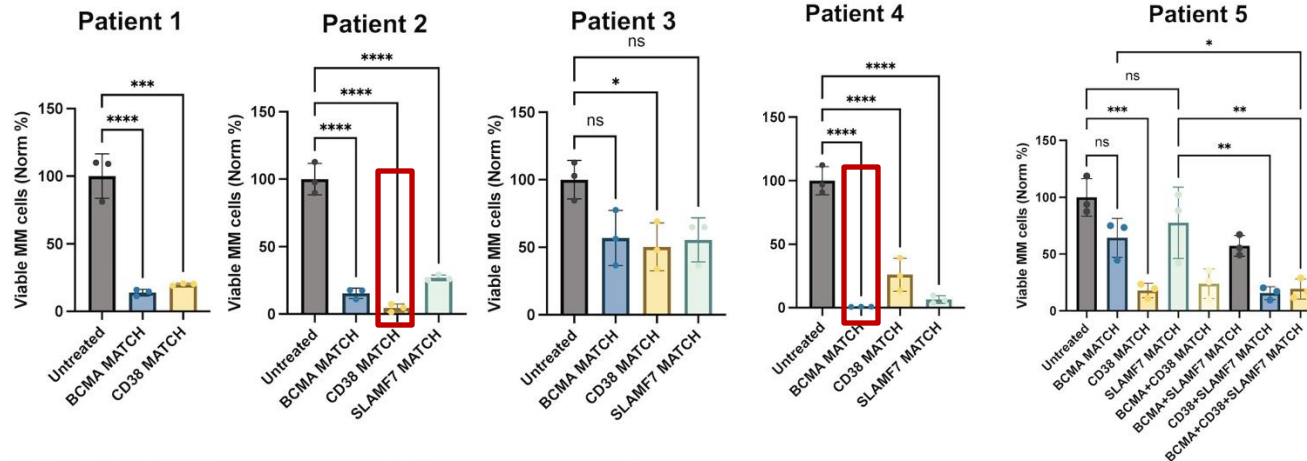
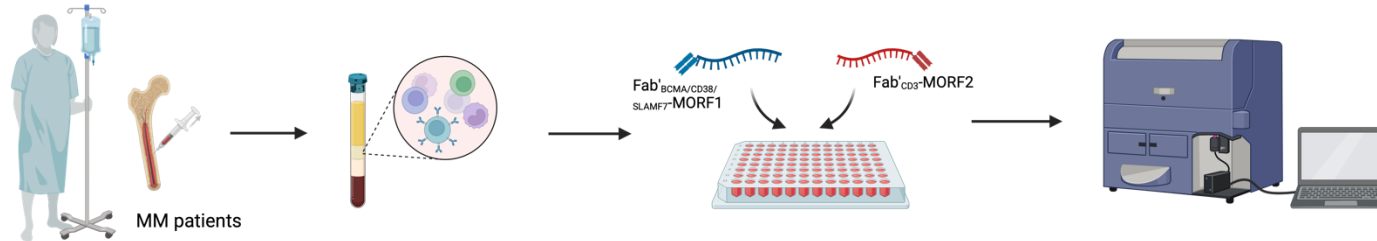
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(1) Bone marrow sample

(2) MNCs isolation

(3) Ex vivo MATCH treatments

(4) Flow cytometry analysis

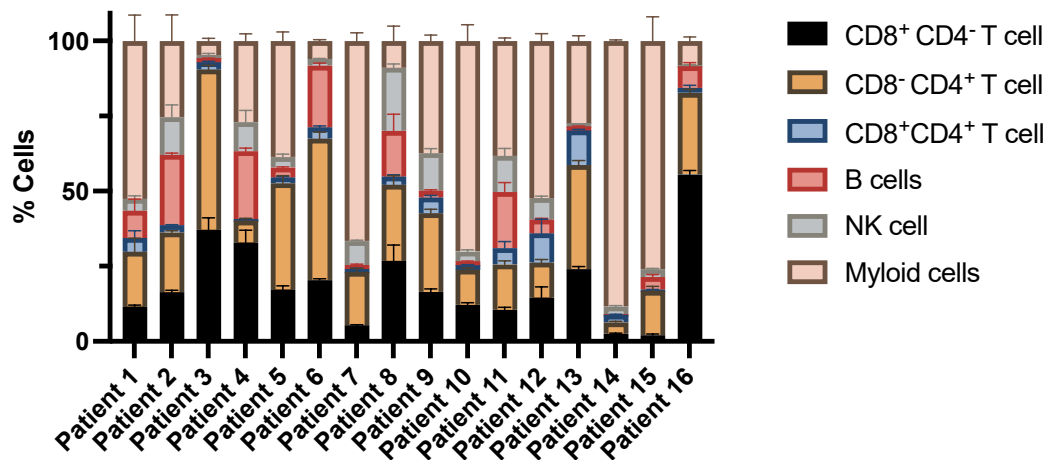


- Different patients exhibited varied responses to MATCH.
- Trispecific MATCH offers a solution to the challenge of tumor heterogeneity.

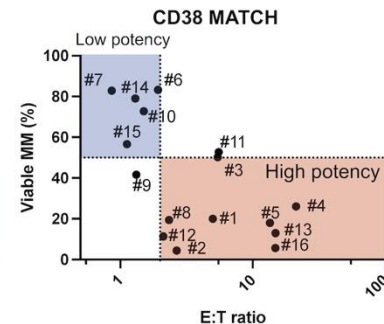
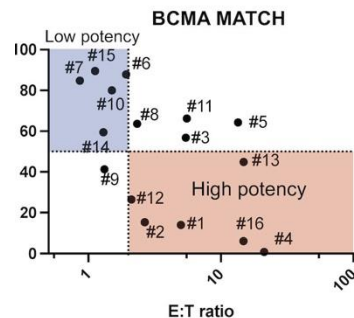
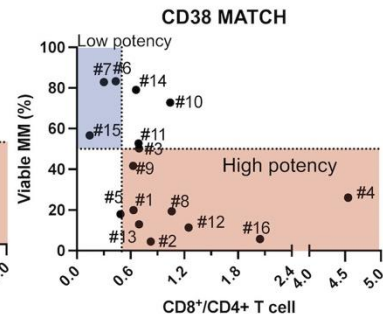
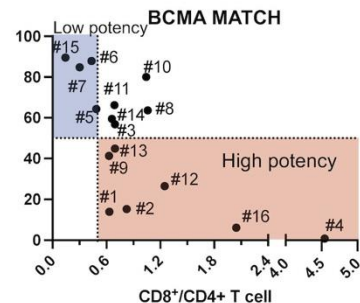
Explore the Translational Potential of MATCH Therapy (ctd)

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Immune Composition



- The response is influenced by both the CD8⁺/CD4⁺ T cell ratio and the effector-to-target (E:T) cell ratio.



Overcome T cell Exhaustion

E:T = 1:2

- co-culture
- BCMA MATCH
- BCMA MATCH + PD-1

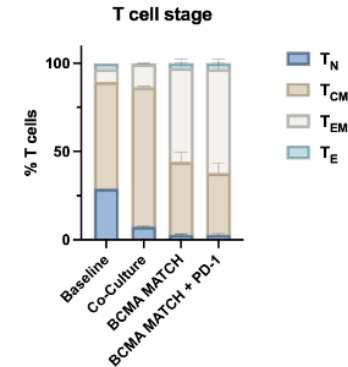
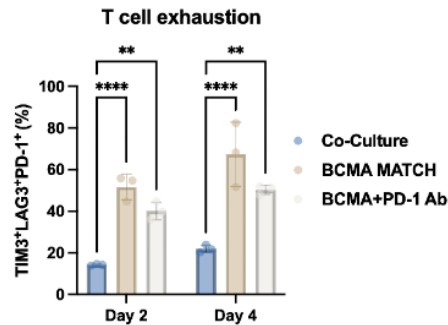
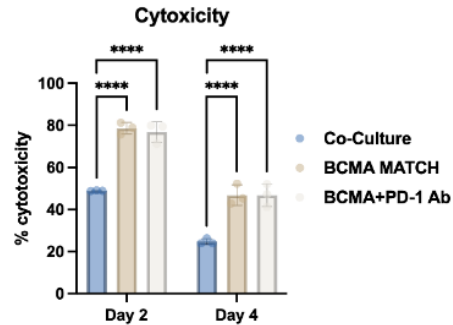
E:T = 1:2 (new MM.1R cells)

- co-culture
- BCMA MATCH
- BCMA MATCH + PD-1

Day 0

Day 2

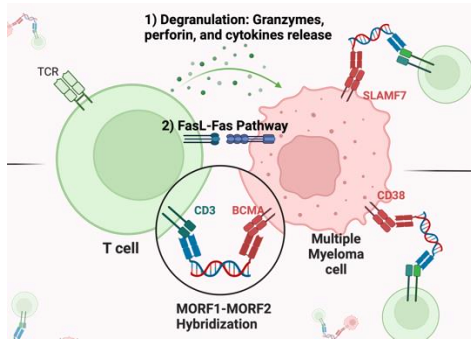
Day 4



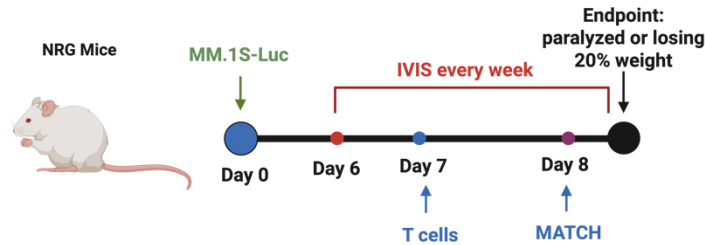
- MATCH can induce cell death in restimulation cycle;
- Combination with anti-PD-1 Ab slows down the T cell exhaustion

Final Remarks and Conclusion

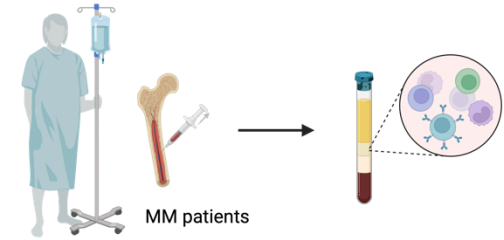
Cellular level



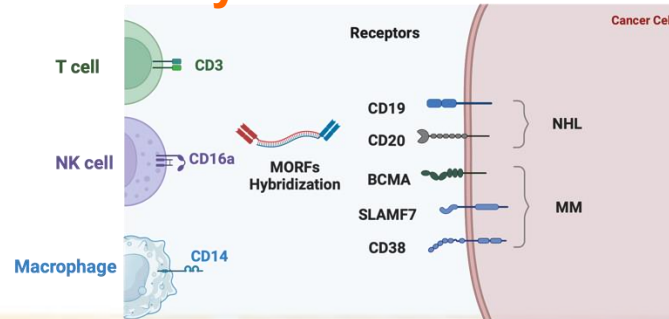
In vivo humanized mouse model



Ex vivo patient-derived sample



Beyond the Horizon...



Acknowledgments



Kopeček/Yang Lab

Dr. Jindřich Kopeček
Dr. Jane Yang
Dr. Jiahui Li
Yingduo Yang
Emma Welsh
Monika Sima
Issac Kendell
Lara Schlickmann
Pavla Kopečková

Collaborators

Dr. Douglas Sborov
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Dr. Donna Cross
Dr. Minna Roh-Johnson

