# THE MAUS LAB 411. BB

#### Volume 1 Issue 1



The lab during a farewell dinner for Irene in Boston's North End, June 2021

## WHAT'S NEW WITH THE CAR-TOLOGISTS?

The Maus Lab and the Cellular Immunotherapy Program (CIP) have had a productive year! We published 3 primary research articles, including articles in *Science Translational Medicine* on <u>CARs that can be turned ON</u> or OFF, in *Molecular Therapy* on how the <u>signaling within T cells change</u> when CARs use different co-stimulatory domains, and the *Journal of Immunotherapy for Cancer* on using artificial antigen presenting cells to manufacture more cost-effective CAR T cells. We also published 5 reviews and 2 clinical perspectives. Marcela also contributed to 18 additional articles! We're excited to share that we submitted a record 8 abstracts to the American Society of Hematology annual meeting, to be held virtually and in Atlanta, GA in December, and 4 were selected for oral presentations and 4 for posters. Congratulations to all — this is an amazing accomplishment! Read on to find out more about what we've been up to and our achievements this year.

### Current Lab Members

Marcela Maus, MD, PhD Stephanie Bailey, PhD Trisha Berger, PhD Amanda Bouffard Korneel Grauwet, PhD Kirsten Grazewski Lu Huang, PhD Max Jan, MD, PhD Michael Kann Tamina Kienka Felix Korell, MD Adam Kuo Rebecca Larson Mark Leick, MD Diego Salas, MD, PhD Andrea Schmidts, MD Emily Silva Harrison Silva Marc Wehrli, MD, PhD

#### **Immune Monitoring Lab**

Kathleen Gallagher, PhD Eva Elder Elba Gonzalez Kathleen Ho Katelin Katsis

## IN THIS ISSUE

- Dip in the CIP: Lab news from the past 6 months
- Maus Lab Notebook: Dig into our Science Translational Medicine article on switchable CARs
- Clinical trial update: Our TriPRIL CAR starts its journey on the clinical road
- Maus lab by the numbers: Grants and trainees and trials, oh my!
- Member spotlight: Meet Becca, a 6<sup>th</sup> year immunology PhD student in the lab
- CAR-eer track: Find out what Selena, a former technician in the lab, is up to now

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<u>Maus Lab</u>

Cellular Immunotherapy Program

MASSACHUSETTS GENERAL HOSPITAL CANCER CENTER Cellular Immunotherapy Program

## DIP IN THE CIP: NEWS UPDATES

#### **Honors and Awards**

- Marcela was awarded the ASGCT Outstanding New Investigator Award. Well deserved, Marcela!
- Marcela was also featured in the Immuno-Oncology 360° <u>Autumn Newsletter</u> describing the Maus lab's work to optimize CAR T cell therapy across tumor types.
- Bryan Choi, MD, PhD, a former fellow in the lab and neurosurgery resident, accepted an Assistant Professor position in the Neurosurgery Department at MGH and opened his lab. Congrats, Bryan!
- Congratulations to Max Jan, MD, PhD, for also accepting a faculty position in the MGH Cancer Center! Max is starting his lab this fall.

#### Lab Members

- This summer we welcomed three new members to the Maus lab. Felix Korell, MD is from Germany and Diego Salas, MD, PhD is from Spain. Both are doing postdoctoral fellowships in the lab. Kirsten Grazewski recently graduated from Tufts University and is a Research Technician.
- The Immune Monitoring lab also welcomed Eva Elder, Elba Gonzalez, Kathleen Ho as new members!
- The lab has been quite proliferative in the past few months! Irene, Marc, and Stefanie all welcomed new babies to their families. Congratulations on your growing families!
- This summer we also bid farewell to Irene, who was Marcela's first postdoctoral fellow. Irene was a tremendous leader in the lab and will be greatly missed. Best of luck in California, Irene!
- We also bid farewell to Sonika, a technician in the lab who was accepted to medical school. Congratulations and best of luck, Sonika!

#### Grants

- The Maus lab was awarded a Gateway for Cancer Research grant! This grant will help support one of our clinical trials for CAR T cells in brain tumors.
- Mark Leick, MD, was awarded an ASCO Young Investigator Award, and Diego Salas, MD, PhD was awarded a grant from the Spanish Society of Medical Oncology. Congratulations, Mark and Diego!

## MAUS LAB NOTEBOOK: CARs that switch ON and OFF

The latest <u>publication</u> from the Maus Lab stemmed from the work of Max Jan, MD, PhD, a postdoc in the lab who is now an Assistant Professor at MGH. Max was co-mentored by Marcela and Benjamin Ebert, PhD. His project focused on preventing CAR T cell overactivation, which leads to exhaustion (decreasing persistence and efficacy) or toxicities. To address this problem, Max and others from the Maus Lab developed CAR T cell receptors that can be turned ON or OFF by the presence of a drug, lenalidomide.

The ON switch works by separating the CAR into two parts: the extracellular antigen binding domain combined with the CD28 costimulatory domain and another CD28 costimulatory domain combined with the signaling domain CD3z. In the presence of lenalidomide, these parts will dimerize, allow for downstream signaling from CD3z, turning the T cell ON. In the absence of lenalidomide, dimerization will not occur and the CAR will not signal, even if it binds to its antigen.



The OFF switch works by combining the entire CAR with a degron tag. When lenalidomide binds the tag, it recruits a ubiquitin ligase, which degrades the CAR. This reduces CAR expression on the cell surface, thereby preventing interaction with its antigen and downstream signaling. We demonstrated that both methods work to limit toxicity-inducing cytokine production while maintaining anti-tumor function. These strategies are a novel solution to CAR T cell overactivation, which can be quickly translated to the clinic.

According to *Science Translational Medicine*'s <u>attention score</u>, this article is in the top 5% of articles getting online attention, with coverage by 11 news outlets and tweeted 374 times.

## CLINICAL TRIAL UPDATE: TriPRIL CAR T cells

TriPRIL is a novel type of CAR T cell that we developed to target multiple myeloma (MM). MM is a cancer of plasma cells (mature B cells that produce antibodies) and is very difficult to treat. Most patients will relapse despite being treated with multiple types of therapies. Recently, CAR T cells targeting B cell maturation antigen (BCMA), a marker specific to plasma cells, were approved by the FDA after showing promising results in clinical trials. However, patients can still relapse following treatment with these CAR T cells. We aimed to improve CAR T cells for MM by targeting two antigens on MM cells. In a project led by Andrea Schmidts, MD, a postdoc in the lab, we <u>showed</u> that MM cancer cells could be effectively targeted with a CAR composed of a natural ligand to two receptors on MM cells, BCMA and transmembrane activator and CAML interactor (TACI). When this ligand, APRIL, was used in its natural trimeric formation as the antigen binding domain of the CAR, the CAR T cells effectively targeted MM cells in vitro and in our mouse models.

These encouraging results led us to initiate a clinical trial of TriPRIL CAR T cells in patients with relapsed or refractory multiple myeloma. We submitted an investigational new drug application to the FDA and it was approved — the trial officially opened in September! This is the second trial the Cellular Immunotherapy Program has opened with a CAR developed entirely in the Maus Lab. Congratulations to the entire Maus Lab and CIP team for this amazing accomplishment! We can't wait to see how this new CAR performs!



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	In the past year	Total Cumulative	
Publications			
Primary Research Articles	3	10	
Review Articles	5	23	
Clinical Perspectives	2	3	
	In the past year	<b>Total Active</b>	<b>Total Cumulative</b>
Grants received			
NIH R01	1	3	3
Other NIH or Government	-	4	5
Foundation	1	1	5
MGH	-	-	3
Trainee Fellowships	3	7	19
Sponsored Research Agreements	2	3	3
Trainees			
Postdocs	2	7	11
PhD graduate students	1	2	4
Master's grad students	1	1	2
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## MAUS LAB BY THE NUMBERS

#### Investigator Initiated Clinical Trials

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Product	Disease	Status	<b>Registration Number</b>	
CAR37	B & T cell lymphoma	Recruiting	NCT04136275	
TriPRIL	R/R Multiple Myeloma	Recruiting	<u>NCT05020444</u>	
Axi-cel + prophylactic anakinra	R/R Large cell Lymphoma	Recruiting	NCT04150913	
Tisa-cel	Primary CNS Lymphoma	Recruiting	<u>NCT04134117</u>	
CAR-TEAM-E	Glioblastoma	IND Submitted		
CD79b19	R/R Large cell Lymphoma	IND in progress	Patients Treated: 3	
			1	

## MEMBER SPOTLIGHT: REBECCA LARSON



Becca is a sixth year Immunology PhD Student at Harvard. She decided to pursue a PhD to deepen her knowledge of cancer immunology. She is researching CAR T cell resistance in glioblastoma and dual-targeting therapies for multiple myeloma and hopes to bring our findings from the lab bench to the clinical bedside. Becca has a passion for putting together teams and working on projects as a unit. She said, "My favorite part of the Maus lab is the people. I am firm believer that the best innovations come from a collaborative culture where enthusiastic scientific conversation is interwoven in everyday small talk. The Maus Lab is a unique group of motivated scientists who are eager to share results, ask questions, and help both technically and intellectually." In the future, Becca wants to become a project leader at a company. It is important to her that she sees the positive impact of her work on people. Outside of her science life, she likes to teach HIIT dance group fitness workouts, bake, go for long walks on the esplanade, and travel to Europe as much as possible.

# CAR-EER TRACK: Selena Lorrey

Selena joined the Maus Lab in 2016 as a research technician. She primarily worked on BCMA-targeting CAR T cells for multiple myeloma, while supporting the overall function of the lab. In 2018, Selena went on to pursue her PhD at Duke University. Now, she is a 4<sup>th</sup> year graduate student in the Fecci Lab as part of the Duke Brain Tumor Immunotherapy Program. She said, "Working in the Maus Lab allowed me to grow as a person and scientist. I acquired valuable lab skills, while learning what to expect from graduate school and how to interact within the working world. My experiences with Marcela and Maus lab has opened doors for me within the scientific community and I feel incredibly fortunate to have started my career in the Maus Lab. The people in the lab really made it fantastic. I now consider them both dear friends and colleagues." Selena's overall goal is to find a career that intersects research and medicine, where she can make a difference in the lives of cancer patients.



# CAR-ING TOGETHER: SUPPORTING THE MAUS LAB

Thanks to the generosity of our donors, we've been able to develop multiple novel cell therapies, of which the first few have now entered clinic, and we hope many more will follow. Our mission is to develop cutting-edge cell therapies to effectively treat patients with cancer. Your donations have enabled us to remain steadfast in that mission. We are enthusiastically working to develop the next generation of CAR T cells and combination immunotherapies to improve patient outcomes.

With your help, we can make a difference in the lives of cancer patients who are in need of more treatment options. Contributions to the Cellular Immunotherapy Program help us develop new ideas, translate our findings to patients, and train the next generation of scientists and physicians to carry out our mission. Click here to donate.



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