THE MAUS LAB 411. BB

August 2022

Current Lab Members Marcela Maus, MD, PhD

Antonio Almazan Stefanie Bailey, PhD

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Maus lab farewell dinner for Marc and Adam in Boston's South End

The Maus Lab and the Cellular Immunotherapy Program (CIP) have had a busy summer. Here's the 411(BB) on what we've been up to since our last issue: We now have our own website! Check out www.mauslab.com to learn more about who we are and what our research entails. Marcela was featured in an article in Healio-check it out to learn more about our fearless leader! Our paper describing CD70-targeting CARs for AML was published in Cancer Cell. You can read more about this project in this Issue. The CIP and IML contributed to a clinical trial of CD19-targeting CAR T cells for primary CNS lymphoma, which was published in <u>Blood</u>. We published a review on CAR T cell-tumor interactions in the journal Med—congratulations to Felix on his first publication from the lab! We contributed a chapter on CAR T cell biology to the textbook Gene and Cellular Immunotherapy for Cancer, released earlier this summer. Marcela has also contributed to 12 other publications through collaborations in the past year. Our We've also had quite a bit of change in terms of lab members this summer, with ten people joining us and six taking the next steps in their careers. Read on to learn more about our people and projects!

Trisha Berger, PhD Filippo Birocchi, PhD Amanda Bouffard Diane Brunett Magdi Elsallab, MD, PhD Elijah Darnell, MD Alessandro Gasparetto Korneel Grauwet, PhD Lu Huang, PhD Michael Kann Tamina Kienka Felix Korell, MD Marcos Labrado Rebecca Larson, PhD Mark Leick, MD Merle Phillips Diego Salas, MD, PhD Emily Silva Valentina Supper Hana Takei Marc Wehrli, MD, PhD

Immune Monitoring Lab (IML) Kathleen Gallagher, PhD Elba Gonzalez Charlotte Graham, MD Won-Ho Lee Hadley Wiggin

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Maus Lab

Cellular Immunotherapy Program

DIP IN THE CIP: NEWS UPDATES

Honors and Awards

- In addition to her profile in <u>Healio</u>, Marcela was also quoted in a <u>USA today article</u> and featured in an ad for MGH in The New York Times.
- The lab attended two more conferences this spring: the American Society for Gene and Cell Therapy (ASGCT) in Washington, DC and the American Association of Immunology (AAI) in Portland, OR
 - 3/3 of our abstracts for ASGCT received oral presentations. Congrats Mark, Stef, and Korneel!
 - Becca and Katie presented posters at AAI. Well done!
- Stefanie Bailey received a travel award to the ASGCT conference and was invited to the SITC Sparkathon, a 3-day training program for emerging leaders in cancer immunotherapy. Congrats, Stef!
- Adam Kuo successfully defended his Master's thesis. Congrats, Adam!

Lab Members

- This summer we've welcomed eight new people to the lab:
 - Filippo Birocchi, PhD, is a postdoctoral fellow who his received his PhD at the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy.
 - Eli Darnell, MD, is a hematology/oncology fellow who recently finished his residency at MGH
 - Madi Elsallab, MD, PhD is a fellow in the Regulatory Sciences program at Harvard.
 - Marcos Labrodo and Allessandro Gasparetto are students who joined us for the summer
 - HanaTakei, Antonio Almazan, and Valentina Supper are new technicians in the lab
- We also bid farewell to three lab members this summer, who will be greatly missed:
 - Harry, a technician in the lab, is entering a PhD program at UNC-Chapel Hill
 - Grace, a recent high school graduate who assisted in the lab, is attending Cornell College
 - Adam, a Masters grad student, is moving to California to work at Stanford with Crystal Mackall

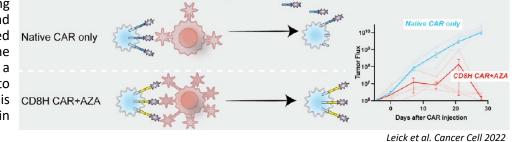
Grants

- Mark Leick was awarded a Clinical Investigator Award from the Damon Runyon Foundation and a K12 Clinical Scientist Career Development Award through MGH. Congratulations, Mark!
- Filippo Birocchi was awarded a fellowship from the American Italian Cancer Foundation. Congrats!

MAUS LAB NOTEBOOK

One of the things that makes CAR T cell an ideal treatment for cancer is that they can actively seek out and destroy cancer cells. They do this by targeting antigens expressed on tumor cells that are not expressed on normal cells or expressed on cells that are dispensable (like B cells). While this has worked well for B cell cancers, there are not currently CAR T cells approved for use against myeloid cancers due to the lack of an antigen that is safe to target. In a <u>study</u> led by Mark Leick, MD and published in *Cancer Cell*, we developed and optimized CAR T cells for acute myeloid leukemia (AML) by targeting CD70, an antigen highly expressed on AML and normally expressed only on activated immune cells. The CAR uses the natural ligand of CD70, CD27, as the region that binds CD70 on the tumor cells. While this CAR T cell worked marginally well, Mark et al. discovered the efficacy could be improved by increasing the binding of CD70-tareting CARs to the tumor cell using two methods. Treating the cancer cells with azacitidine (AZA) increased CD70 levels, which made more target antigen available for the CAR T cells to bind to. During this interaction, CD27 can be cleaved, to form soluble CD27, which weakens the interaction. To prevent cleavage, we tested a variety of modified hinge regions for the CAR and found that a CD8 hinge region (CD8H) prevented cleavage of CD27 and strengthened CAR T cell binding to CD70 on cancer cells. The combination of both methods (CD8H + AZA) was highly

effective at controlling cancer growth in vitro and in mouse models (noted by tumor flux in the graph). This could be a promising strategy to translate to the clinic! This study was also featured in an MGH press release.



IML UPDATE

What's the IML?

The Immune Monitoring Lab, directed by Dr. Kathleen Gallagher, provides comprehensive immune monitoring to aid in the research of immune-based therapies. Their work specializes in immune profiles of disease and analysis of immune testing and response.

Lab Members

- This summer, the IML welcomes two new members to the lab:
 - Hadley Wiggin and Won-Ho Lee are joining the IML as research techs
- The IML bid farewell to two members in the beginning of summer who are advancing in their careers. We couldn't be more proud!
 - Katie Katsis, a medical technologist in the IML, started a new position in the biotech industry.
 - Eva Elder, a research technician in the IML, was accepted to the University of Minnesota Medical School.
- Elba González has accepted a new position in the IML as Program Coordinator. Congrats, El!

Current assays in Development

- ddPCR for monitoring CAR-T expansion
- T cell intracellular cytokine staining assays
- T cell CD107 degranulation assay

MAUS LAB BY THE NUMBERS

	In the past year	Total Cumulative	
Publications	9	45	
Primary Research Articles	5	15	
Review Articles	2	25	
Perspectives/Commentaries	2	5	
	In the past year	Total Active	Total Cumulative
Grants received	7	20	44
NIH R01	-	3	3
Other NIH or Government	1	5	6
Foundation	-	1	5
MGH	-	-	3
Trainee Fellowships	5	8	24
Sponsored Research Agreements	1	3	3
Trainees	7	15	31
Postdocs	3	9	14
PhD graduate students	1	2	5
Master's grad students	_	_	2
Research Technicians	3	4	10

Investigator-Initiated Clinical Trials

Product	Disease	Status	Registration Number	
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: 30)
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MEMBER SPOTLIGHT: STEFANIE BAILEY, PHD



Stefanie is a tried-and-true Texan, born in the panhandle and raised in a small town in west Texas called Andrews. She stayed in the desert of west Texas to obtain her Bachelor of Science in Biology from Lubbock Christian University before moving to the beaches of Charleston, SC to pursue her PhD in Immunology from the Medical University of South Carolina. Stefanie's research focus thus far has been on improving CAR-T therapies in both solid and hematologic malignancies. While her PhD work was centered more on the selection of effective T cell subsets, her postdoctoral focus has been on genetically editing bulk T cells to maintain efficacy but mitigate toxicity in CAR-T patients. Being from Texas, Stef loves all things southern--the heat, Mexican food, college football and all things fried. In her free time, she enjoys reading, running, traveling, and spending time with family. Being near the water--lake, ocean or even thunderstorms--is her happy place.

Stef's goal is to become an independent investigator at a research institution where she will run a lab focusing on CAR T cell research in solid tumors. When asked what her favorite thing about the Maus lab is, she said "I love that even though we all come from different backgrounds, personally and professionally, everyone is respectful and genuinely strives to help others. The unique characteristics and skills of each individual in the lab fosters our growth as scientists and significantly advances our shared goal of curing cancer."

CAR-EER TRACK: IRENE SCARFO, PHD

Irene is from Pinerolo, Torino, Italy and completed her PhD in Biomedical Sciences and Oncology at the University of Torino before starting as a in the Maus lab in 2016 as Marcela's first postdoctoral fellow. During her five years in the lab, Irene contributed to X manuscripts and led the preclinical work for CAR37, which is now in clinical trial. She is currently a Senior Scientist at ArsenalBio, leading the development of inducible, logic-gated CAR T cells for solid tumors. Her overall career goal is to to develop and bring to the clinic cellular therapies for cancer patients while also helping and supporting the career of other scientists. Irene said, "Marcela's lab is a cutting-edge science center of excellence where I refined my scientific background and improved my team collaboration skills to openly discuss



projects effectively. With the multiple opportunities of taking part to the submission of INDs, I've been able to gain a 'vision' mindset for the research goal that ultimately prepared me for my current role. The variety of projects, the numerous collaborations with academic labs and biotech companies have helped me in managing a diverse team. Marcela is an incredible female leader who taught me science and the managerial aspect of a lab by example."

CAR-ING TOGETHER: SUPPORTING THE MAUS LAB

Thanks to the generosity of our donors, we've developed multiple novel cell therapies, which 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. 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



Maus Lab

out our mission. Click here to donate.

