Name: Hadas Weinstein-Marom **Date: April 5, 2026**

CURRICULUM VITAE

1. Personal Details

Permanent Home Address: Kibbutz Dafna, Upper Galilee, 1223500, Israel

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2. Higher Education

A. Undergraduate and Graduate Studies

Period of Study	Name of Institution and Department	Degree	Year of Approval of Degree
2010-2015	Hebrew University of Jerusalem, Sharett Institute of Oncology. Faculty: Medical Sciences Department: Cell Biology, Immunology & Cancer Research	Ph.D.	2016
2005-2008	Hebrew University of Jerusalem; Inter-Faculty Graduate Biotechnology Program	M.Sc.	2010
2001-2004	Hebrew University of Jerusalem, Faculty of Agriculture, Food and Environment, Biochemistry and Food Science	B.Sc.	2004

B. Post-Doctoral Studies

Period of Study	Name of Institution, Department and Host	Degree	Year of Completion
2017-2018	Tel Aviv University; Ella Institute for Immuno-Oncology, Chaim Sheba Medical Center; Advisor: Dr. Michal J. Besser	-	2018

3. Academic Ranks and Tenure in Institutes of Higher Education

Dates	Name of Institution and Department	Rank/Position
2026-present	Tel-Hai University, Faculty of Sciences & Technology MIGAL - Galilee Research Institute	Senior Lecturer, Head of Laboratory of Cellular Immunotherapy & Synthetic Biology
2021-2026	Tel-Hai College. Faculty of Sciences & Technology, department of Biotechnology	*Lecturer, PI, Immunology Lab
2015-2021	Tel-Hai College, Biotechnology Dept.	Junior Faculty member
2004-2015	Tel-Hai College, Biotechnology Dept.	Teaching Assistant

4. Offices in Academic Administration

Dates	Name of Institution and Department	Rank/Position

2021-present	Tel-Hai University. Faculty of Sciences & Technology, department of Biotechnology	*Head of the pre-medicine track

5. Scholarly Positions and Activities outside the Institution

- 4. 2025 - Group leader of the new Laboratory for Cellular Immunotherapy & Synthetic Biology at MIGAL - Galilee Research Institute.
- Scientific Co-founder of GentiBio and former member of its scientific advisory board.

6. Participation in Scholarly Conferences

a. Active Participation

Date	Name of Conference	Place of Conference	Subject of Lecture/Discussion	Role
*April 2026	Annual Meeting: Israel Society for Clinical Laboratory Sciences (ISCLS)	Tel Aviv	Lecture: Synthetic Immunology Tools for T Cell–Based Therapies	Invited speaker
*Feb. 2026	11th FISEB Congress (ILANIT)	Eilat, Israel	Lecture: New synthetic immunology tools for diverse clinical applications	Invited speaker
*March 2025	Annual Meeting of the Israel Immunological Society (IIS)	Tel-Aviv University	Poster presentation: Generation of type 1-like regulatory T cells via transduction of human CD4+ T cells with membrane-attached IL-10	Selected: Poster presentation

Date	Name of Conference	Place of Conference	Subject of Lecture/Discussion	Role
*Feb. 2023	10th FISEB Congress (ILANIT)	Eilat, Israel	Flash talk and Poster presentation: New genetic adjuvants for enhancing the antitumor capacities of human T cells in adoptive cell therapy	Selected: Flash talk and Poster presentation
Sept. 2019	The Joint Scientific Meeting of the (IIS) and the Israel Society for Cancer Research (ISCR)	Tel Aviv, Israel	Oral presentation: The pioneer round of translation and MHC-I peptides presented to cytotoxic T lymphocytes.	Selected: Oral presentation
Feb. 2017	8th FISEB Congress (ILANIT)	Eilat, Israel	Oral presentation: Enhancing the effector functions of T cells with a combination of new mRNA adjuvants for improving adoptive cell therapy.	Selected: Oral presentation
Feb. 2016	5th Translational Research Day	Safed, Israel	Poster Presentation: Membrane-attached cytokines expressed by mRNA electroporation: potent T cell adjuvants for adoptive cell therapy	Selected: Poster presentation
May 2016	14th Annual Meeting of the Association for Cancer Immunotherapy (CIMT)	Mainz, Germany	Poster Presentation: Enhancing the effector functions of T cells with a combination of new mRNA adjuvants for improving adoptive cell therapy	Selected: Poster presentation

Date	Name of Conference	Place of Conference	Subject of Lecture/Discussion	Role
May, 2014	12th Annual Meeting of the CIMT	Mainz, Germany	Poster Presentation: Membrane-attached cytokines expressed by mRNA electroporation: new T cell genetic adjuvants for adoptive cell therapy	Selected: Poster presentation
Feb. 2013	40th Annual Meeting of the IIS	Beer-Sheba, Israel	Oral and Poster presentation: Membrane-attached cytokines expressed by mRNA electroporation: new T cell genetic adjuvants for adoptive cell therapy	Selected: Oral and Poster presentation

8. Research Grants

a. Grants Awarded

Role in Research	Co-Researchers	Topic	Funded by/ Amount	Year
PI*	Prof. Gideon Gross	GentiBio grant for innovative research in adoptive cell therapy	$370,000	1.9.2020-31.5.2021
PI*	Prof. Gideon Gross	See above	$360,000	1.7.2022-31.6.2023
PI*		Using antigen-specific type 1 regulatory (Tr1) cells for preventing on-target off-tumor	Vatat Kol Kore (MOST). 2y, 350,000 NIS total.	2026-2027

		toxicity in adoptive T cell therapy of cancer		
PI*	Rostislav Novak MD/Ph.D. Rambam Health Care Campus	Overcoming ECM-Mediated Immune Exclusion in Sarcoma Using GD2 CAR-T Cells and LOX Inhibition	RTICC Collaborative Grants for Multidisciplinary Cancer Research – Technion $30,000/y 2y.	2026-2027
PI*	Ofrat Beyar Katz MD/Ph.D. Head of Cellular Immunotherapy Rambam Health Care Campus	A new CAR-T cell therapy for Non-Hodgkin Lymphoma	Israel Cancer Association (ICA) NIS90,000/y, 2y	2026-2028

b. <u>Submission of Research Proposals – Pending</u>

Role in Research	**Co-Researchers**	**Topic**	**Funded by**	**Year**
PI*	Ofrat Beyar Katz MD/Ph.D. Rambam Health Care Campus Chen Buxbaum MD Rambam Health Care Campus Yuval Shaked Ph.D. Technion	Developing a novel, multi-component CAR-T cell therapy for glioblastoma (GBM) to overcome current therapeutic barriers	ISF - Israel Science Foundation MAVRI - Biomedical Research Grants	2026-2029

c. Submission of Research Proposals – Not Funded

Role in Research	Co-Researchers	Topic	Funded by	Year
PI*		A novel gene-based approach for adoptive T cell therapy of melanoma	Melanoma Research Alliance (MRA) – Young investigator award	2024
PI*	Richard Harbottle, Germany	A universal platform for enhancing efficacy and safety of genetically engineered antitumor T cells	DKFZ-MOST - Binational Israel-Germany program	2024
PI*		Genetically engineered human type I regulatory T cells for immunotherapy	Israel Science Foundation (ISF) – personal research grants	2024
PI*		A new approach for redirecting T cells against tumor antigens	Israel Cancer Research Fund (ICRF)	2024
PI*		Inducible genetic reprogramming of tumor-infiltrating lymphocytes for the treatment of melanoma	Israel Cancer Association (ICA)	2024
PI*		A new logic gate in adoptive T cell therapy, of cancer	ISF	2023
PI*	Richard Harbottle, Germany	Single-step engineering of anti-tumor T cells using a non-viral, non-integrating, high-capacity DNA vector	DKFZ-MOST	2022

9. Scholarships, Awards and Prizes

- Selected participant for the European project "R&I PEERS" - for Improving Gender Equality in Research and Innovation, Horizon 2020.
- Selected participant (with full scholarship) in the 2019 Winter School of the CIMT Academy of Translational Cancer Immunology.
- Selected as 'best lecturer of the year', Biotechnology Dept. Tel-Hai College, October 2018.
- Selected participant (with full scholarship) in the 9th German-Israeli – Cancer Research School on Cancer Stem Cells and Tumor Heterogeneity. Grainau, Germany, March 2018.
- Selected as 'best lecturer of the year', Biotechnology Dept. Tel-Hai College, October 2023

10. Teaching

a. Courses Taught in Recent Years

Year	Name of Course	Type of Course: Lecture/ Seminar/ Workshop/ High Learn Course/ Introduction Course (Mandatory)	Degree	Number of Students
2015-2021	Molecular Biology (advanced)	High Learn Course	B.Sc.	40-60
2015-present	Genetics of malignant diseases	High Learn Course	B.Sc.	40-60
2004-present	Antibodies in Biotechnology	Lab course	B.Sc.	40-60
2004-present	Antibodies in Biotechnology	High Learn Course	B.Sc.	40-60
2004-present	Animal Cell Culture	Lab course	B.Sc.	40-60
2004-present	Animal Cell Culture	High Learn Course	B.Sc.	40-60
2004-present	Laboratory in Cell Biology	Lab course/ lecture	B.Sc.	250-300

2004-2015	Laboratory in Vertebrates & Invertebrates	Lab course	B.Sc.	80

b. Supervision of Graduate Students

Ph.D. students

Name of Student	Title of Thesis	Degree	Date of Completion / in Progress	Co-supervisor
*Avi Pinchanski	Development of new CARs for treating B cell malignancies	Ph.D.	In Progress Started 01/01/2025	Technion. Co-supervisor: Dr. O. Beyar Katz
*Dayana Blokon	A novel gene-based approach for adoptive T cell therapy of melanoma	Ph.D.	In progress Started 01/10/2024	Hebrew University. Co-supervisor: Prof. M. Lotem

M.Sc. Students

Name of Student	Title of Thesis	Degree	Date of Completion / in Progress	Co-supervisor
Lee Dayan	Rational design of multi-system TCR-like CAR constructs	M.Sc.	In progress	-
Ghydaa Abu Asalih	Overcoming ECM-mediated immune exclusion in sarcoma	M.Sc.	In progress	-
Noam Suliman	A new approach for preventing on-target off-tumor toxicity in adoptive T cell therapy of cancer	M.Sc.	In progress	
*Eliya Avraham	New CARs for the treatment of melanoma	M.Sc.	In progress	-

Name of Student	Title of Thesis	Degree	Date of Completion / in Progress	Co-supervisor
*Roy Agam	Development of new CAR and logic gate platforms	M.Sc.	2025	-
*Tal Harris	Inducible genetic reprogramming of antitumor T cells	M.Sc.	2025	-
Pinchanski Avi	Development of new enhancing chimeric antigen receptors for adoptive cell therapy	M.Sc.	2023	-
Maya Levi	Selective cancer immunotherapy	M.Sc.	2022	-
Oren Shoraki	Immunotherapy of celiac disease	M.Sc.	2021	Gideon Gross
Sivan Gino	New immunotherapy for inflammatory diseases	M.Sc.	2021	Gideon Gross
Jenny Borzenko	New inhibitory chimeric antigen receptors	M.Sc.	2021	Gideon Gross
Dayana Blokon	New designs for chimeric antigen receptors	M.Sc.	2020	-
Sara Posner	New targets for anti-inflammatory Tregs	M.Sc.	2020	Gideon Gross
Lior Malka	New arrangements of Genetic adjuvants for adoptive T cell therapy	M.Sc.	2020	Gideon Gross
Ofir Levin	New chimeric antigen receptors	M.Sc.	2020	Gideon Gross
Nofar Shmuel	Inducible expression of adjuvant genes for cancer immunotherapy	M.Sc.	2019	Gideon Gross

11. Miscellaneous

Leading the 2019 Tel-Hai-MIGAL iGEM team

Taken from the iGEM website: "The iGEM Foundation is an independent, non-profit organisation dedicated to the advancement of synthetic biology, education and competition, and the development of an open, collaborative, and cooperative community."

On the yearly iGEM competition: "Multidisciplinary student teams from all over the world compete for medals and awards by designing, building, and testing projects using cutting-edge synthetic biology."

The iGEM team I led for the 2019 competition included 12 undergraduate students from different programs at Tel-Hai and 4 M.Sc. students from our MIGAL Lab. In our scientific project, we developed a new logic AND gate for cancer immunotherapy. The entire project involved a lot of work in many areas with the local community. We won a silver medal.

Patents:

Title	Stage	PCT/WO No.	NP Filing date	Granted Patents
CAR-TILs and CAR-TCR-T cells in adoptive T cell therapy	Prov			
Genetically reprogrammed Tregs expressing membrane-bound Il-10	National phase	WO2019180724	2020-09-22	JP, AU
Blocking chimeric antigen receptors for prevention of undesired activation of effector and regulatory immune cells	National phase	WO2021044213	2022-03-03	
Genetically reprogrammed Tregs expressing CARs	National phase	WO2020194306	2021-09-26	
Systems and uses thereof for creating synthetic transcriptional logic 'and' gates based on pre-mRNA trans-splicing	National phase	WO2020261277	2022-01-25	

Chimeric antigen receptor comprising CD40 cytoplasmic domain and uses thereof	National phase	WO2021048850	2021-03-11	
Chimeric membrane-bound cytokines incorporating costimulatory elements for enhancing anti-inflammatory function	PCT	PCT/IL2023/050812		
Site-specific activation of regulatory T cells	PCT	PCT/US2023/032868		

12. **Professional Experience**

Non-Academic Activity & Positions

- 2012-2015: Teaching in the Sidney Warren Science Education Center for Youth at Tel-Hai College.
- Instructing undergraduate students of the Biotechnology Dept. at Tel-Hai College n their research projects at the Immunology Lab of MIGAL: Since completing my PhD in 2016, I have mentored undergraduate students in their research projects, guiding two students each year. Notably, almost all graduates of these research projects have continued to pursue a master's degree at Tel-Hai or other academic institutions, with some advancing to a PhD degree (two under my supervision) or at other institutions. This experience has allowed me to support students in developing their research skills, critical thinking, and academic growth
- Engaged in the National Science Day organized by the Ministry of Science and the European Researchers' Night.
- Conducted scientific activities and experiments to promote science accessibility for young children, elementary school and high school students.
- Delivered scientific lectures to senior citizens in various forums within and beyond the Upper Galilee region.
- During COVID-19, scientific lectures were delivered online, and science activities were filmed for both the general public and children as part of European Researchers' Night initiatives.

PUBLICATIONS

A. Ph.D. Dissertation

Membrane-Attached Cytokines Expressed by mRNA Electroporation: New T Cell Genetic Adjuvants for Adoptive Cell Therapy (2016)

75 pages

English

Hebrew University of Jerusalem, Sharett Institute of Oncology. Faculty: Medical Sciences Department: Cell Biology, Immunology & Cancer Research under the supervision of: Prof. Tamar Peretz and Prof. Gideon Gross

The thesis was published as detailed below (Refs. No. 9, 10, 11).

D. Articles in Refereed Journals

131 Citations by 114 documents
15 Documents
7 *h*-index

Published (and accepted for publication)

1. Roas, K., Kovalski, I., Mouhadeb, O., Aminov, T., **Weinstein-Marom, H,** Nissim, L. (2026). Modular and Scalable Synthetic Gene Circuits for Complex Functions Within Minimal Computational Layers in Human Cells. Accepted for publication in *Nature Communications*.
2. Blokon-Kogan, D., Davidson, S., Levi-Mann, M., Gross, G. and **Weinstein-Marom, H.** (2026). Retroviral transduction of human CD4+ T cells with membrane-attached IL-10 generates type 1-like regulatory T cells. *Human Gene Ther*. April 2, Online ahead of print.
3. *Cohen, I., Khoury, M., Yuxiang, H., Blokon-Kogan, D., Gengrinovitch, S., Eitam, H., Avraham-Kelbert, M., **Weinstein-Marom, H.**, Xu, P. and Bar-Sela, G. Cannabidiol polarizes neutrophils towards immunosuppressive cancer, supporting phenotype. *Front. Immunol.,* Sec. Molecular Innate Immunity (July 2025) Vol. 16. IF=5.8, 0 citations.
4. *Feigelson, S. W., Dadosh, T., Sapoznikov, A., **Weinstein-Marom, H.,** Blokon-Kogan, D., Avraham, Y., Unger, T., Gross, G., Dahan, R. and Alon. R. (2025). CD32B1, a multi-functional non-signaling scaffold for antibody decoration on T cell microvilli. *Front. Immunol.*, Vol. 15. IF=5.8, 0 citations.
5. *Kakabadse, D, Chen, D., Fishman, S., **Weinstein-Marom, H.**, Davies, J., Wen, L., Gross, G[#]. and Wong, S.F[#] (2024). Regulatory CD4+ T cells redirected against pathogenic CD8+ T cells protect NOD mice from development of autoimmune diabetes. *Front. Immunol.*, Vol. 15. ([#]Equal contribution.)

IF=5.8. Q1, 5 citations.

6. *Chen, D., Kakabadse, D., Fishman, S., **Weinstein-Marom, H.,** Davies, J., Boldison, J., Thayer, T.C., Wen, L., Gross, G. and Wong, S.F. (2023). Novel engineered B lymphocytes targeting islet-specific T cells inhibit the development of Type 1 Diabetes in Non-Obese Diabetic Scid mice. *Front. Immunol.* Sep. 4.

   IF=8.8, Q1, 6 citations.

7. *Blokon-Kogan, D., Levi- Mann, D., Malka-Levy, L., Itzhaki, O., Besser, M.J., Shiftan, Y., Szöőr, Á., Vereb, G., Gross, G., Abken, H. and **Weinstein-Marom, H.** (2022). Membrane anchored IL-18 linked to constitutively active TLR4 and CD40 improves human T cell anti-tumor capacities for adoptive cell therapy. *J. Immunother. Cancer,* July 23.

   IF=12.5. Oncology 25/45, Q1; Immunology 18/161, Q1, 7 citations.

8. *Savanur, A.M., **Weinstein-Marom**, H. and Gross, G. (2021). Implementing logic gates for safer immunotherapy of cancer. *Front. Immunol*. Nov 4; 12:780399.

   IF=7.5, Q1, 44 citations.

9. Levin-Piaeda, O, Levin, N., Danieli, A., **Weinstein-Marom, H#.** and Gross, G#. (2021). The Intracellular Domain of CD40 is a Potent Costimulatory Element in Chimeric Antigen Receptors. *J. Immunother.,* 44, 209-213. (#Equal contribution.)

   IF=4.1. 75/244, Q2, 9 citations.

10. **Weinstein-Marom, H.**, Gross, G., Levi, M., Brayer, H., Schachter, J., Itzhaki, O., and Besser, M.J. (2021). Genetic modification of tumor-infiltrating lymphocytes via retroviral transduction. *Front. Immunol.*, Vol. 11.

    IF=5.1 39/159 Q1, 8 citations.

11. **Weinstein-Marom, H**., Hendel, L., Avigad-Laron, E., Margalit, A. and Gross, G. (2019). MHC-I presentation of peptides derived from protein products of the pioneer round of translation. *FASEB. J.* 33, 11458-11468.

    IF=5.0. 58/297, Q1, 4 citations.

12. **Weinstein-Marom, H.**, Levin, N., Pato, A., Peretz, T., Eisenberg, G., Lotem, M., Itzhaki, O., Besser, M.J. and Gross, G. (2019). Combined expression of genetic adjuvants exerts multiple immunostimulatory effects on antitumor T cells. *J. Immunother.* 42, 43-50.

    IF=4.1. 75/244, Q2, 7 citations.

13. Levin, N., **Weinstein-Marom, H.**, Pato, A., Itzhaki, O., Besser, M.J., Peretz, T., Eisenberg, G., Lotem, M. and Gross, G. (2018). Potent activation of human T cells by mRNA encoding constitutively active CD40. *J. Immunology* 201, 2959–2968.

IF=4.9. 45/159, Q2, 12 citations.

14. **Weinstein-Marom, H.**, Pato, A., Levin, N., Susid, K., Itzhaki, O., Besser, M.J., Peretz, T., Margalit, A., Lotem, M. and Gross, G. (2016). Membrane-attached cytokines expressed by mRNA electroporation act as potent T cell adjuvants. *J. Immuother.* 39: 60-70.

    IF=4.1. 85/244, Q2, 21 citations.

15. Lazarus, D.[#], **Weinstein-Marom, H.[#]**, Fishman, S., Yossef, Y., Zuri, D,. Barnea, E., Admon, A., Margalit, A. and G. Gross, G. (2015). Efficient peptide recovery from secreted recombinant MHC-I molecules expressed via mRNA transfection. *Immunol. Lett.* 165: 32-38. ([#]Equal contribution.)

    IF=2.5. 90/151, Q3, 6 citations.

E. Articles or Chapters in Scientific Books (which are not Conference Proceedings)

Published

1. *__Hadas Weinstein-Marom__, Dayana Blokon-Kogan, Maya Levi- Mann, Chaja Katzman, Shira Shalev, Masha Zaitsev, Michal J. Besser, Ronnie Shapira-Frommer, Gideon Gross, Orit Itzhaki, Lior Nissim. (2023) Genetic modification of tumor infiltrating lymphocytes, peripheral T cells and T cell model cell lines. Book chapter: *Methods in Molecular Biology* (Springer Nature). MIMB, volume 2748. https://www.springer.com/series/7651. 1 citation.

I. Summary of my Activities and Future Plans

1. Membrane-Attached Cytokines for T Cell Therapy

During my Ph.D., I developed a strategy to enhance the survival and function of adoptive T cells by expressing key cytokines (IL-2, IL-12, and IL-15) as integral T-cell membrane proteins. Systemic administration of these cytokines is often associated with severe toxicity, limiting their clinical use. By attaching them to the cell membrane via mRNA electroporation, I confined cytokine availability to therapeutic T cells, preventing unwanted systemic effects.

The engineered cytokines supported the ex vivo growth of human CD8+ and CD4+ T cells for six days post-transfection, demonstrating comparable effects to high-dose soluble IL-2. Membrane-bound cytokines also enhanced activation markers such as CD25, CD69, 4-1BB, and OX40 when combined with TLR4 signaling. These findings support the potential application of membrane cytokines in improving adoptive T cell therapy.

2. Synergy Between Membrane Cytokines and Genetic Adjuvants in T Cell Therapy

Building on my Ph.D. research, I investigated the cooperative effects of membrane cytokines and other genetic adjuvants, such as constitutively active TLR4 and CD40. These genetic modifications were designed to autonomously enhance T cell function upon mRNA electroporation.

In both peripheral blood CD8+ T cells and tumor-infiltrating lymphocytes (TILs), these engineered adjuvants significantly upregulated key activation markers (CD25, OX40, 4-1BB, CD127, CD28), improved cytotoxic activity, and increased IFN-γ and TNF-α secretion. Notably, predefined mRNA mixtures encoding these adjuvants synergistically enhanced melanoma-specific T cell responses, demonstrating their potential in cancer immunotherapy.

3. Optimizing Retroviral Transduction for Tumor-Infiltrating Lymphocytes (TILs)

During my postdoctoral research, I developed an optimized protocol for retroviral transduction of TILs, allowing for efficient genetic modification to improve their therapeutic efficacy. Given the resurgence of TIL therapy due to its ability to target tumor-specific neoantigens, this advancement was critical in ensuring high transduction efficiency and functional enhancement of T cells.

Using this protocol, we achieved >70% expression of an anti-CD19 chimeric antigen receptor (CAR) in TILs, resulting in strong IFN-γ secretion in response to CD19+ target cells. This protocol provides a reproducible approach to enhancing TIL function for clinical applications.

4. CD40 as a Costimulatory Element in CAR-T Cell Therapy

As a principal investigator, I led a study exploring the use of CD40 as a novel costimulatory domain in second- and third-generation CAR-T cells. The costimulatory domain in CAR constructs plays a crucial role in regulating T cell activation, persistence, and anti-tumor efficacy.

We compared CD40 to the widely used 4-1BB domain in CAR constructs. Our results showed that CD40 triggered potent NF-κB activation and was comparable to 4-1BB in enhancing T cell activation markers, cytokine secretion, and cytotoxicity. Notably, donor-dependent differences in response to CD40 and 4-1BB suggested a potential for personalized approaches in CAR-T cell design. These findings highlight CD40 as a promising alternative costimulatory domain in next-generation CAR therapies.

5. Membrane-Anchored IL-18-Based Genetic Adjuvants for Cancer Immunotherapy

I initiated and led the development of a composite genetic adjuvant that integrates IL-18, TLR4, and CD40 into a single membrane-bound construct. The goal was to amplify T cell activation by simultaneously engaging the cytokine receptor, toll-like receptor, and TNF receptor pathways.

This "all-in-one" genetic modification was tested in CAR-T cells and melanoma patient-derived TILs. Engineered T cells exhibited spontaneous upregulation of T-bet, increased IFN-γ and TNF-α secretion, and enhanced melanoma cell killing. Notably, the IL-18-TLR4-CD40 construct was more potent than membrane IL-18 alone, demonstrating the value of integrating multiple costimulatory signals into a single construct. This approach provides a novel way to improve adoptive T cell therapy outcomes while avoiding the systemic toxicity associated with cytokine administration.

6. Generation of Human Type 1 Regulatory T (Tr1)-Like Cells via Membrane IL-10

As part of my work as a PI, I developed a method for generating Tr1-like cells through membrane-attached IL-10 rather than soluble IL-10. Tr1 cells are FoxP3-negative regulatory T cells that secrete IL-10 and play a role in immune suppression. Their therapeutic use requires efficient protocols for stable and reproducible generation.

Using retroviral transduction, I successfully engineered human CD4+ T cells to express membrane-bound IL-10, leading to stable IL-10 expression and allowing for simple purification using magnetic beads. Purified cells exhibited a homogenous Tr1-like phenotype (CD49b+, LAG-3+, PD-1+, pSTAT3+) and maintained a central memory phenotype. This approach overcomes the limitations of uncontrolled IL-10 secretion and offers a promising strategy for generating regulatory T cells for immune modulation