RICE
Biotech Launch Pad

Hybrid Advanced Molecular Manufacturing Regulator (HAMMR) for Cancer Immunotherapy

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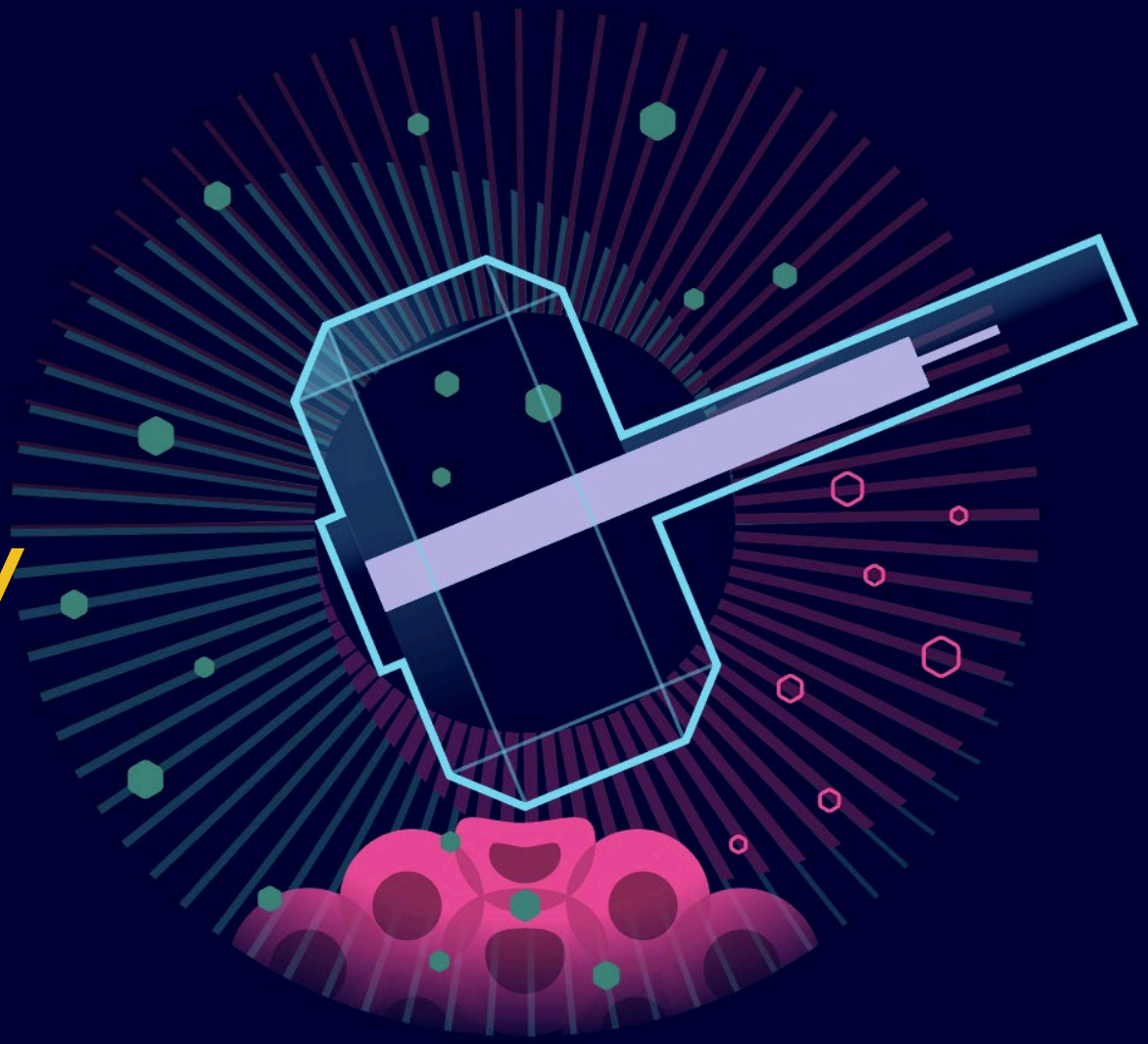
https://biotechlaunchpad.rice.edu/



What if we could boost response to solid tumor therapy *from 10% to >50 %?*

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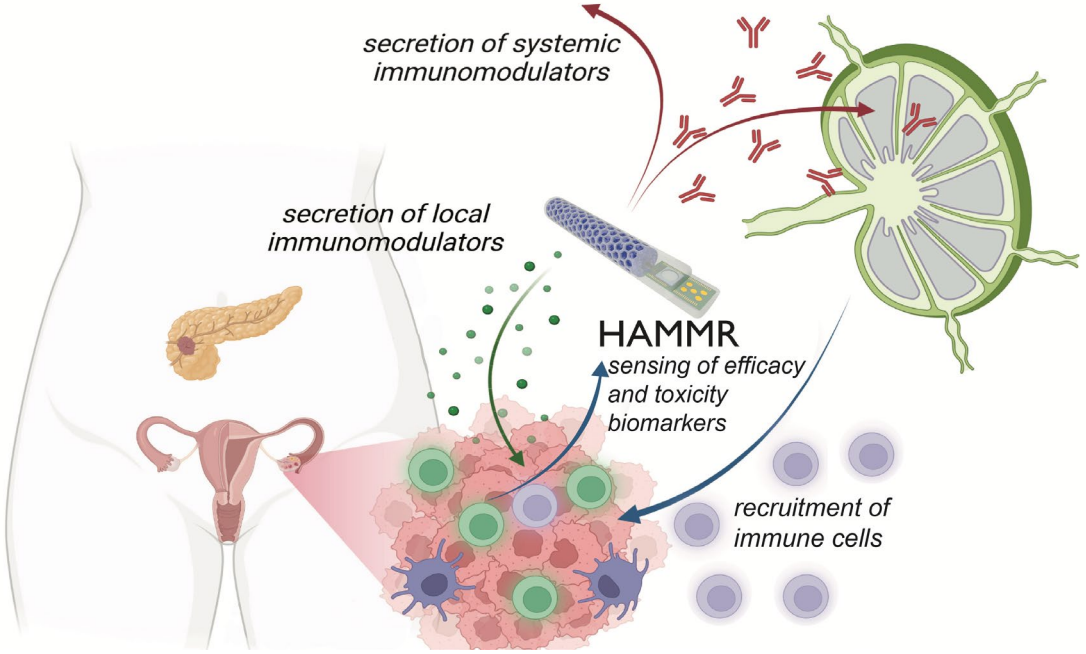
- **Peritoneal cancers**, such as ovarian and primary colorectal cancers, **cause more than a third of all cancer deaths** in the United States**.**
- Today, activating the immune system against solid tumors often fails because it becomes toxic to the patient before inducing an effective immune response. **Only 5-15% of patients effectively respond.**
- An effective treatment could **save approximately 187,000 American lives annually**.
- More broadly, patients with solid tumors, such as those found in peritoneal cancers, often do not respond effectively to **current immunotherapies** since activating the patient's immune system against solid tumors often **becomes toxic before it becomes effective**.



Develop a Sense-and-Respond Cancer Therapy
Implant Technology

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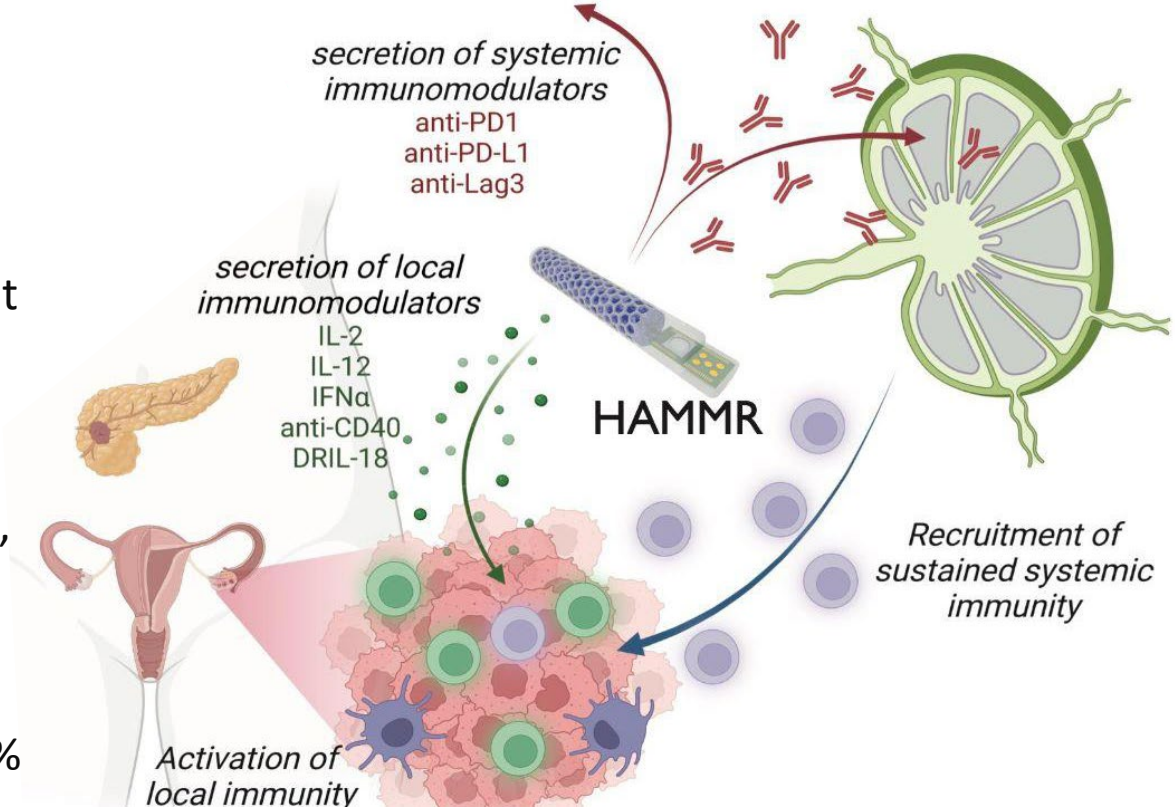
Project THOR: Targeted Hybrid Oncotherapeutic Regulation

- **19 investigators,** Engineers, Scientists, Clinicians, and Industry partners dedicated to developing this groundbreaking cancer therapy platform over the next five years.
- **Develop HAMMR**, a small device that can be implanted adjacent to tumors through a minimally invasive procedure.
- **Real-time Adaptive Therapy:** By continuously monitoring the tumor's environment, producing tailored immunotherapy drugs, and adjusting doses in real time, HAMMR can safely and effectively eliminate cancer.
- **The impact** is to reduce cancer-related deaths by more than 50%



Partners

RICE · THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History® · Carnegie Mellon University · JOHNS HOPKINS UNIVERSITY · Stanford University · UNIVERSITY of HOUSTON · Georgia Institute of Technology

Disrupt biologics development paradigm
Implantable pharmacies

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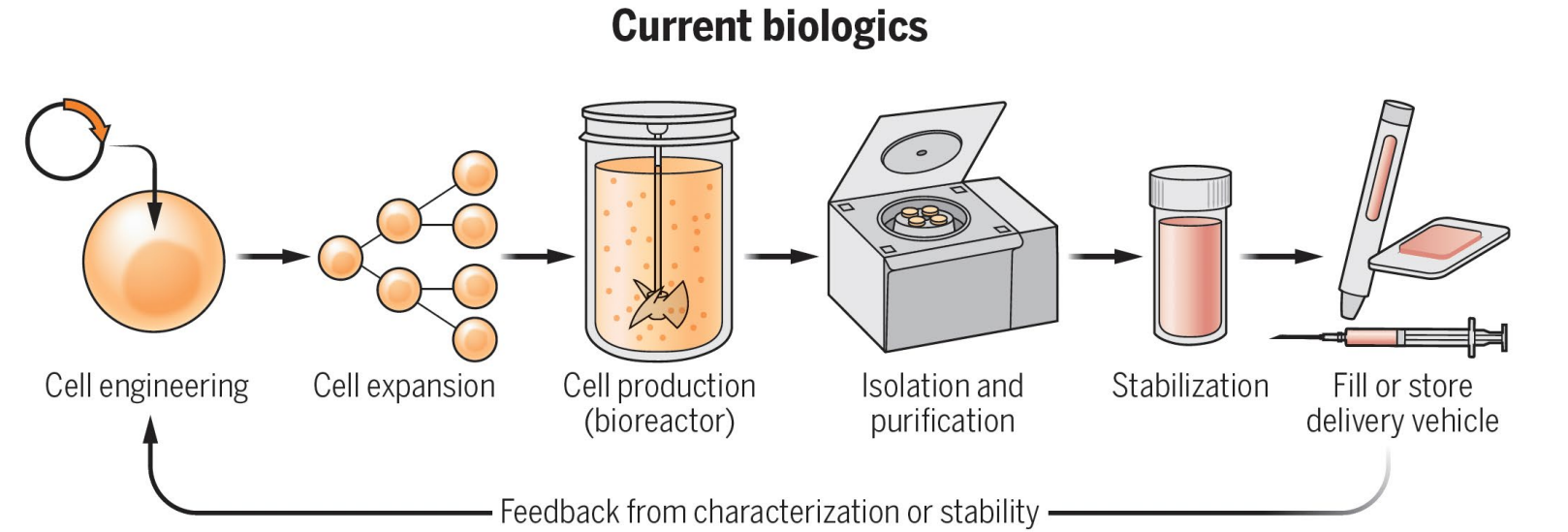

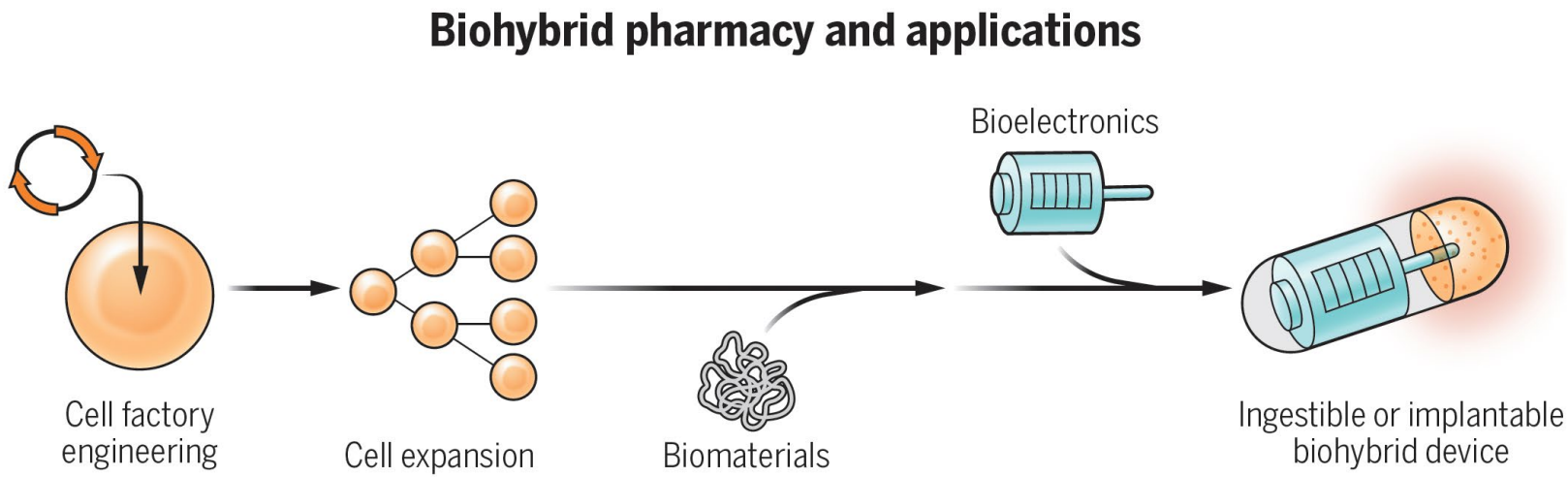

Source: Rivnay, Sheehan, Veiseh. Science. Oct 2024

Today, biologics are expensive to manufacture, requiring isolation, purification, formulation, stabilization and packaging, with each step increasing the cost of biologics.

Biohybrid pharmacies address the short half-lives of most biologics while avoiding immunogenicity associated with modified or recombinant biologics.

Immunomodulatory Polymers Enables Long-Term Cell Viability without immunosuppression

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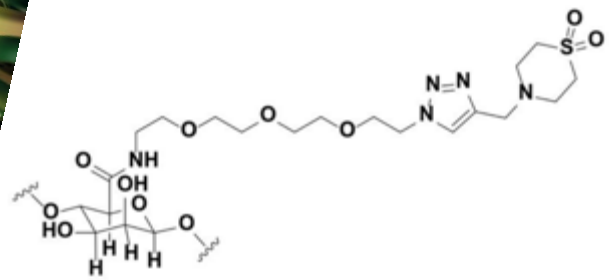

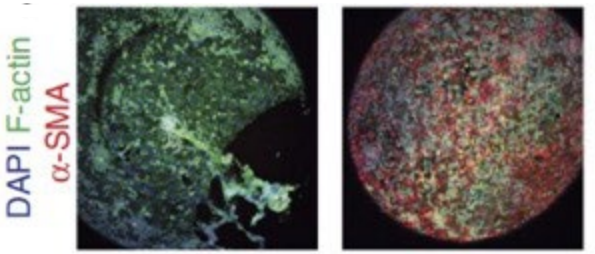

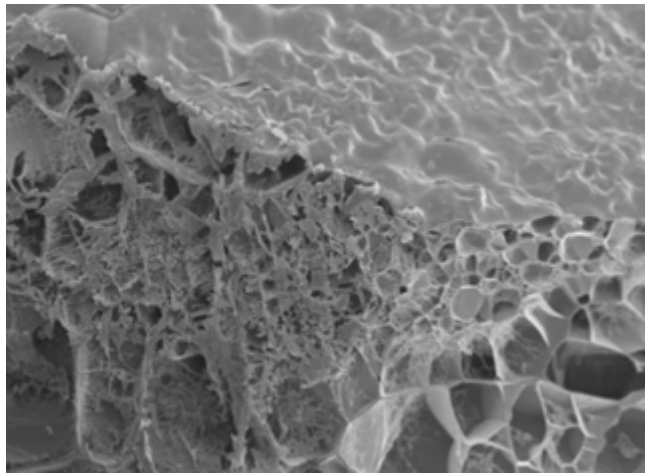

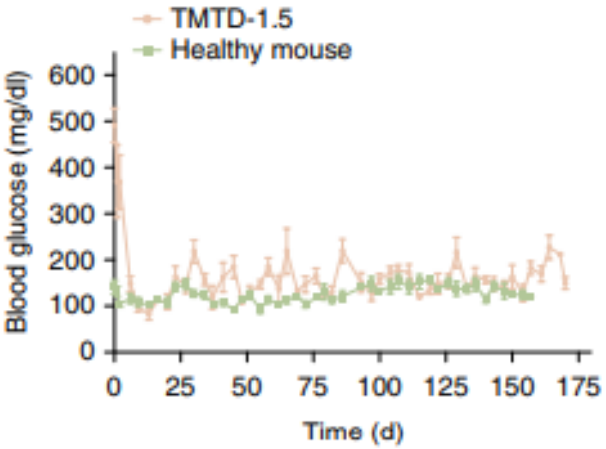

Vegas and Veiseh et al., *Nat Med,* 2016

Implanted cells deliver a consistent biologic *therapeutic for ≥1 year*

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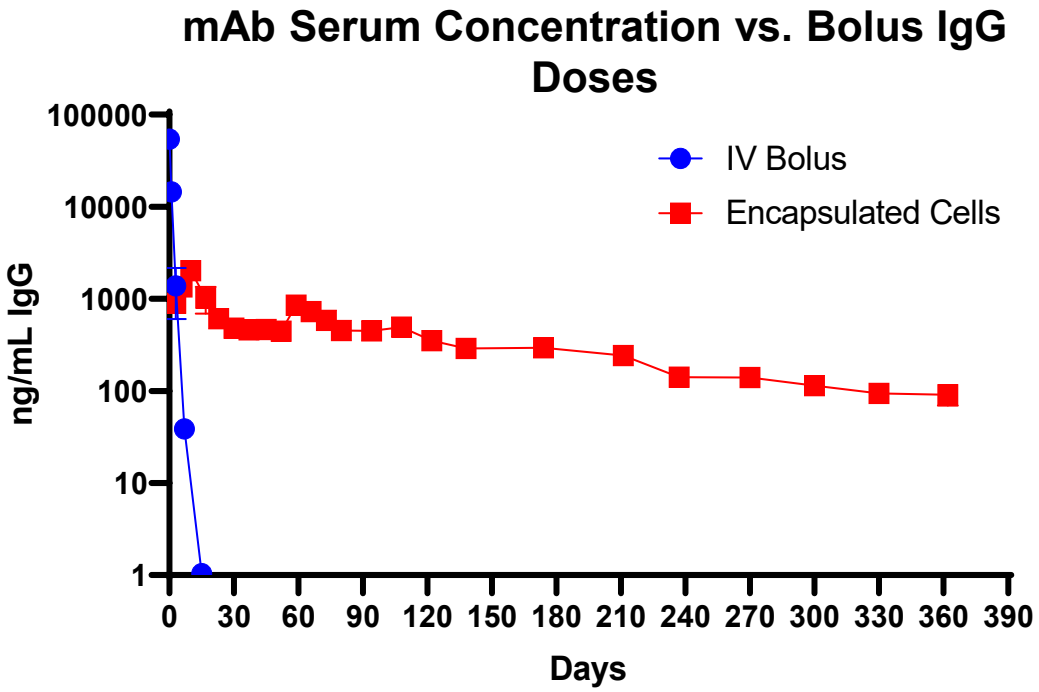
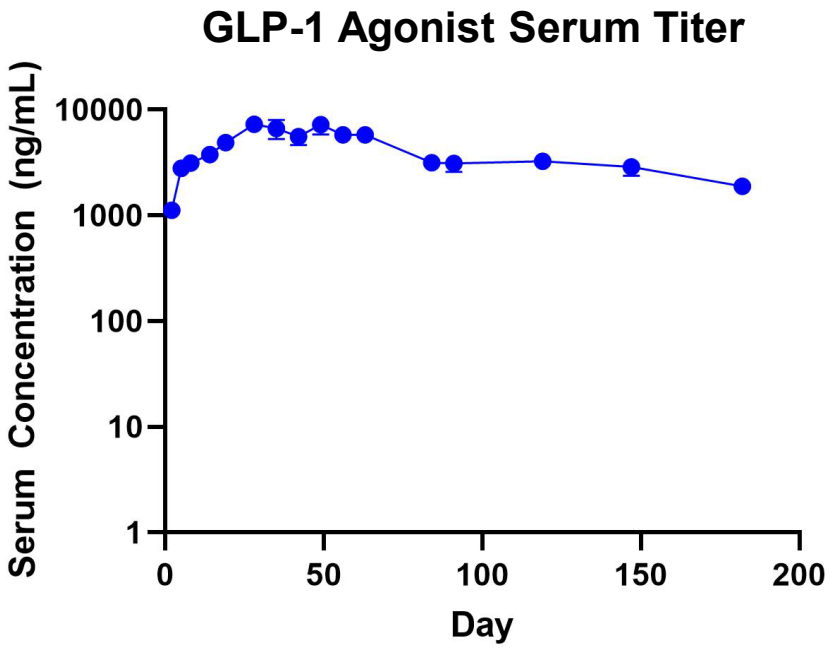
1-year durability



6-month durability



Treatment can be delivered for different periods of time, depending on patients' needs

In Chemotherapy-Treated Ovarian Cancer Patients
Reduced Effector Cell Immune Signaling in Tumors

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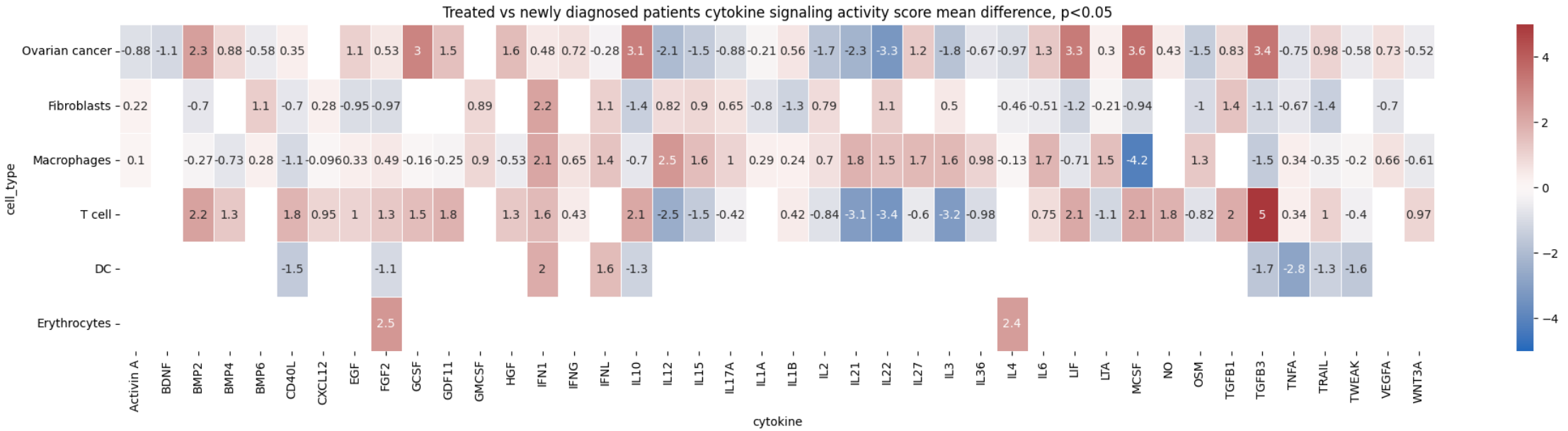
In tumor cells, chemo - treated patients showed higher MCSF, TGFB3, and LIF signaling and lower IL12, IL21, and IL22 signaling compared to treatment naïve samples.



*Newly diagnosed: patient 3, 5 (cohort 1 sample), 6; treated: patient 1, 2, 4, 5, (cohort 2 sample), 7, 8, 9, 10, 11; patient 21, 22, 23 excluded from analysis due to missing clinical status

*Mean difference of Cytosig activity score, Wilcox rank sum test, p-val < 0.05

Cytokine factories deliver potent, persistent, and regulated dosing to tumor-containing cavity

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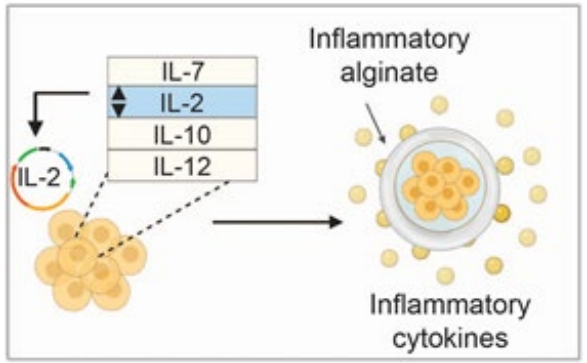
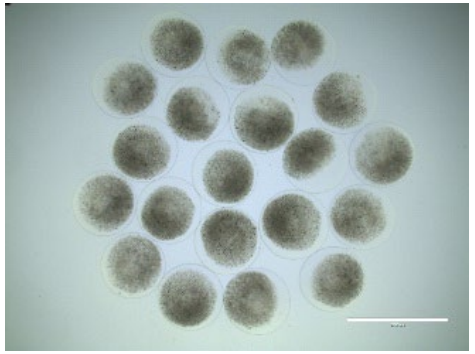
SCIENCE ADVANCES | RESEARCH ARTICLE

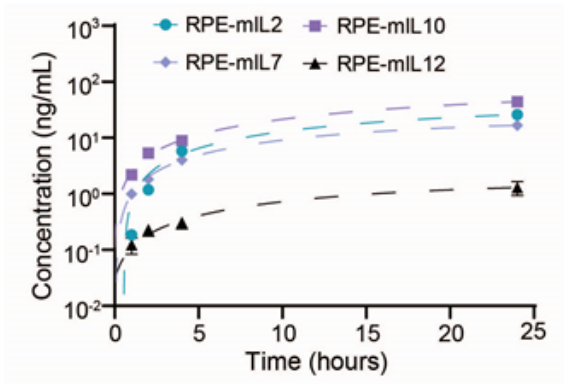
CELL BIOLOGY

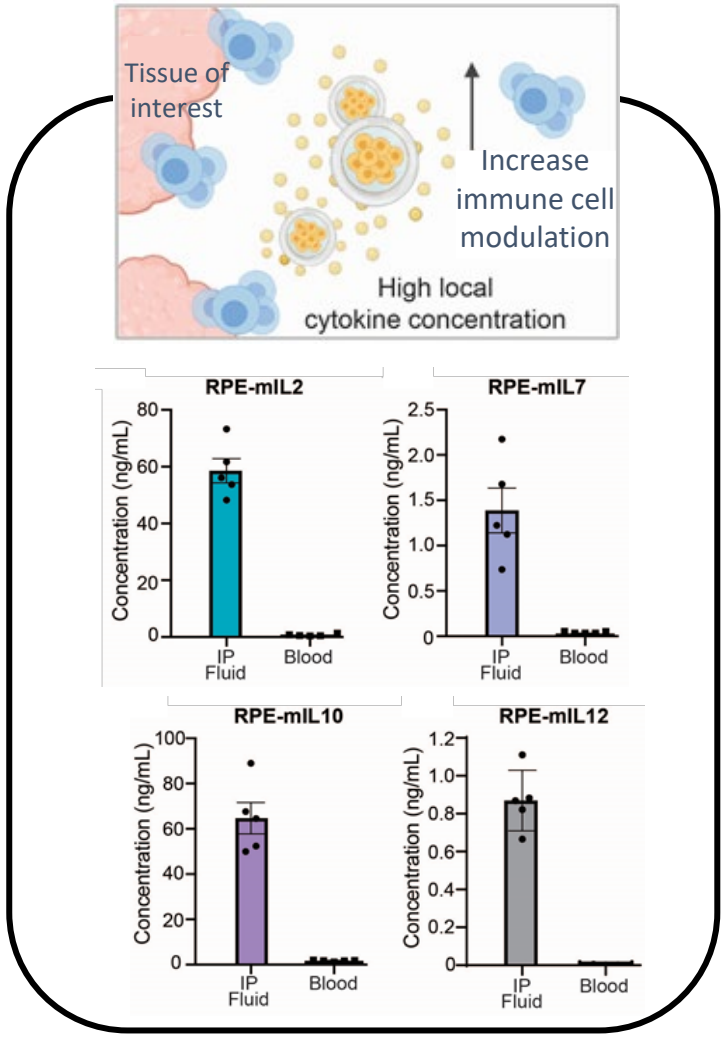
Clinically translatable cytokine delivery platform for eradication of intraperitoneal tumors

Amanda M. Nash[1], Maria I. Jarvis[1], Samira Aghlara-Fotovat[1], Sudip Mukherjee[1], Andrea Hernandez[1], Andrew D. Hecht[1], Peter D. Rios[2], Sofia Ghani[2], Ira Joshi[2], Douglas Isa[2], Yufei Cui[1], Shirin Nouraein[1], Jared Z. Lee[3], Chunyu Xu[4], David Y. Zhang[1], Rahul A. Sheth[5], Weiyi Peng[4], Jose Oberholzer[2,6], Oleg A. Igoshin[1], Amir A. Jazaeri[7], Omid Veiseh[1]*









PHASE 1 DOSE ESCALATION AND SAFETY STUDY
SUPPORTS FURTHER CLINICAL DEVELOPMENT

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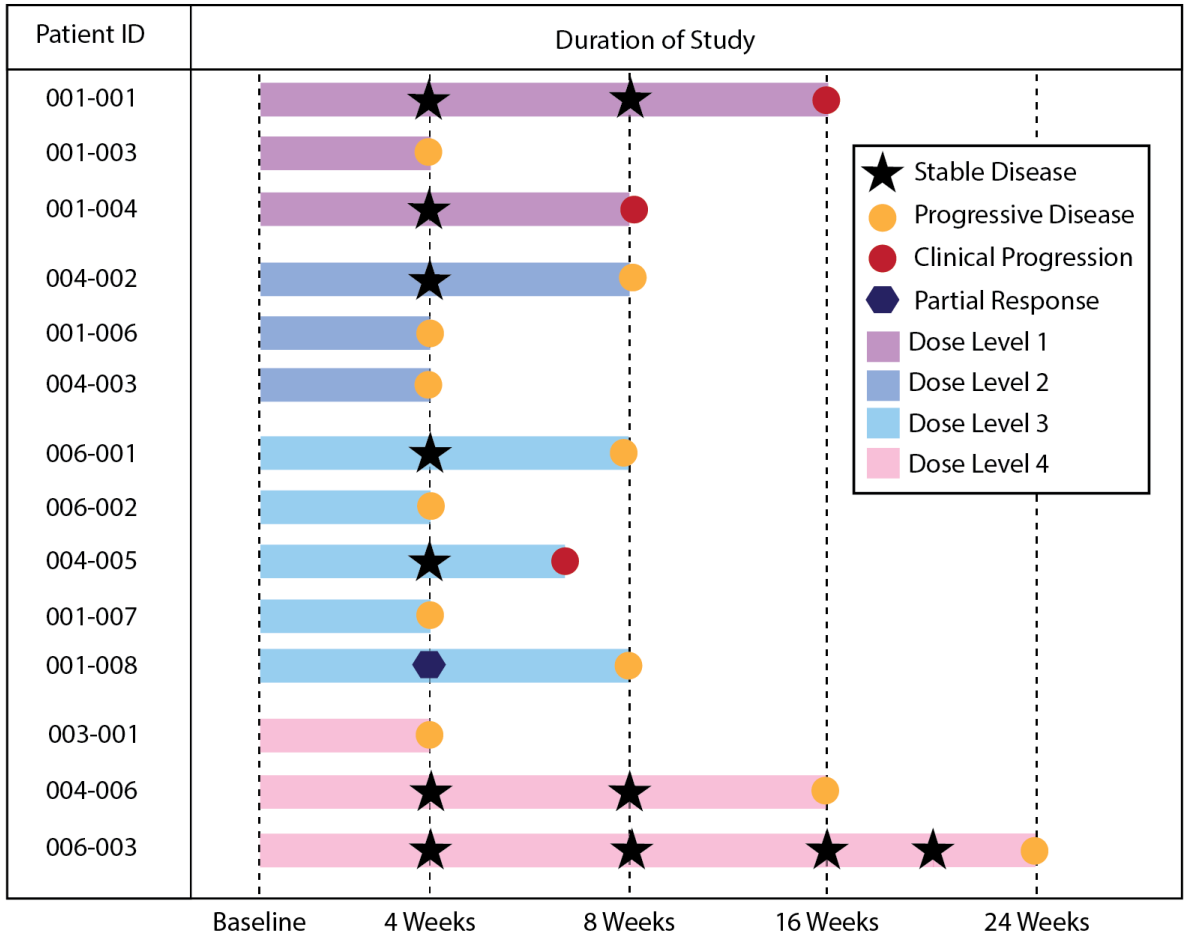
- **Phase 1 trial:** RPE-IL2 as a monotherapy in peritoneal platinum-resistant ovarian cancers: Accomplished 4 out of 5 dose levels

Safety

- No dose-limiting toxicities observed across dose ranges
- AEs were in the grade 1-2 range and profile was characteristic for IL2 treatment

Survival

- 2 patients with stable disease at 8 weeks
- **1 patient with stable disease at 20 weeks**



Biomarker Activity

IL2 primes the immune T cells for CTLA4 inhibition

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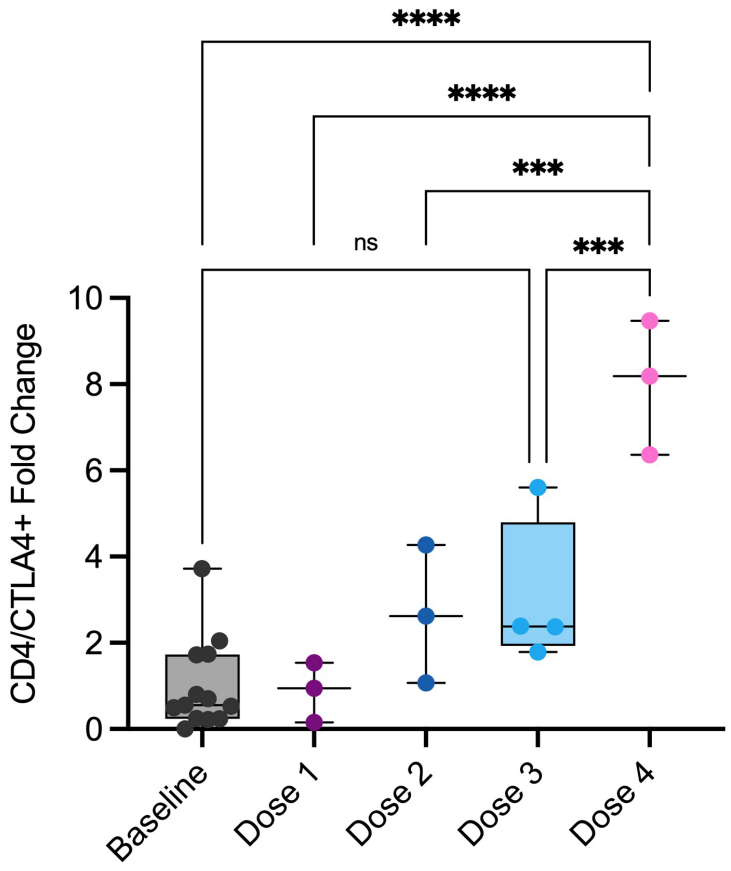
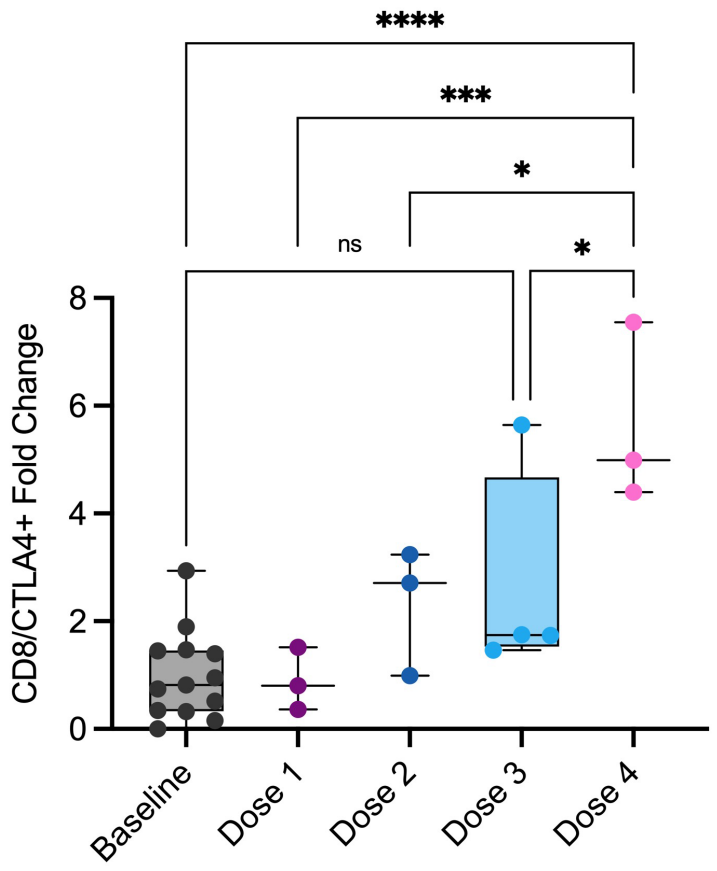
- CTLA4 **C**ytotoxic **T** **L**ymphocyte **A**ssociated protein **4**
- T cell checkpoint expressed on activated cytotoxic T cells
- Robust CTLA4 expression at dose level 4
- Local cytokine production activates cytotoxic T cells
- Cytokines prime the immune system for effective checkpoint inhibition
- **Combination biologics** are needed to **boost and improve survival outcomes**

Dose-dependent CTLA4 expression





Developing HAMMR
An entirely new way of treating cancer

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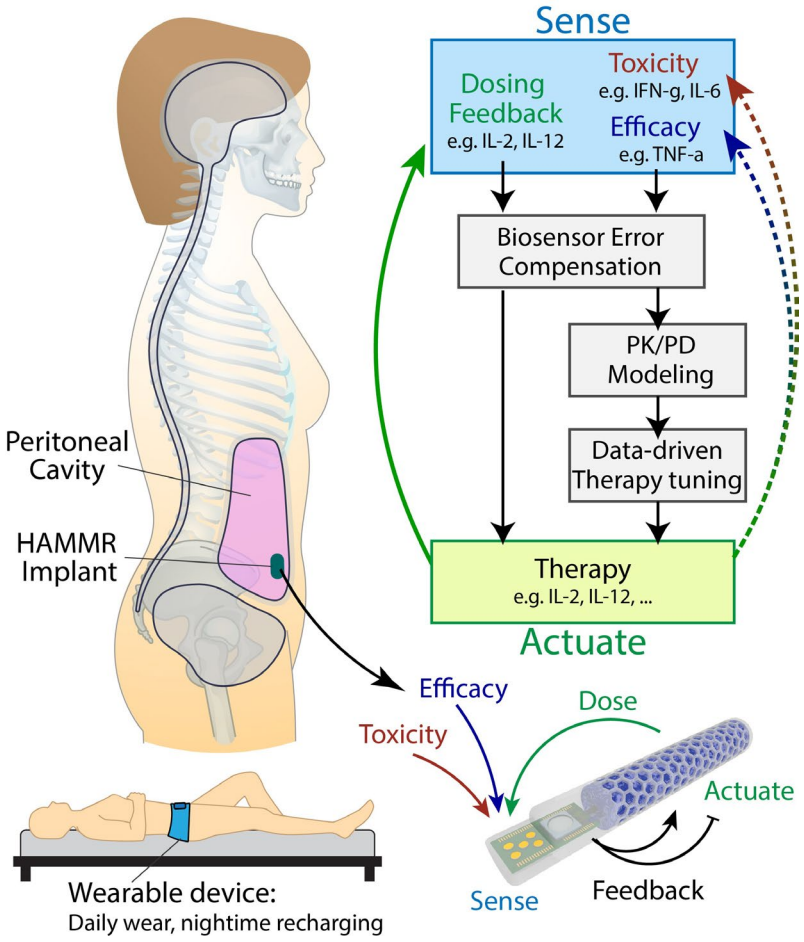
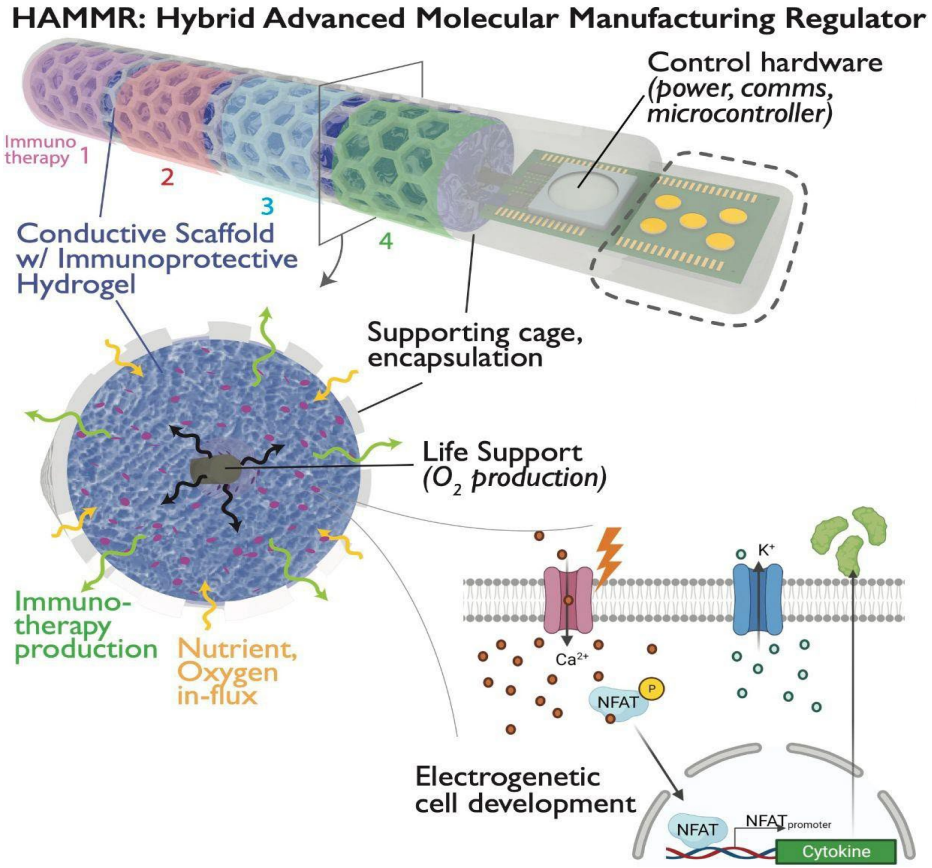
- **The HAMMR Device** will monitor cancer progression
- Deliver the therapy, providing **patient-specific closed-loop regulation** of immunomodulating molecules
- The implant will also **reduce the burden on the patient's** daily life
- The integrated system will enable homesteading of advanced therapies, providing a **broader range of care to underserved communities**.



A small biohybrid device containing engineered cells and bioelectronics to control them



Cells are engineered to secrete cancer *immunomodulators* *in response to electrical stimulation*

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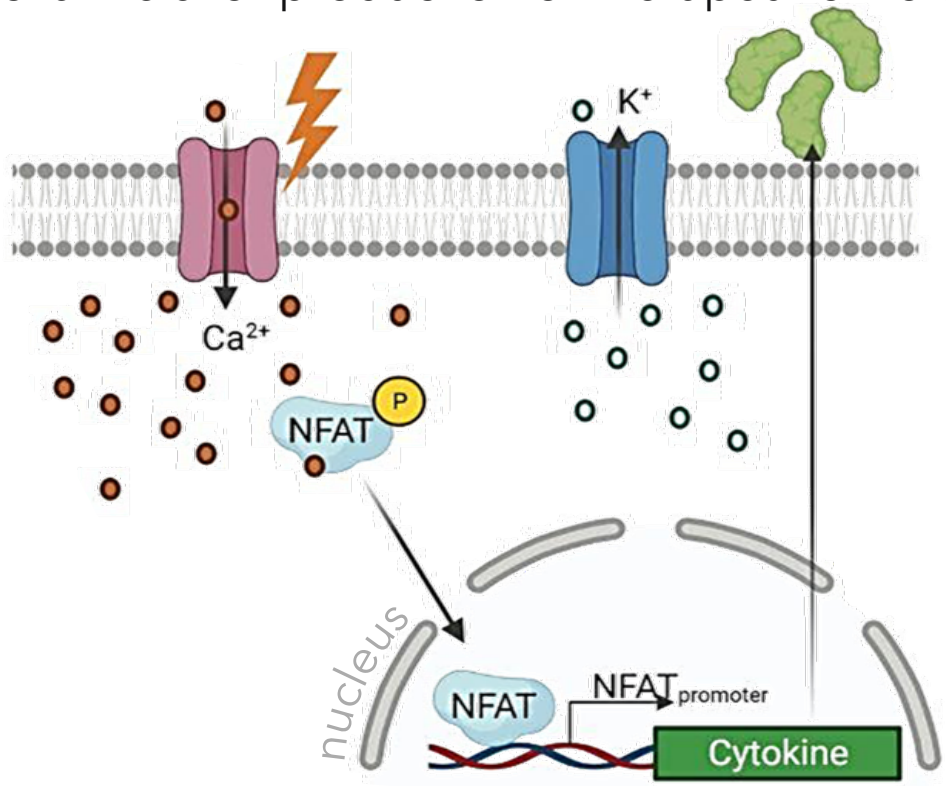
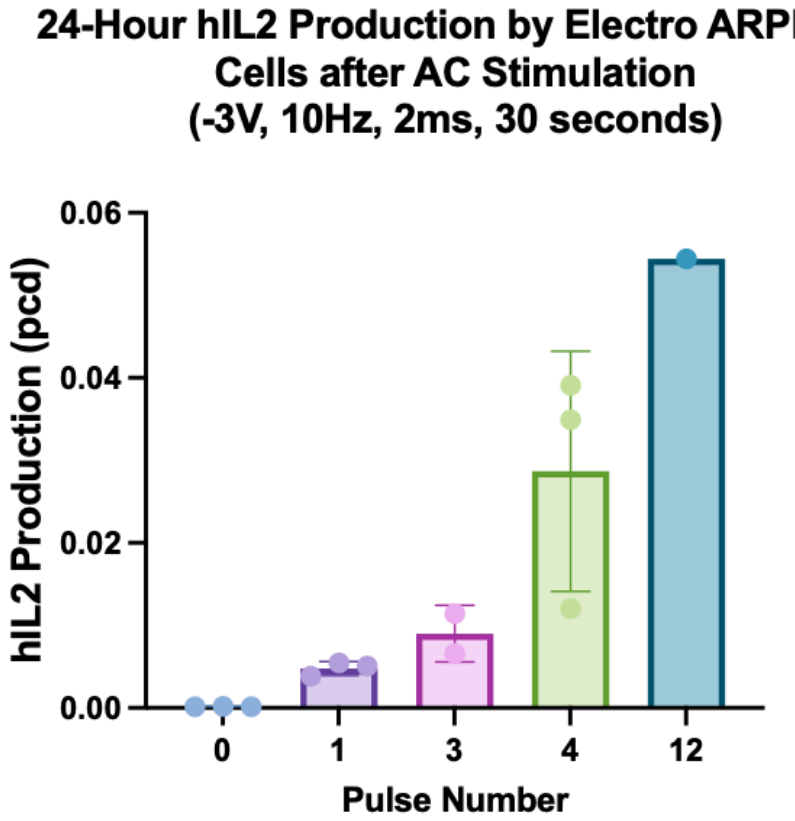
Human cells are synthetically engineered to express electrically-responsive membrane channels for production of therapeutic molecules



Electrical pulse stimulation enables controlled cytokine production



Feedback-regulated immunotherapies

Enable safer and more effective immunotherapy

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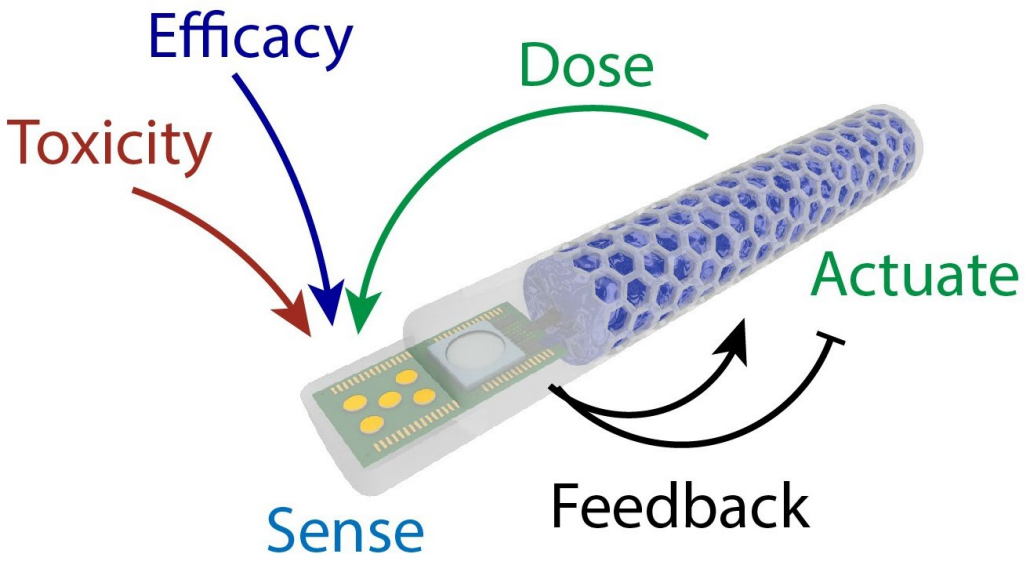
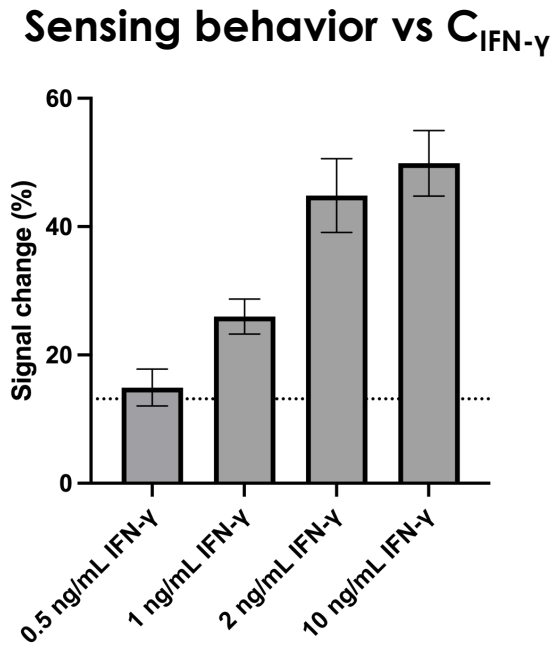
Integrated HAMMR device with actuator and sensors



Real-time sensing of immune activation



Device elicits robust anti-tumor immunity
across multiple tumor models

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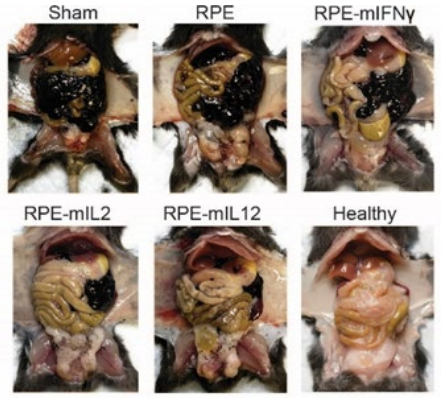
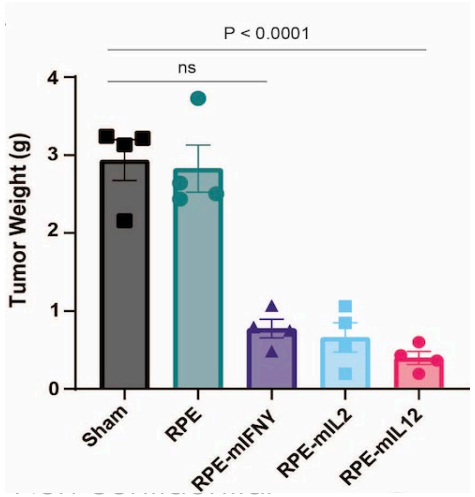
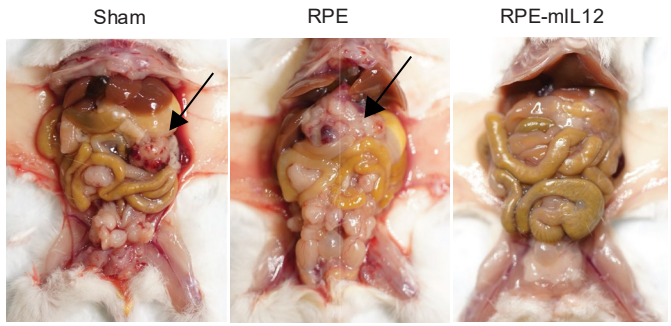
Local Therapy (device adjacent to tumors):

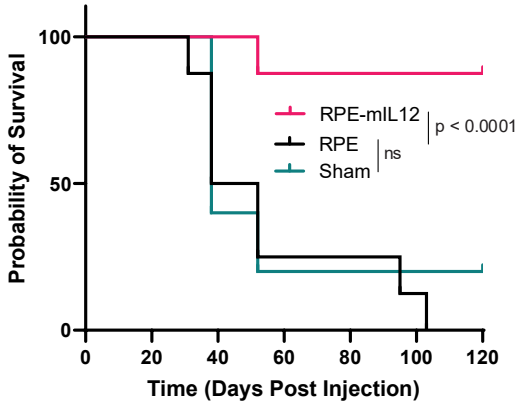
Metastatic (peritoneal) melanoma



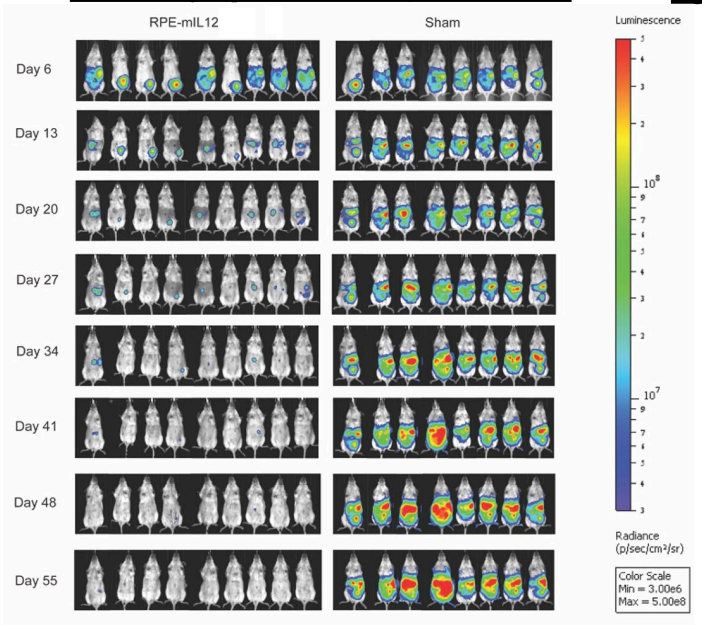


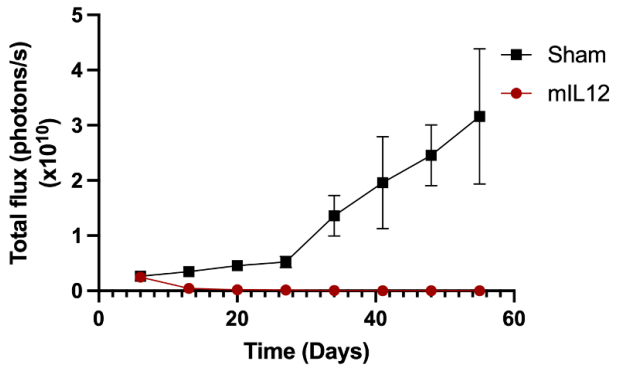
Primary (peritoneal) pancreatic



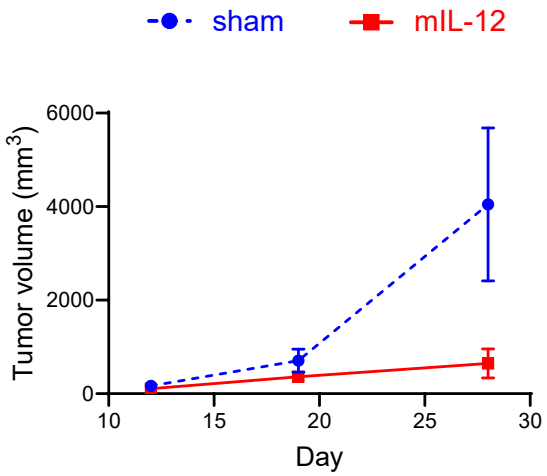


Primary (peritoneal) Ovarian





Lymph node metastatic melanoma



First-in-human trial HAMMR Device
Scheduled to begin in the next 18 months

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- A phase 1 Clinical Trial for a combination product will be conducted to assess the safety and feasibility of using the HAMMR device in humans.
- An IND application will be submitted for the first-in-human trial.
- HAMMR devices will be prepared and validated in compliance with GMP Manufacturing requirements.
- The trial will be led by Dr. Amir Jazaeri, M.D., at the MD Anderson Cancer Center.

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The HAMMR will be implanted for 4, 8, 12, and 16 weeks in ~10-20 patients. Blood, ascites fluid and biopsy will be collected to monitor the performance of the therapy. Long term follow up will be done every 8 weeks.

Bioelectronic device enables long-term delivery for *from user-controlled devices*

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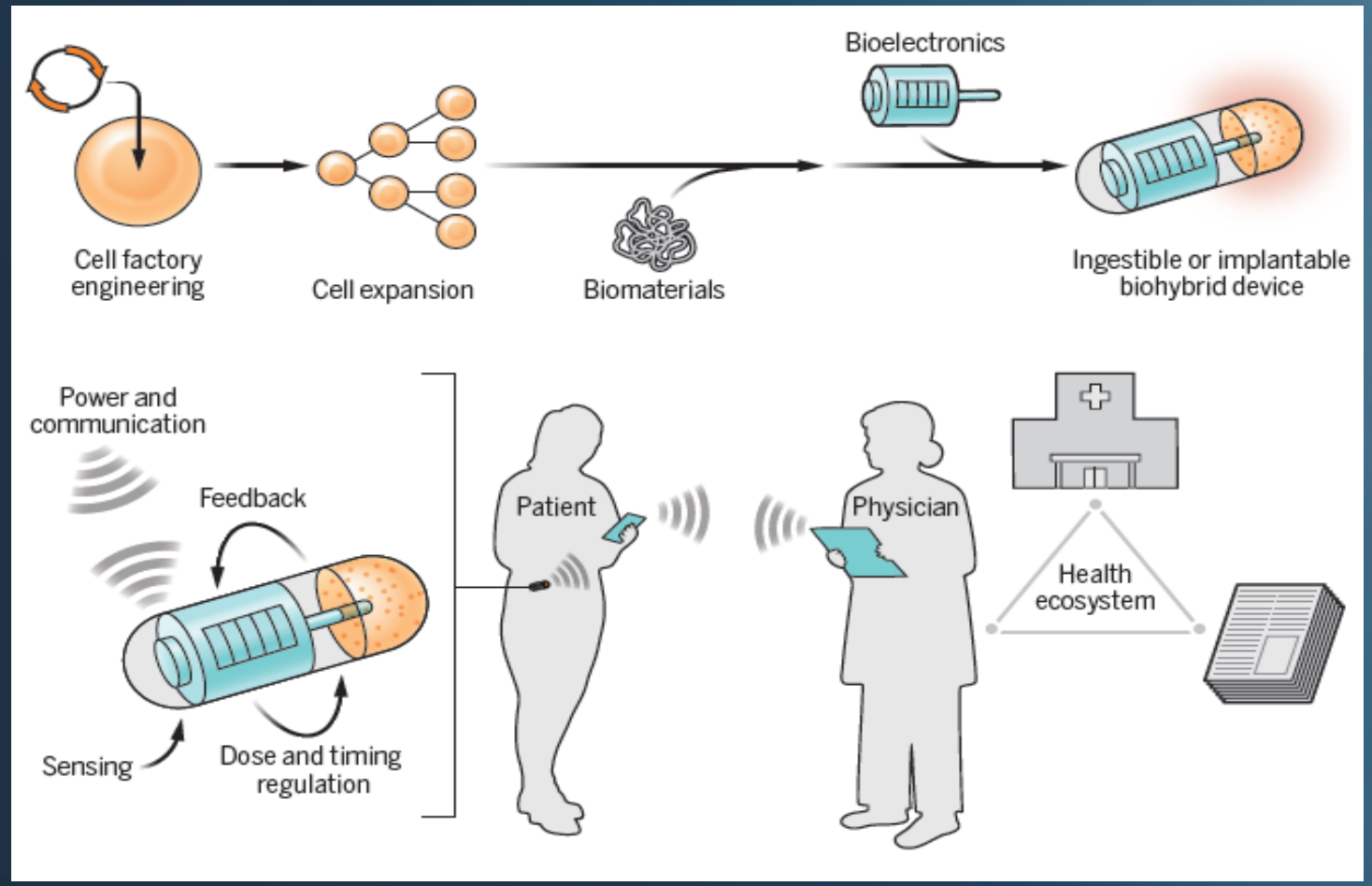


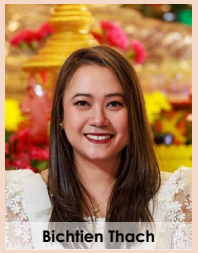
Source: Rivnay, Sheehan, Veiseh. Science. Oct 2024

Veiseh Lab Team

Veiseh Lab

Staff


Christian Schreib, PhD


Bichtien Thach

Postdoctoral Researchers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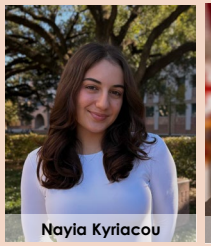
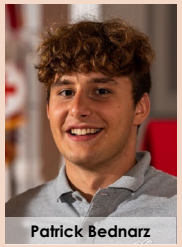
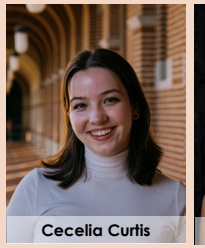
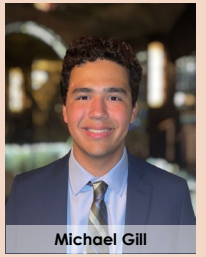
Undergraduate Students


Nayia Kyriacou


Patrick Bednarz


Cecelia Curtis


Giann Ruiz


Michael Gill


Prasi Desai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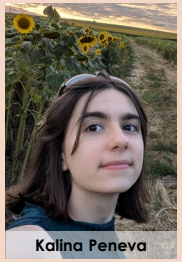
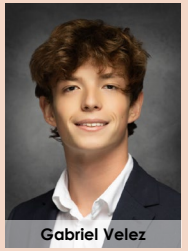
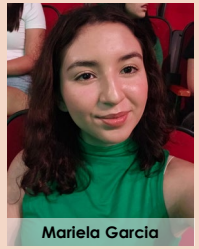

Kalina Peneva


Gabriel Velez


Mariela Garcia


Naayaa Mehta


Jewel Moore-Young

Graduate Students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Anthony Davis


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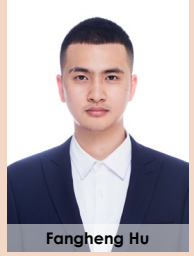
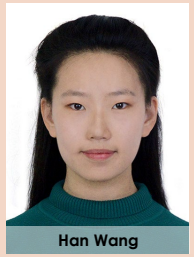
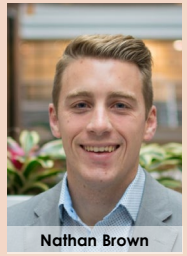
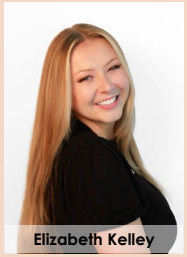
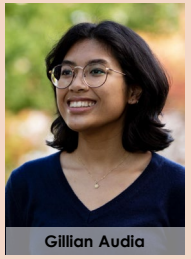

Fangheng Hu

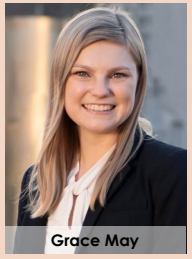

Han Wang


Nathan Brown


Elizabeth Kelley


Chris Wright


Gillian Audia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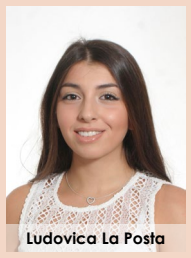
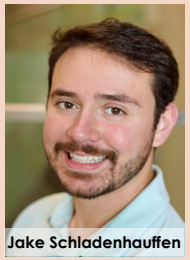
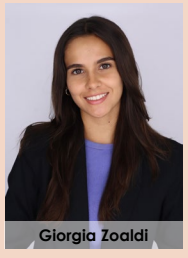
Kailyn Nunez


Jacob Cabler


Alejandra Cobos Perez


Ludovica La Posta


Jake Schladenhauffen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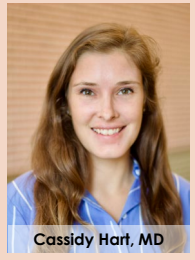
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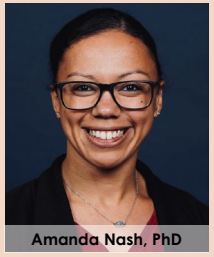
Graduate/Post-Doctoral Alumni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