Telephone Meeting

University of Connecticut Board of Trustees
Committee for Research, Entrepreneurship and Innovation

Thursday, September 28, 2023

AGENDA

Meeting held by Telephone:
Public Call in #: (415) 655-0002 US Toll
Access Code: 2621 161 3696

Public Streaming Link (with live captioning): https://ait.uconn.edu/bot

(A recording of the meeting will be posted on the Board website https://boardoftrustees.uconn.edu within seven days of the meeting.)

Call to order at 1:00 p.m.

1. Public Participation*
   *Individuals who wish to speak during the Public Participation portion of the Thursday, September 28, meeting must do so 24 hours in advance of the meeting’s start time (i.e., 1:00 p.m. on Wednesday, September 27) by emailing BoardCommittees@uconn.edu. Speaking requests must include a name, telephone number, topic, and affiliation with the University (i.e., student, employee, member of the public). The Committee may limit the entirety of the public comment to a maximum of 30 minutes. As an alternative, individuals may submit written comments via BoardCommittees@uconn.edu, and all comments will be transmitted to the Committee.

2. Minutes from the June 29, 2023, Meeting

3. Glycogen Storage Disease Research
   Presentation by Youngmok Lee, Ph.D.
   Assistant Professor, Department of Pediatrics

4. Pioneering Research in Cell Analysis and Modeling
   Presentation by Pedro Mendes, Ph.D.
   Professor, Department of Cell Biology
   Director, Center for Quantitative Medicine

5. Board of Trustees Statement in Support of the University’s Initiatives on Sustainability and the Environment

6. Other Business

7. Executive Session (as needed)

8. Adjournment

PLEASE NOTE: If you are an individual with a disability and require accommodations, please e-mail the Board of Trustees Office at boardoftrustees@uconn.edu prior to the meeting.
Glycogen Storage Disease Research

Youngmok Lee Ph.D
Assistant Professor
GSD Lab, Department of Pediatrics
UConn Health
What is GSD, Glycogen Storage Disease?
A metabolic disorder caused by a deficiency of an enzyme or transport protein affecting glycogen synthesis, glycogen breakdown, or glucose production, typically in liver and/or muscle.
Currently, 15 different types of GSD have been identified.
Type Ia GSD
Prior to 1971, glycogen storage disease type Ia was almost universally fatal marked by extreme failure to thrive, life-threatening hypoglycemia, and acidosis.
In 1982, uncooked cornstarch therapy was introduced as a slow-release glucose source, and the prognosis improved dramatically.

→ Blood sugar can be maintained 3-4 hours
→ Survival of the patients are greatly improved

Required to keep drink cornstarch every 3-4 hours including night-time (no sleep through night)

Skipping a cornstarch dose or digestive problem can result in severe hypoglycemia may lead to death.
Bench to Bedside
Gene Therapy Development for GSD-Ia

1996: Mouse model characterization
2009-2018: Gene therapy vector development and test
2018-Present: Human Clinical Trial
Efforts on gene therapy development
Efforts for gene therapy development

Long-term safety and efficacy evaluations
Successful Phase I/II study and on-going Phase III trial
Next Target
GSD-Ia → Ib

: Different gene but identical symptoms
Glycogen Storage Disease type Ib

- The first goal of dietary management with UCCS (Uncooked Corn Starch) is prevention of hypoglycemia, however, it is challenging due to IBD
- Long-term complications: hepatic adenomas, kidney disease, and osteoporosis
- Neutropenia has been managed with regular injections of G-CSF. SGLT2 inhibitor has been recently introduced
GSD-Ib Gene therapy development
## Summary of results - comparison with previous gene therapies

<table>
<thead>
<tr>
<th>Year</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>2007</td>
<td>• Showed improvement in survival</td>
</tr>
<tr>
<td></td>
<td>• Short-term gene expression in both liver and bone marrow</td>
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<tr>
<td>2009</td>
<td>• 2007+</td>
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<tr>
<td></td>
<td>• Longer term gene expression (only RT-PCR)</td>
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<tr>
<td></td>
<td>• Improved growth rate</td>
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<tr>
<td></td>
<td>• Short-term improvement in neutropenia</td>
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<tr>
<td></td>
<td>• No Fasting glucose test</td>
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<tr>
<td>2017</td>
<td>• 2009+</td>
</tr>
<tr>
<td></td>
<td>• Long term expression of hG6PT</td>
</tr>
<tr>
<td></td>
<td>• Tolerate fasting 24h</td>
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<tr>
<td></td>
<td>• Native G6PT promoter was less active</td>
</tr>
<tr>
<td></td>
<td>• No effect in improvement in neutropenia in aged mice</td>
</tr>
<tr>
<td>Present</td>
<td>• 2017+</td>
</tr>
<tr>
<td></td>
<td>• Stronger gene expression <em>in vitro</em></td>
</tr>
<tr>
<td></td>
<td>• Neonatal to Adult (so far) lasting activity</td>
</tr>
<tr>
<td></td>
<td>• ANC increased</td>
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</tbody>
</table>
Gene Therapy Development for GSD-Ib

2003
- Mouse model characterization

2023
- Gene therapy vector development and test

2024-2025
- Human Clinical Trial

Current state of development

UCONN HEALTH
Thank you
Acknowledgement

GSD Lab. members

Charles Arends, Ph.D. candidate
Gene therapy developments for GSD-Ia and Ib
Investigation of immune function in GSD-Ib

Yasir Ameen, Research Assistant
Establishment of method for in vitro gluconeogenesis

Alicia Mitchell, MD Candidate, Class of 2026
Correction of lipogenesis by the regulation of G6P flow in a GSD-Ia

Samantha DeRosa, M.D./Ph.D. Student
2023 Fall Lab Rotation
Investigation of kidney functions of GSD-Ia
Pioneering Research in Cell Analysis and Modeling

Pedro Mendes
Richard D. Berlin Center for Cell Analysis & Modeling
pmendes@uchc.edu

https://health.uconn.edu/cell-analysis-modeling/
Pioneering software for simulation of cell/biochemical kinetics


The Virtual Cell Project

- 25,000+ registered users
- Graphical interface for biologists
- Reaction rules or networks
- Kinetics, diffusion, advection, membrane transport, electrophysiology
- Compartmental (ODE), spatial (PDE), deterministic, stochastic and network-free simulations
- Searchable model database
- Pathway database support
- Experimental data integration
- Virtual Microscopy
- SpringSaLaD for mesoscale
• Has now a well-established worldwide user-base
• > 1000 publications use COPASI
• Over 100 papers published yearly using COPASI
• Over 10,000 downloads per year
• 120 MS or PhD theses

http://copasi.org/Research
Moving from the cell upwards: multi-scale simulation

• Develop computational methods for combining multi-omics datasets and different modeling frameworks into multi-scale simulations.
• Apply these approaches to build simulations of whole microbiomes, which span molecular to multi-cellular scales.
CCAM Startup founded by C. Acker, L. Loew and P. Yan
Develops sensors and technology for imaging electrical activity in cells, tissue and organs.

Sinus rhythm in live open chest pig heart

After induction of arrhythmia

Sept. 8, 2023: $1.9M NIH SBIR grant awarded to Potentiometric Probes for voltage sensing in cardiac systems