TECHNION
Israel Institute of Technology

September 2023

Dear Friends,

As we approach a new academic year, I wanted to extend my warmest greetings and express my sincere appreciation for your invaluable support to The Schneur Diabetes Research Center.

With immense pleasure, I am enclosing our latest report on "Engineered Insulin-Responsive Muscle Tissue: Restoring Long-Term Insulin Sensitivity to Type 2 Diabetes Patients." This report represents the collective efforts of my group and myself in the effort to combat insulin resistance effectively. Our excitement continues to grow as we witness remarkable successes in engineering muscle tissue to restore insulin sensitivity in patients.

I wish to express my gratitude for your support, which is the bedrock of our endeavors. Without your generous contributions and interest in elevating the standard of care for diabetes patients, none of this would have been possible. Your commitment to our cause is an inspiration.

Once again, I extend my sincerest appreciation for your support and belief in our mission. I am honored to have you as partners in this transformative journey.

With warm regards and best wishes,

Shulamit Levenberg

Prof. Shulamit Levenberg
Director of The Schneur Diabetes Research Center

The Schneur Diabetes Research Center

2023 Report

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2023

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Israel Institute of Technology

Engineered Insulin-Responsive Muscle Tissue: Restoring Long-Term Insulin Sensitivity to Type 2 Diabetes Patients

Prof. Shulamit Levenberg

Annual Report 2023

SUMMARY

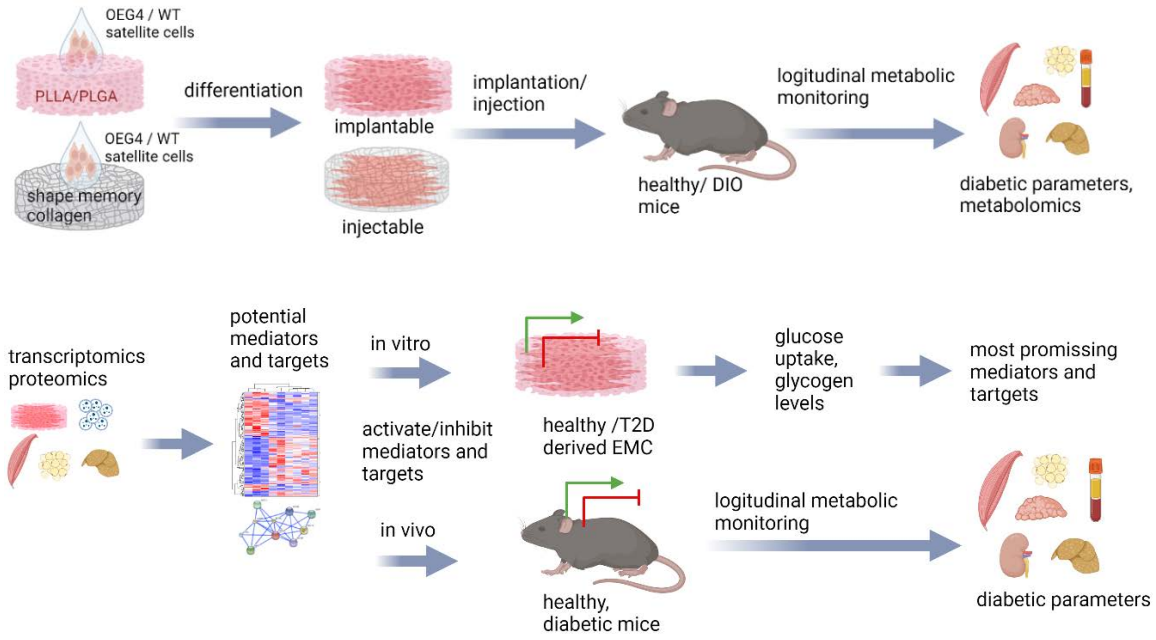
Our research focuses on addressing the challenges of Type 2 diabetes (DM2), a prevalent disease that causes significant suffering and mortality worldwide. We are specifically interested in peripheral tissue insulin resistance and its impact on glucose homeostasis. We aim to develop an innovative solution by engineering muscle tissue that overexpresses the glucose transporter GLUT4. This tissue, when transplanted into diabetic patients, is expected to improve glucose uptake and normalize blood glucose levels. Furthermore, our investigation into the crosstalk between the engineered and host tissues may reveal new treatment strategies for metabolic disorders and advance regenerative tissue engineering.

GOALS

Our primary objective is to develop a long-term solution to peripheral tissue insulin resistance and ultimately find a cure for diabetes. To achieve this, we are constructing an engineered vascularized muscle tissue by genetically modifying myoblasts. The tissue, grafted into diabetes patients using biodegradable scaffolds, will enhance glucose uptake and restore normal blood glucose levels. Additionally, we aim to study the crosstalk mechanisms between the engineered and host tissues, potentially uncovering systemic metabolic effects and opening new avenues for metabolic disorder treatments.

METHOD

We are genetically modifying myoblasts from mice and humans to overexpress the glucose transporter GLUT4. Using these modified cells, we are creating an engineered vascularized muscle tissue. In diabetic mice, we are assessing the tissue's ability to maintain muscle characteristics and enhance glucose uptake. As a preliminary step prior to clinical trials, we are studying the anti-diabetic effects of the tissue on the whole mouse by analyzing RNA and protein samples from various tissues.



RESULTS

We successfully engineered a 3D muscle tissue construct from mouse cells, expressing higher levels of the glucose transporter GLUT4. After transplantation into diabetic mice, the tissue integration led to improved diabetes parameters, including reduced sugar levels during fasting and sugar challenge tests, as well as improved metabolic markers, such as fatty liver. The diabetic condition improvement lasted for three months.

Using human-derived cells, we genetically engineered them to increase glucose uptake. We are currently investigating their ability to reduce glucose levels in immune-deficient diabetic mice.

We developed an injectable shape memory scaffold containing engineered muscle cells for simpler delivery of the treatment. The cells differentiated into muscle fibers and retained viability after passing through an injection needle. After injecting the scaffold into the femoral muscle of mice, we observed integration with the host tissue after 8 weeks. Notably, we observed that the injectable GlUT4-enriched engineered constructs improved glucose homeostasis similarly to our previously tested implants. Ongoing research aims to determine the therapeutic effectiveness of different scaffold amounts to optimize the treatment strategy.

IMPACT

Our project offers an engineered tissue-based therapy administered through intramuscular injection, providing sustained improvement in the diabetic condition and reducing the need for conventional interventions. This represents a significant advancement in treating Type 2 diabetes, and establishes a foundation for addressing other disorder conditions.

CONCLUSION

Our research focuses on developing a specialized cellular system to provide therapeutic tools for Type 2 diabetes. By combining our findings with an understanding of cellular mechanisms, we aim to contribute to breakthroughs in diabetes treatment and related fields.

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ACKNOWLEDGMENT

We express our heartfelt gratitude to the generous donors who invested in our diabetes research project. Your invaluable support brings us closer to finding a cure for this disease that affects millions of people.

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