Developing a Placental Model: Evaluating ECM Composition on BeWo Gene Expression

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Site Information

Tissue Engineering and Biomaterials Laboratory

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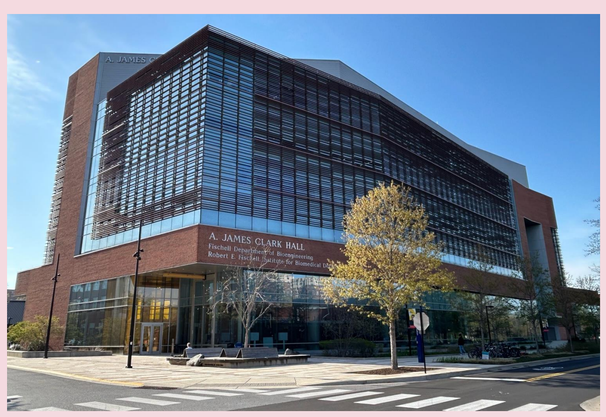
Lab Specialization: Tissue Engineering and 3D Bioprinting

Put simply, this lab builds biological models of human tissues using biologically derived materials and living cells. These models help us study diseases, test treatments, and can even create replacements for damaged or missing tissue.

How does this work?

- We use Gelatin Methacrylate (GelMa), an organic material that mimics the natural environment of cells, to 3D print a scaffold, forming a structure for cells to grow on
  - Cells are seeded onto this scaffold, and over time they grow to fill out this structure



Background

What is Gestational Diabetes?

Gestational diabetes is a condition characterized by elevated blood-glucose levels during pregnancy. It occurs when hormonal changes impair the body's ability to use insulin effectively, leading to insulin resistance and increasing health risks for both the pregnant individual and the developing fetus during pregnancy and after birth.

Why Study the Placenta?

The placenta is a temporary organ that forms during pregnancy and plays a vital role in supporting the developing fetus by regulating the exchange of nutrients, oxygen, waste, and hormones across the maternal-fetal interface. By studying how gestational diabetes impacts placental function, researchers can better understand the condition's impact and work towards improving prenatal care and long-term health outcomes.

The Ethical Challenge

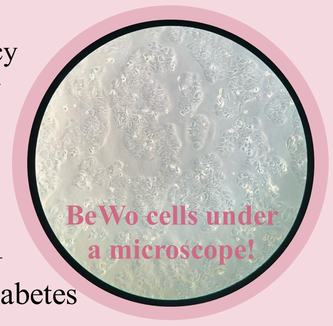
The placenta undergoes many important changes during the early stages of pregnancy. However, due to ethical limitations, placental tissue is collected from full-term pregnancies after birth, as to not risk harm to the developing fetus. By developing an in-vitro placental model, we will be able to study different stages of placental function and development with minimal ethical concerns.

My Project

My project focuses on understanding how different extracellular matrix (ECM) compositions influence the behavior of BeWo cells

- The ECM is a network of proteins and other macromolecules that provides structural and biochemical support to cells. It helps maintain tissue shape, supports cell attachment, enables communication between cells, and guides new cell growth and migration
  - In the placenta, the ECM is especially important for helping trophoblast cells form a monolayer, transport nutrients, and secrete hormones.
- BeWo cells are an immortalized human trophoblast cell line commonly used to model the molecular transport and hormone section functions of the placenta
  - We are using these to mimic placental behavior in early pregnancy

By analyzing how different ECM compositions (gelatin, GelMa, and decellularized placenta ECM) affect BeWo cell gene expression, we can identify the optimal environment for growing the most realistic placental model!



Overall Goal: Create a 3D placental model to study gestational diabetes

Me prepping samples for cDNA synthesis!

Current Progress

1 BeWo Cell Culture

We cultured BeWo cells under two different conditions:

- **Treated condition:** 0.1% gelatin-coated cell culture flasks
- **Untreated condition:** uncoated, standard cell culture flasks

Cells were grown for 1, 2, and 3 days to observe how exposure to different ECM compositions affects their gene expression over time

We will later introduce two additional experiment groups: 10% GelMa and Decellularized pECM coatings

2 RNA Isolation

To understand what the cells are doing, I isolated their RNA by lysing (breaking open) the cell membranes and separating the RNA from the other cellular contents. Since active genes are transcribed into RNA, extracting it allows us to see which genes are expressed.

3 cDNA Synthesis

Since RNA cannot directly assess gene expression, I created complementary DNA (cDNA) from the purified RNA.
This process involves an enzyme known as reverse transcriptase, which builds a DNA strand by using the RNA sequence as a template. The resulting cDNA serves as a more stable representation of the active genetic messages in the cell.

Next Steps

To assess how the different ECM compositions influence BeWo cell behavior, I will perform quantitative reverse transcription PCR (qRT-PCR) to analyze gene expression.

qRT-PCR

qRT-PCR is a technique used to measure the activity level of specific genes. We utilize TaqMan probes, which are short DNA oligonucleotides complementary to the gene of interest, to generate a fluorescent signal. The strength of this signal indicates the amount of each gene expressed, aiding in our evaluation of cellular behavior.

- I have selected primers for genes involved in hormone secretion, molecular transport, and trophoblast function, which are critical to understanding how closely the cells mimic placental behavior under each condition.
- Because each primer corresponds to a specific gene, we can gain insights into how changes in ECM composition influence BeWo cell behavior.

Eventually, these results will help identify the most effective GelMA formulation for supporting realistic placental cell function. This will then guide the development of a 3D bioprinted placenta model to study gestational diabetes!

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