

Pregnancy-Associated Organ-on-a-Chip Models to Pioneer Targeted Therapies

Hagar Labouta, PhD

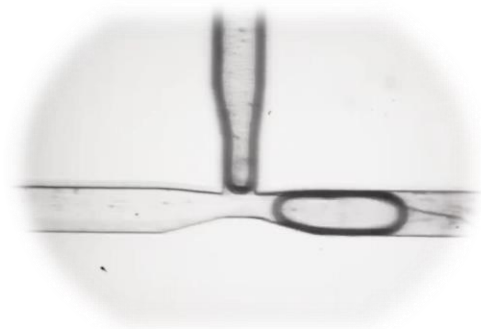
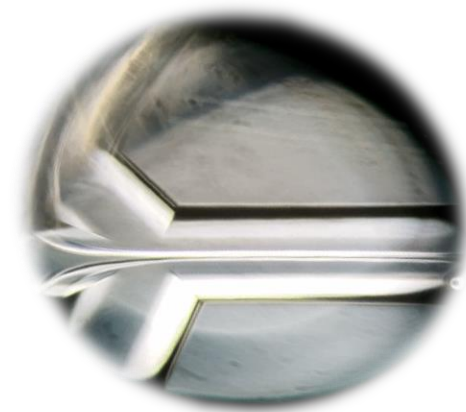
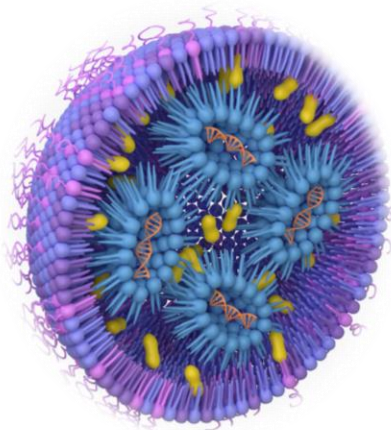
Keenan Professor of Medical Discovery, Unity Health Toronto

Leslie Dan Faculty of Pharmacy, and Institute of Biomedical Engineering,
University of Toronto



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We Design Microfluidic Chips to Optimize & Scale-up Nanoparticle Production



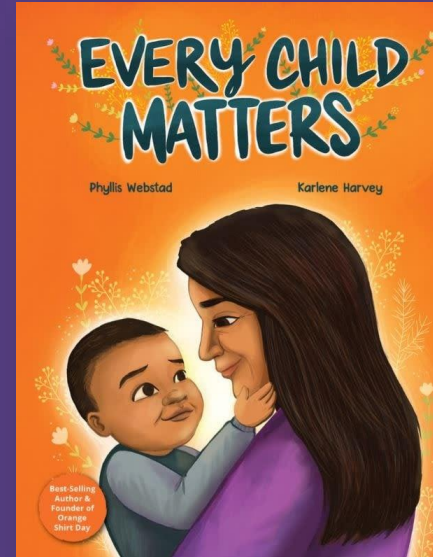
Abdelkarim et al., (2025) Journal of Controlled Release, in press

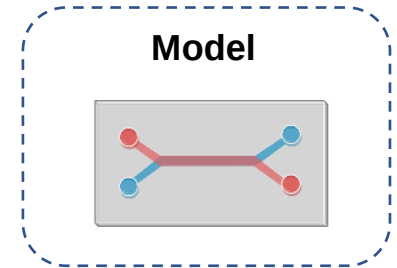
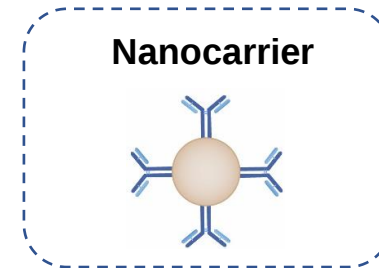
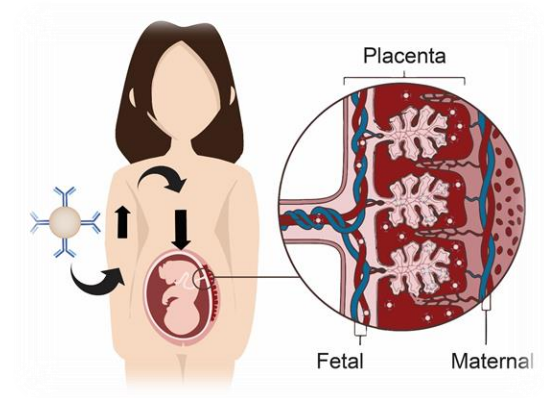
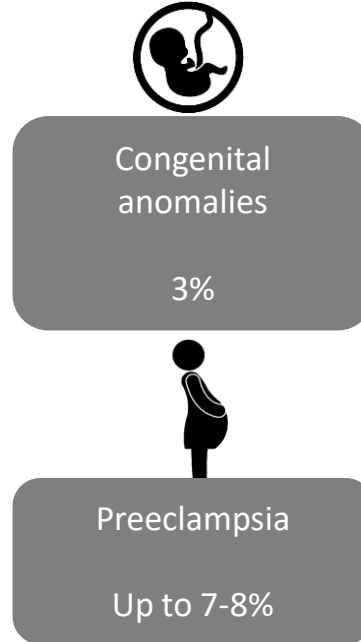
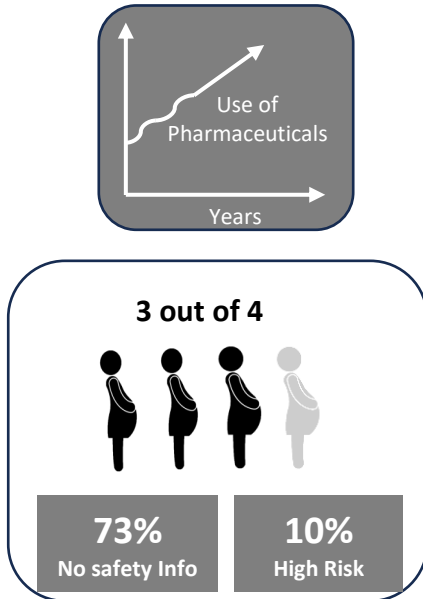
Abostait et al., (2024) Journal of Controlled Release, 376.

Abostait, Tyrrell, et al. (2022) Molecular Pharmaceutics, 16.

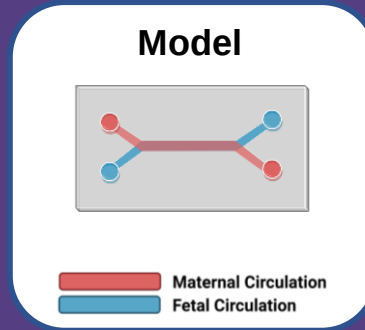
Ali, et. al. (2021) ACS Applied Bio Materials, 6.

Maternal and Fetal Health





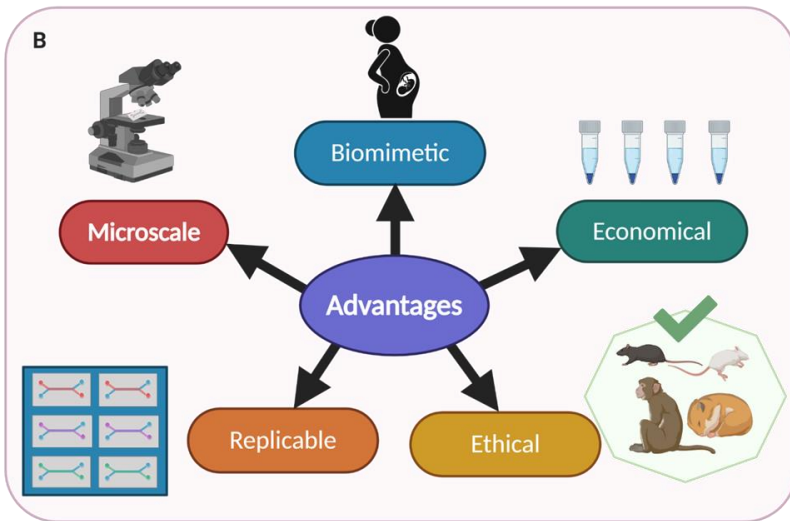
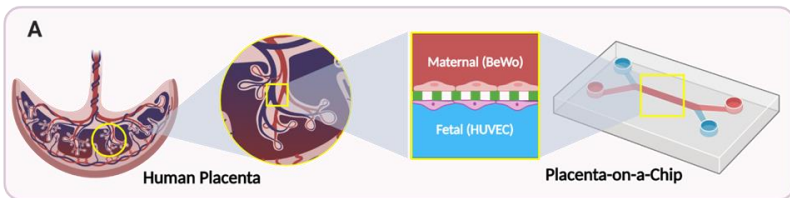
How to Develop A Biomimetic Placental Model?



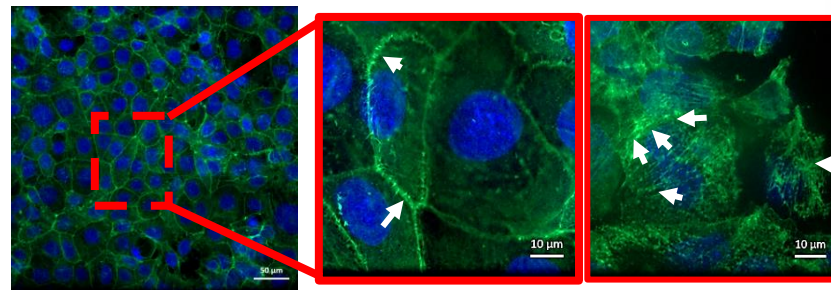
Placenta-on-chip model



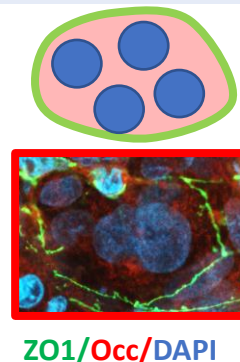
Jack Tyrrell



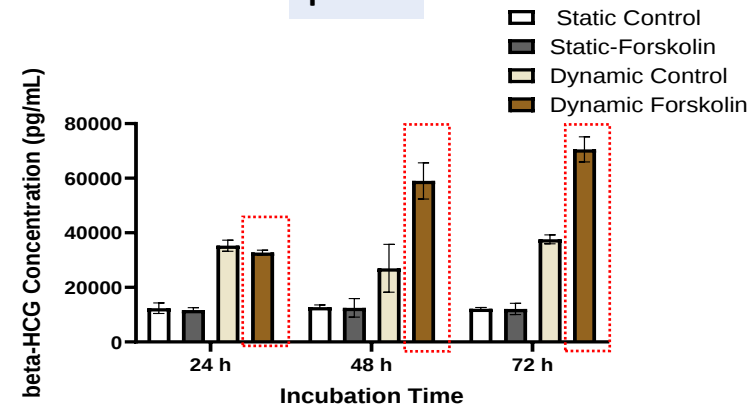
Microvilli formation

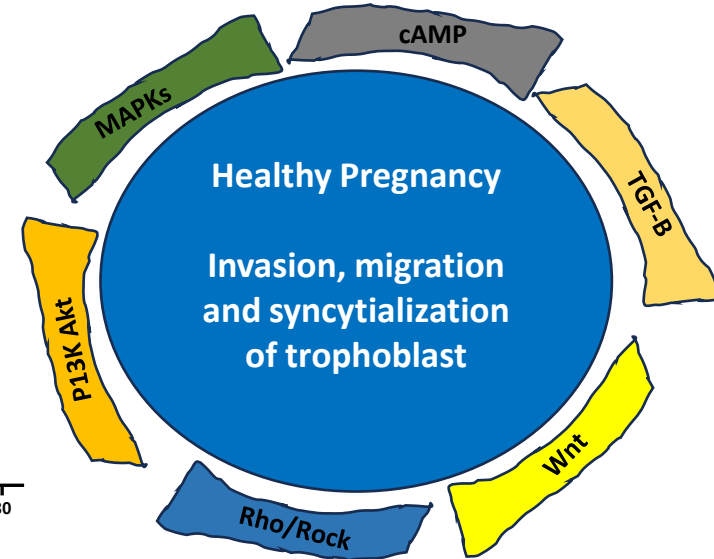


Syncytialization

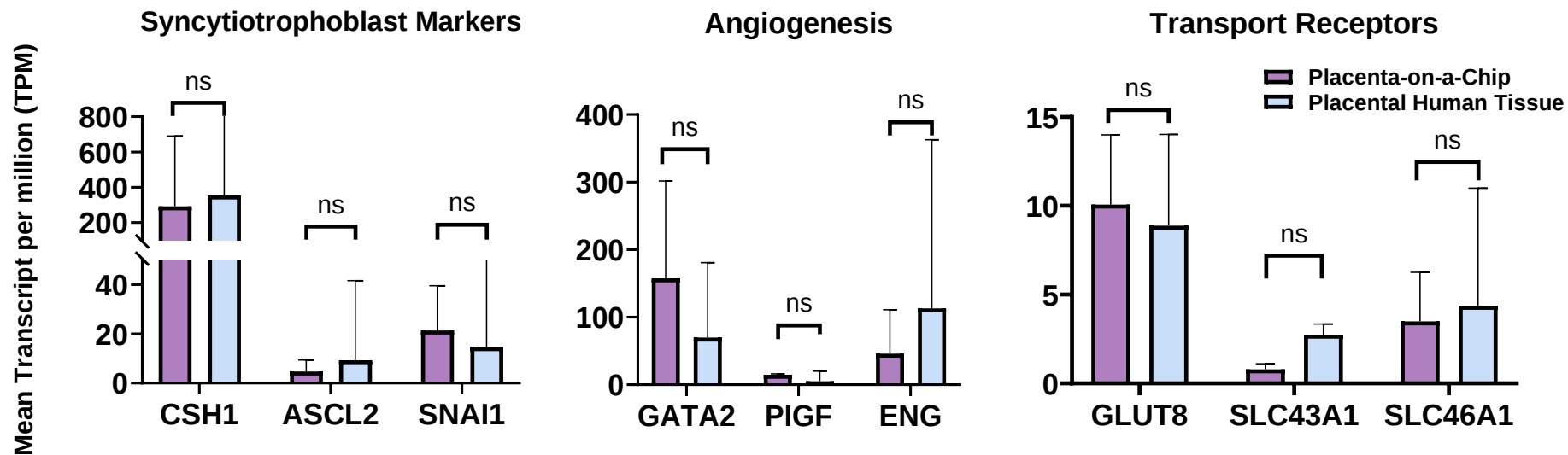


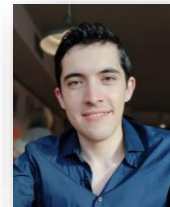
β -HCG





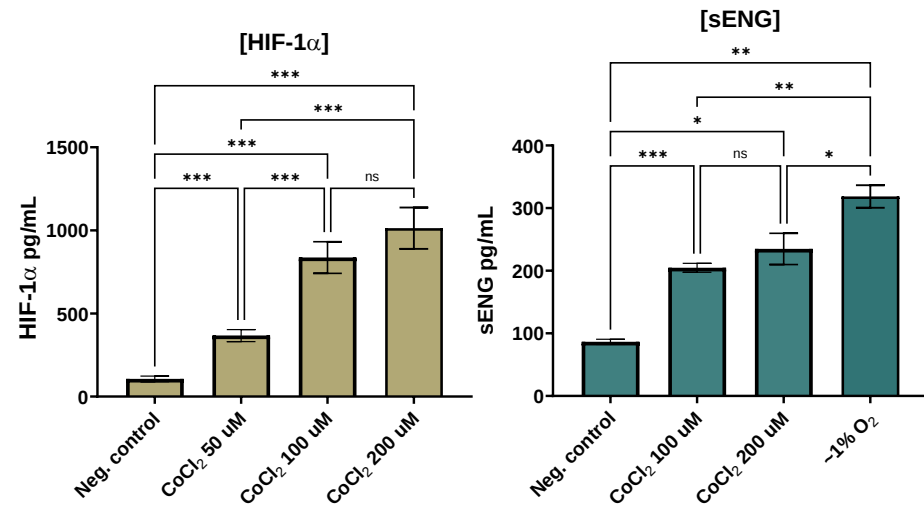
Placenta-on-a-chip recapitulates key markers in human placental tissues



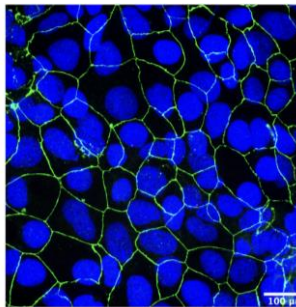


Luis Davalos

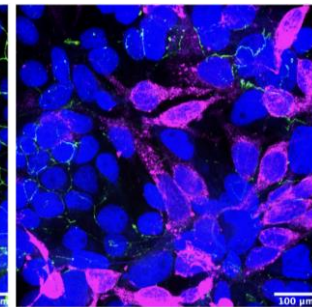
Hypoxic Placenta-on-a-Chip Recapitulates Biomarkers of Preeclampsia



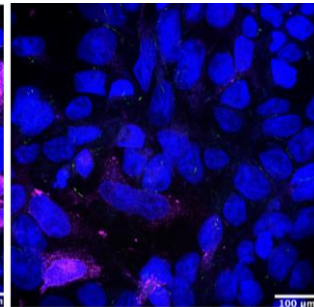
Negative Control



Positive Control



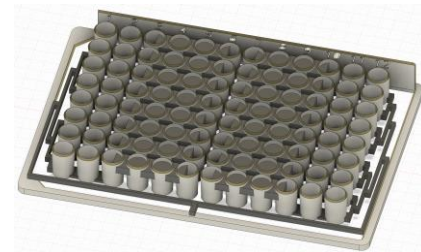
Hypoxia



CELL NUCLEI – HOECHST 33342

TIGHT JUNCTIONS – ZO-1/AJ 48A

SYNCYTIALIZED CELLS (βHCG)

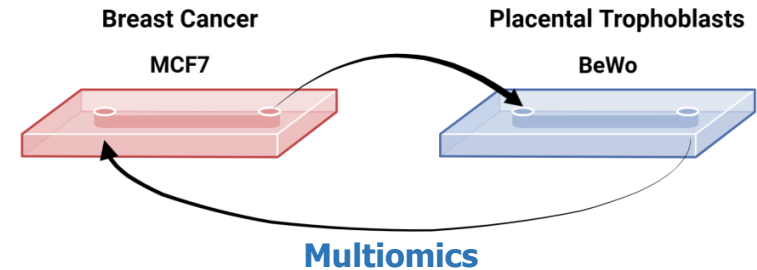
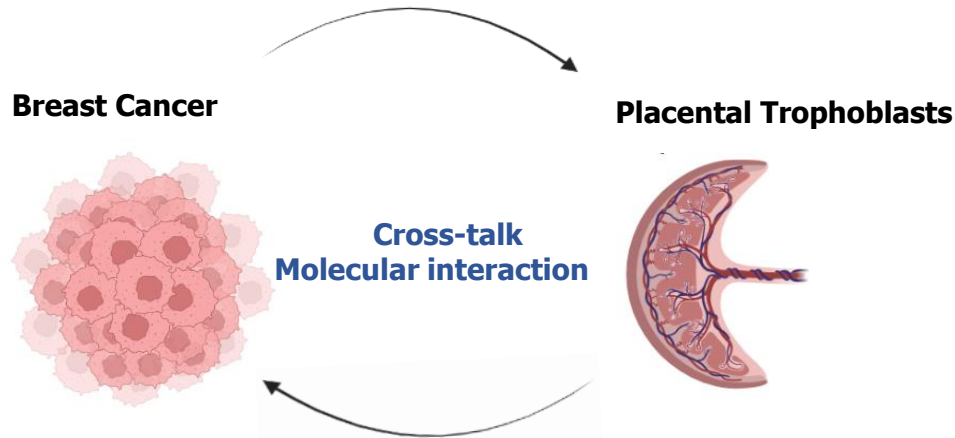
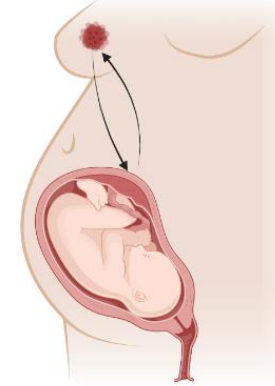


Pregnancy-Associated Breast Cancer (PABC)-on-a-Chip



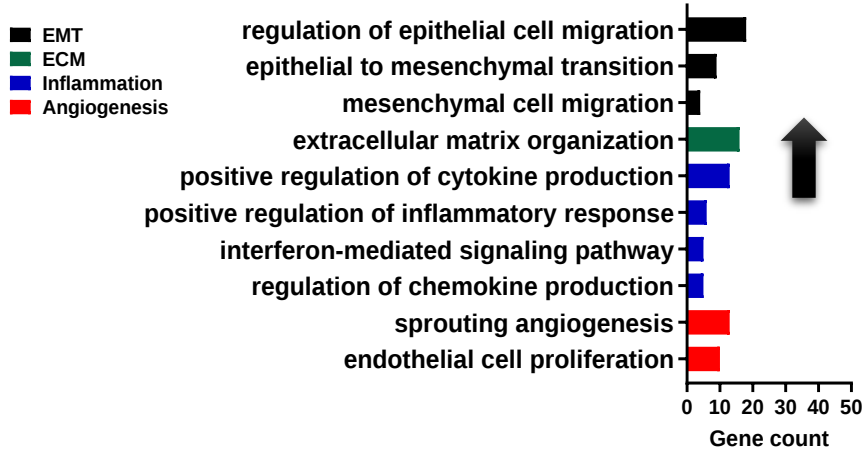
Yasmin Abdelkader

- Most common cancer in pregnancy.
- 5-year survival in PABC (stage III) is 10%
For non-pregnant patients (stage III) survival rate is 72%.



PABC is a metastatic Tumour

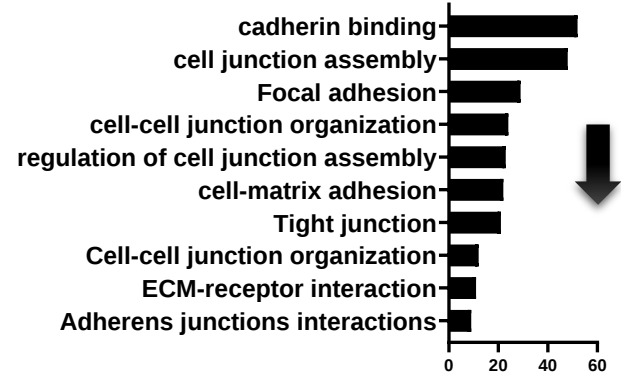
Enhanced Angiogenesis, EMT and Inflammation



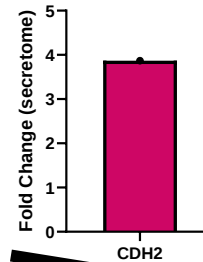
Clinical observations show higher metastasis rates in PABC patients.

Gamble, npj breast cancer, 2023
Jo et al . Cancers 2022.

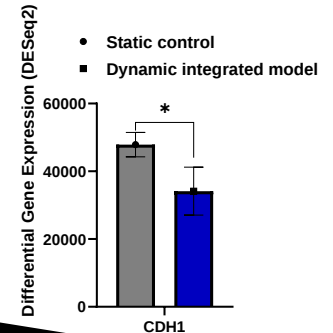
Downregulation of Adherens junction Pathways



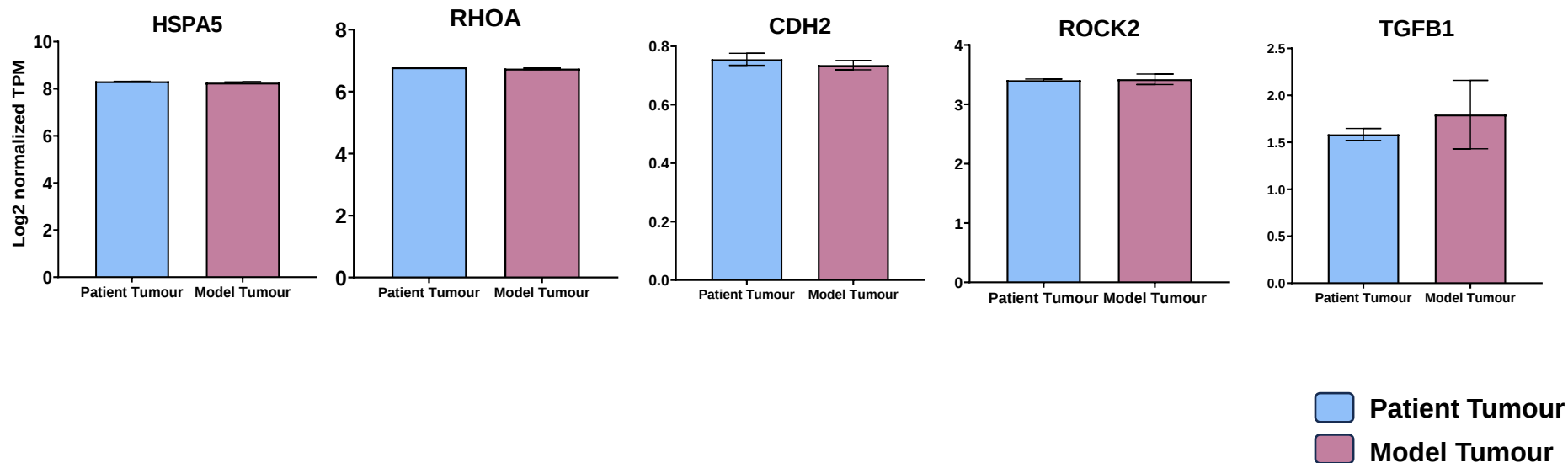
N-Cadherin
Mesenchymal marker



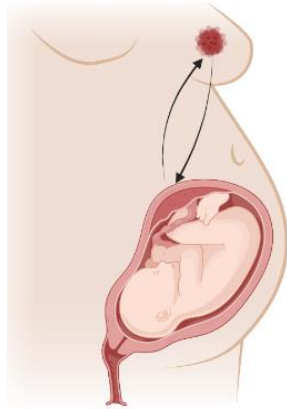
E-Cadherin
Epithelial marker



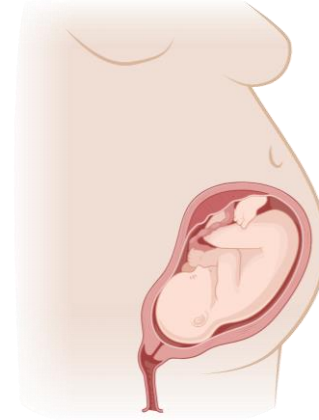
PABC-on-a-chip recapitulates key markers in human PABC tissues



How placenta in PABC differs from healthy pregnancy?



Vs



Breast Cancer

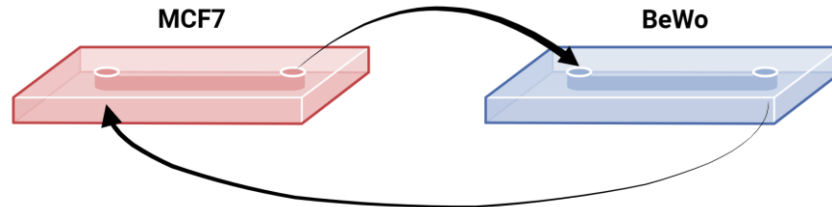
MCF7

Placental Trophoblasts

BeWo

Placental Trophoblasts

BeWo





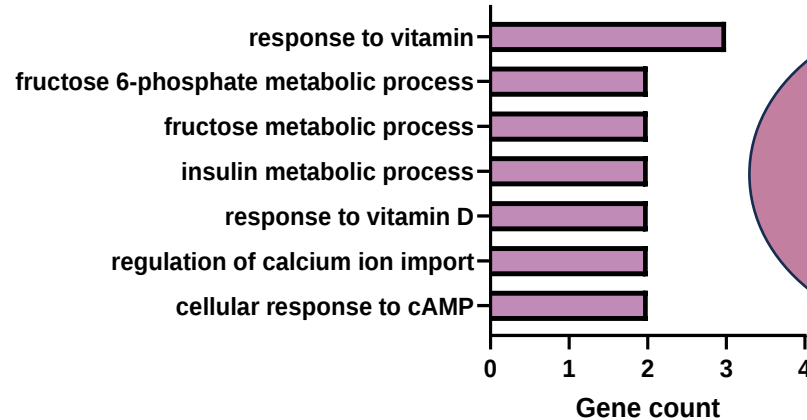
Actin cytoskeleton

Cell Transporters

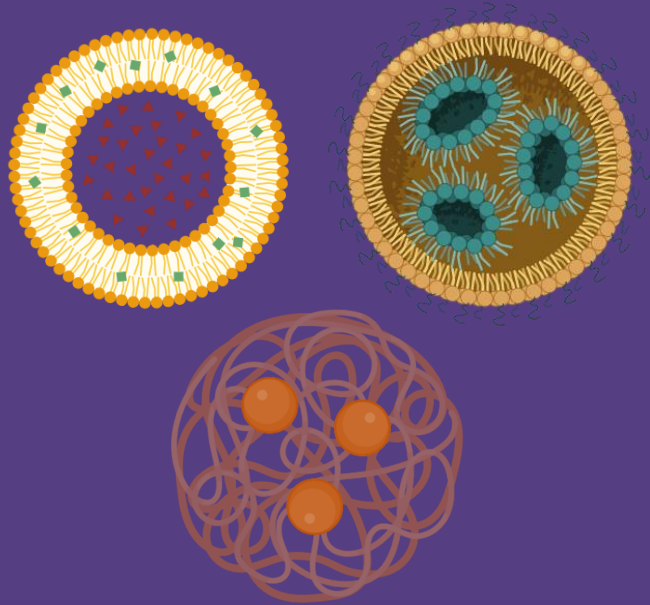
Angiogenesis

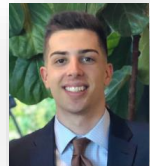
Hormonal secretion

STC1 affected pathways



Prenatal Delivery Systems





Jack Tyrrell



Pauline Chavrier

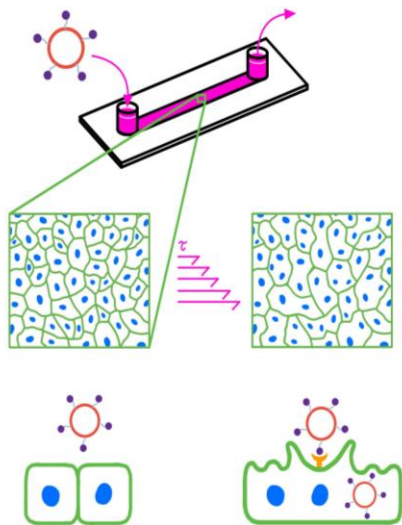
Amr Abostait



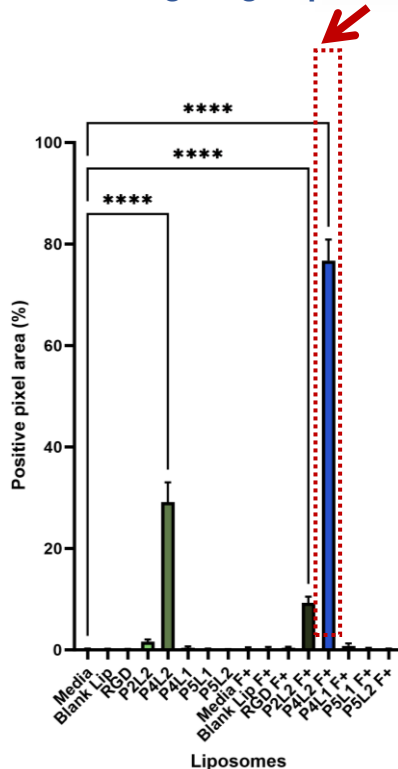
Andrew Tse

Shear Stress-dependant Placental Delivery

placenta-targeted
liposomes

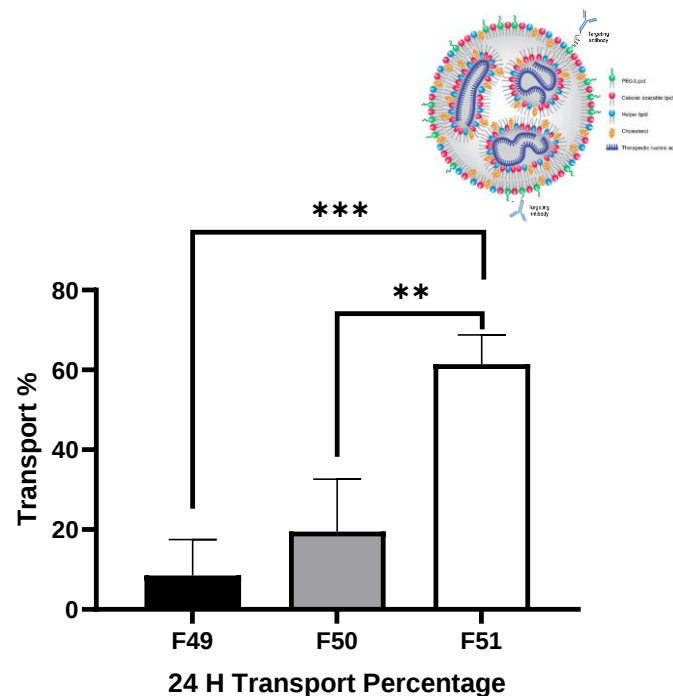


Novel Targeting Peptides



Unpublished

Fetal Drug Delivery



Tse et al., (2022) Biomaterials Science,18.

Abostait et al., (2024) Journal of Controlled Release, 376.

Abostait, Tyrrell, et al. (2022) Molec. Pharm, 16.

EDITORIAL



Defining the landscape of prenatal nanomedicine and a roadmap for future research

Hagar I. Labouta ^{a,b,c}

PRENATAL NANOMEDICINE



Address Physiological Changes in Pregnancy: e.g.

- Pregnancy-Associated Plasma Proteins
- Immune Modulation
- Placental Secretions



Maximize Fetal and Maternal Safety: e.g.

- Fetal and Maternal Un-intended Exposure
- Un-intended Modulation of Placental Barrier and Secretory Functions
- Long-term Developmental Effects



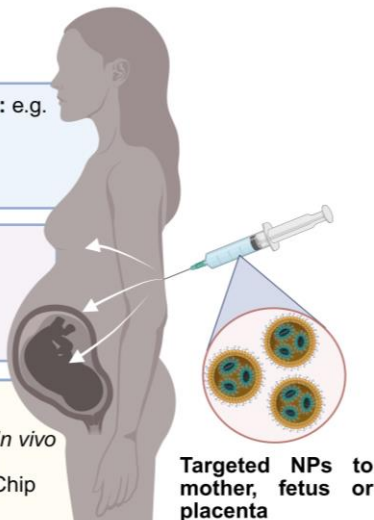
Generate Pregnancy-Associated Models: e.g.

- Integrate Complementary *In vitro*, *Ex vivo* & *In vivo* Models to address Model-Specific limitations
- Validate Pregnancy-associated Organ-on-a-Chip Models



Collaborate with Clinicians and Regulators: e.g.

- Capitalize on translation of lipid NP-based COVID-19 vaccines for use during pregnancy
- Develop Regulatory Guidelines



Intra-amniotic injection



Ex vivo fetal lung



Collaborators:

Christine Allen (University of Toronto)
Teodor Veres, Lidja Malic & Ben Moon (NRC)
Kelsie Thu (University of Toronto)
Howard Berger (University of Toronto)
Tina Buerki-Thurnherr (EMPA)
Max Anikovskiy (University of Calgary)
Richard Keijzer (University of Manitoba)

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Microfluidics Drives Innovation in
Delivery Technologies and Preclinical Testing

Co-editors: Hagar Labouta & Milica Radisic