



Adipose Tissue Biology and Nutrient Metabolism Core (ABM)

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Purpose of ABM Core

Facilitate and foster research on mechanisms regulating adipose tissue mass, distribution, nutrient signaling and depot-specific metabolic and endocrine functions in health and disease.

Provide easy and cost-effective access to carefully quality controlled rodent and human preadipocytes and adipocytes, and banked cell and tissues.

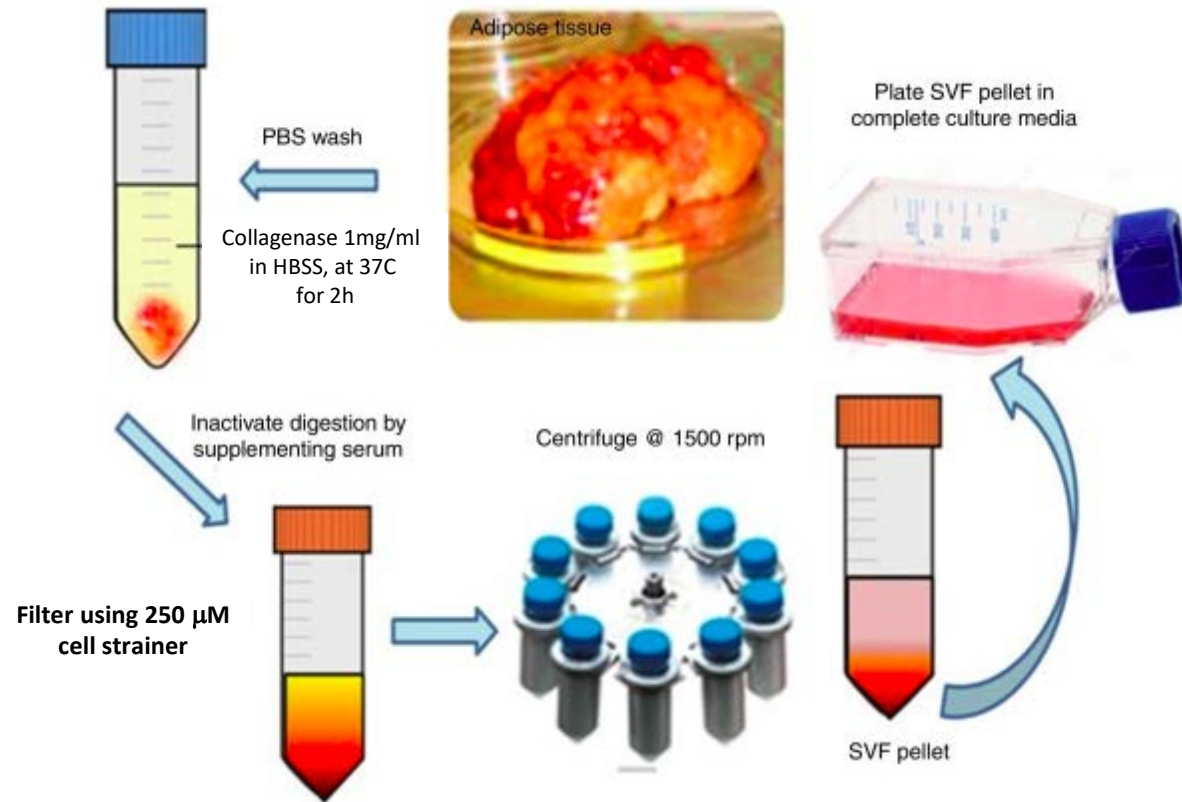
Develop and standardize methods in adipocyte biology as needed by our research base in this rapidly evolving field.

Provide consultative advice, support and training for new investigators and established investigators from the nutrition and obesity fields, as well as other fields, who wish to understand the role of adipose tissues and adipocytes in their clinical/translational studies or model systems.

SERVICES PROVIDED BY THE CORE

Adipose tissue and stromal cells procurement and processing

- Patient Consent.
- Bariatric surgery – surgeon gives pieces of subcutaneous, omental and mesenteric adipose tissues.
- Small piece of each cut for immediate freeze in LiqN₂ , rest is dropped into separate 50ml tube with media.
- Return to core lab for further processing.



- SVF plated on p60 (subcut and mesent) and p100 (omental) and grown to 60% confluent.
- Split cells into 2 (subc and mesent) or 3 p100 plates and grow to 60% confluent.
- Split cells into vials for storage (passage 1) or into p100plates expansion to 60% confluent.
- Repeat for passage 2 and eventually passage 3 stocks.

Lee, MJ and Fried, SK. Optimal Protocol for the Differentiation and Metabolic Analysis of Human Adipose Stromal Cells. [Methods Enzymol. 2014; 538: 49-65](#)

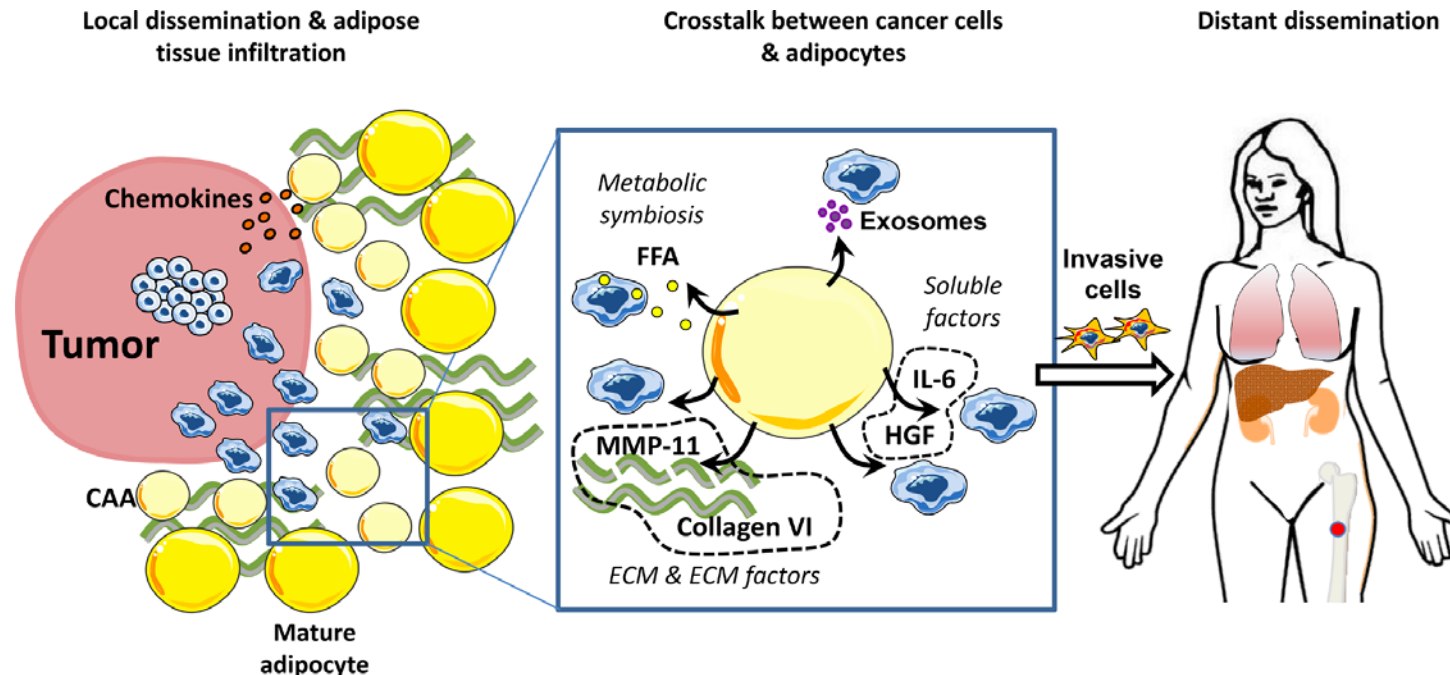
Consulting and collaborations

1. Andrew Emili - Professor Biochemistry BUSM

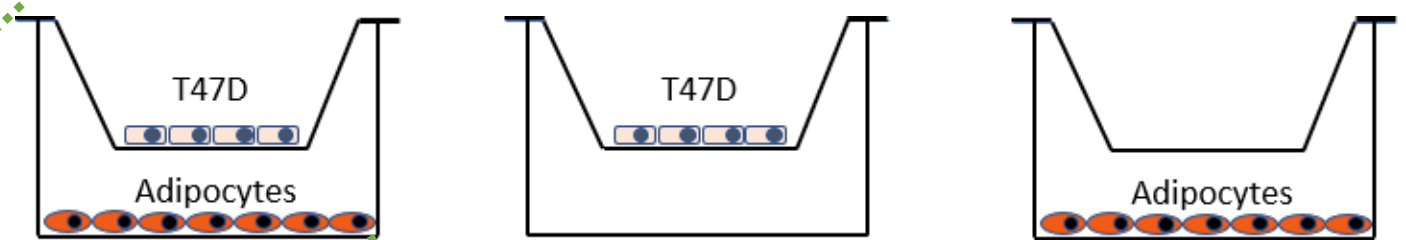


Define the proteome, phosphoproteome and secretome of adipocytes obtained from different depots of normal, prediabetic and diabetic individuals.

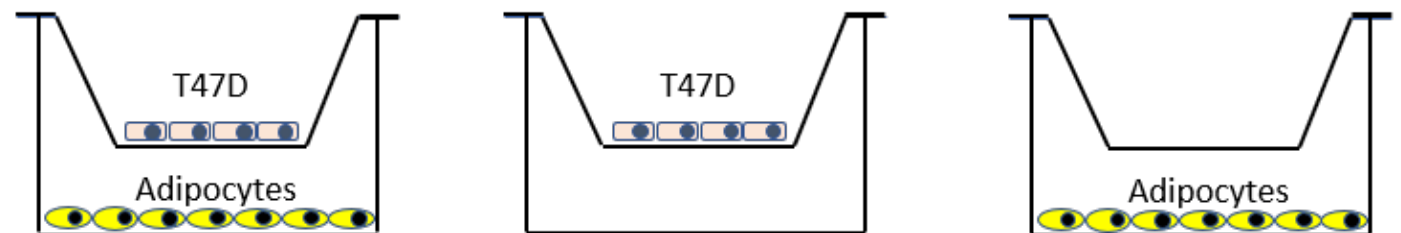
Focus is on adipocytes from mammary adipose of individuals with breast cancer.



Breast cancer + Obese/Non-Diabetic adipocytes



Breast cancer + Obese/Diabetic adipocytes



Transwell insert

Breast cancer cells

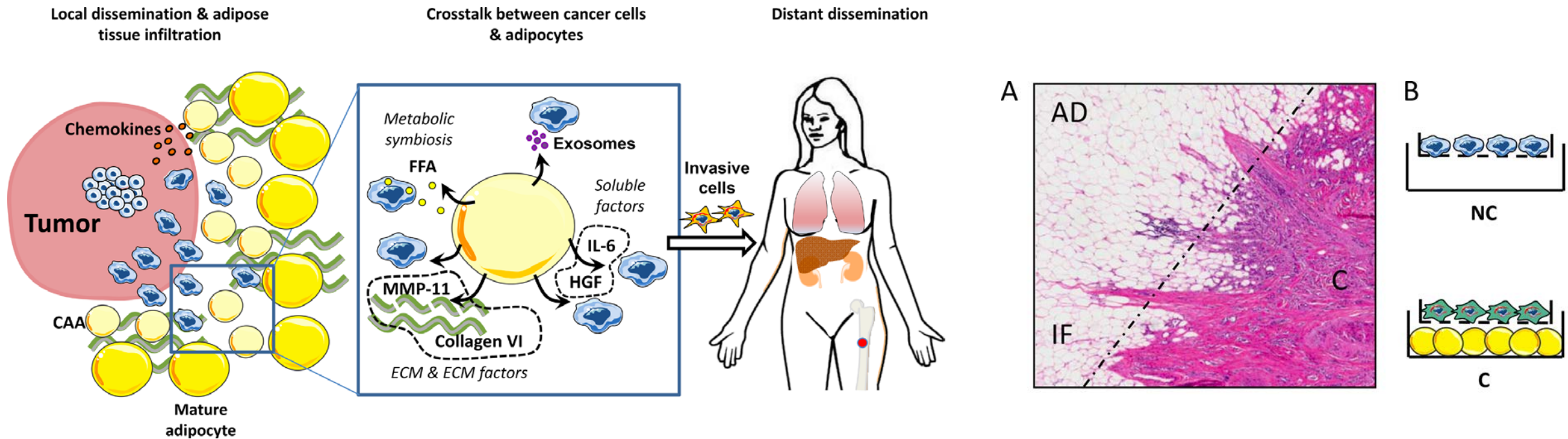
0.4 μm membrane

Adipocytes

Consulting and collaborations

2. Gerald Denis - Associate Professor, Medicine, BUSM

Determine how insulin resistant breast adipocytes drive EMT, invasion and metastasis in ER+ breast cancer.



Consulting and collaborations

3. Carmen Escobedo - visiting PI with Chris Chen (BU) and at the Wyss Institute.

Developing adipose tissue on a chip of human adipocytes from lean and obese individuals.

She requests hands on training in preadipocyte isolation to establish culture under different 3D culture conditions.

Consulting and collaborations

4. MNORC (Michigan) - Ormond McDougall and Carey Lumeng.

Collaborative arrangement between ABM cores of BNORC and MNORC.

BNORC can provide MNORC with samples when available.

MNORC can provide samples from surgical patients

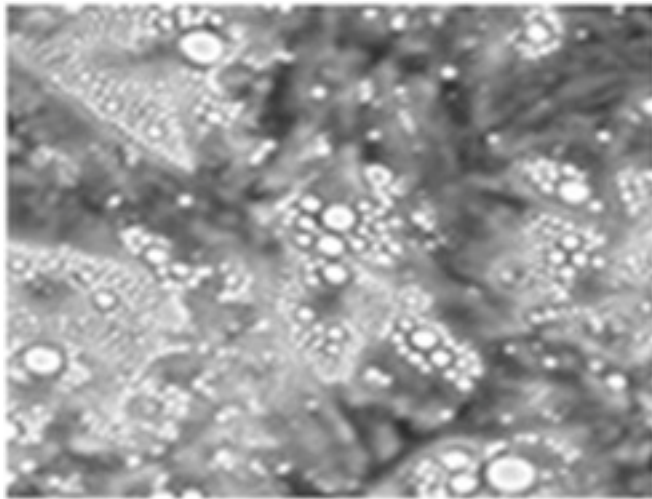
EMERGING TECHNOLOGIES

1. Establish conditions to enhance differentiation of omental adipose stromal cells.
2. Establish conditions to promote differentiation of stromal cells into beige/brite adipocytes.
3. Formation of Organoids from Human Adipose Stromal Progenitors.

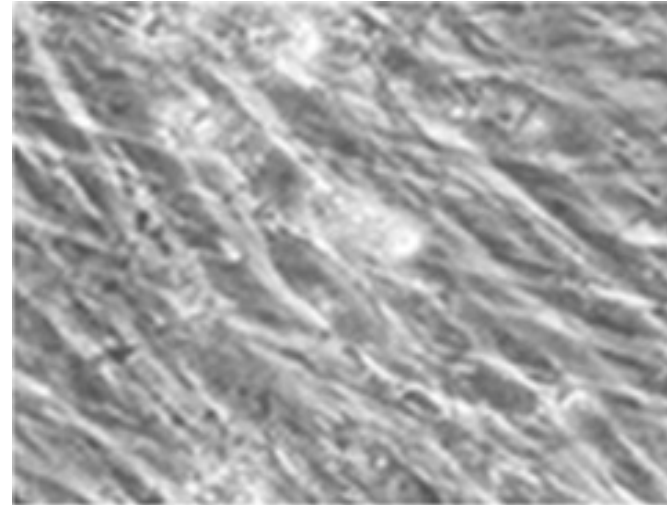
Establish conditions to enhance differentiation of omental adipose stromal cells.

Omental SVF differentiates poorly compared to subcutaneous SVF.

Subcutaneous



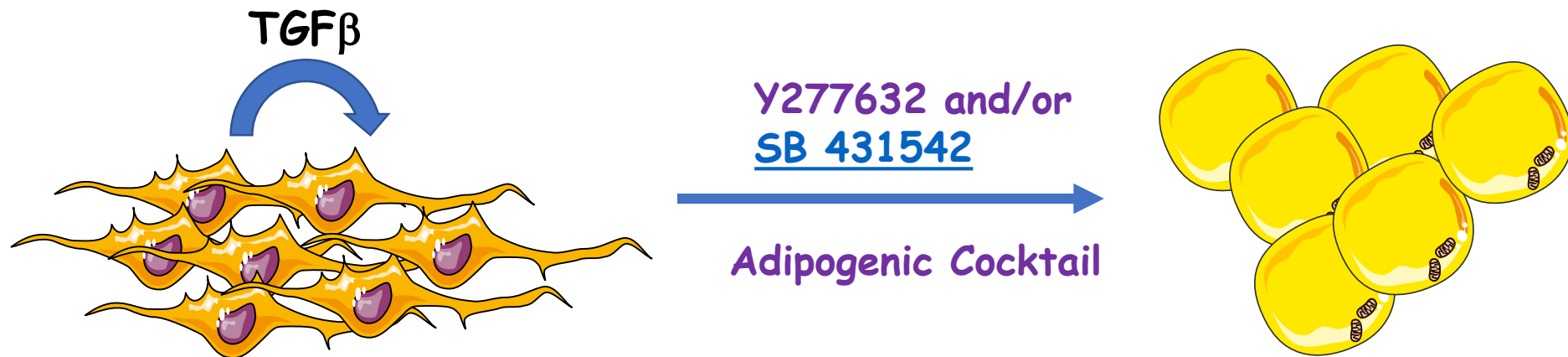
Omental



Lee MJ et al., Impaired Glucocorticoid Suppression of TGF β Signaling in Human Omental Adipose Tissues Limits Adipogenesis and May Promote Fibrosis. *Diabetes*, 68:587,2019.

Establish conditions to enhance differentiation of omental adipose stromal cells.

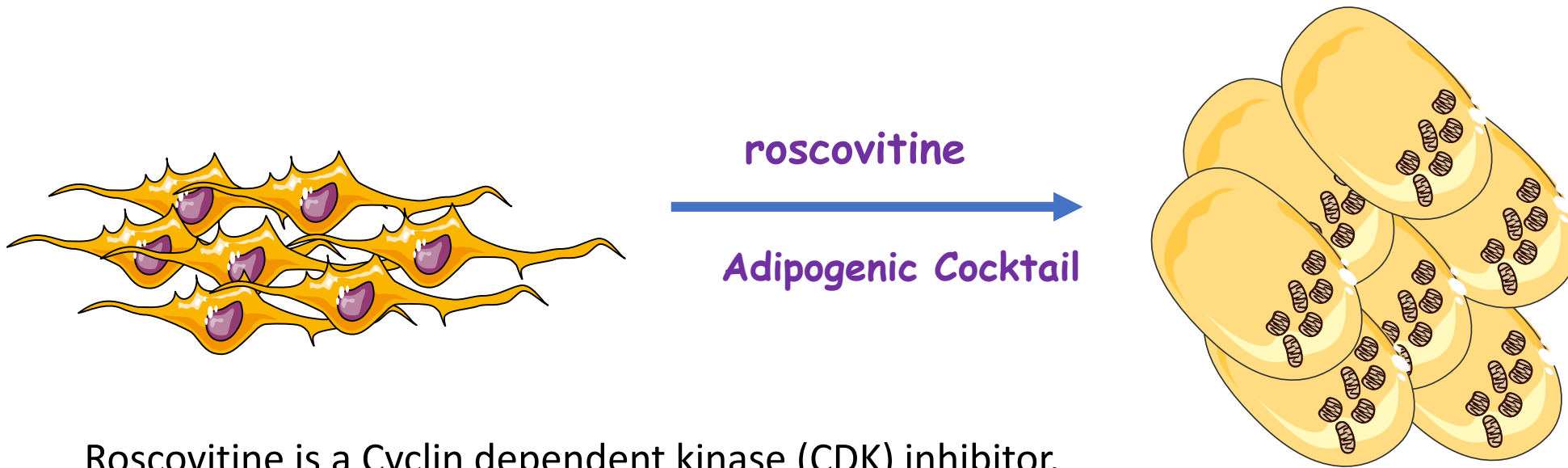
Recent data from Fried and collaborators suggest that the extracellular matrix produced by other omental stroma cells inhibits differentiation by activating TGF β signaling.



Strategy: Expand omental SVF in presence of inhibitors of ECM production as well as blocking TGF β receptors.

Promote the differentiation of stromal cells into beige/brite adipocytes.

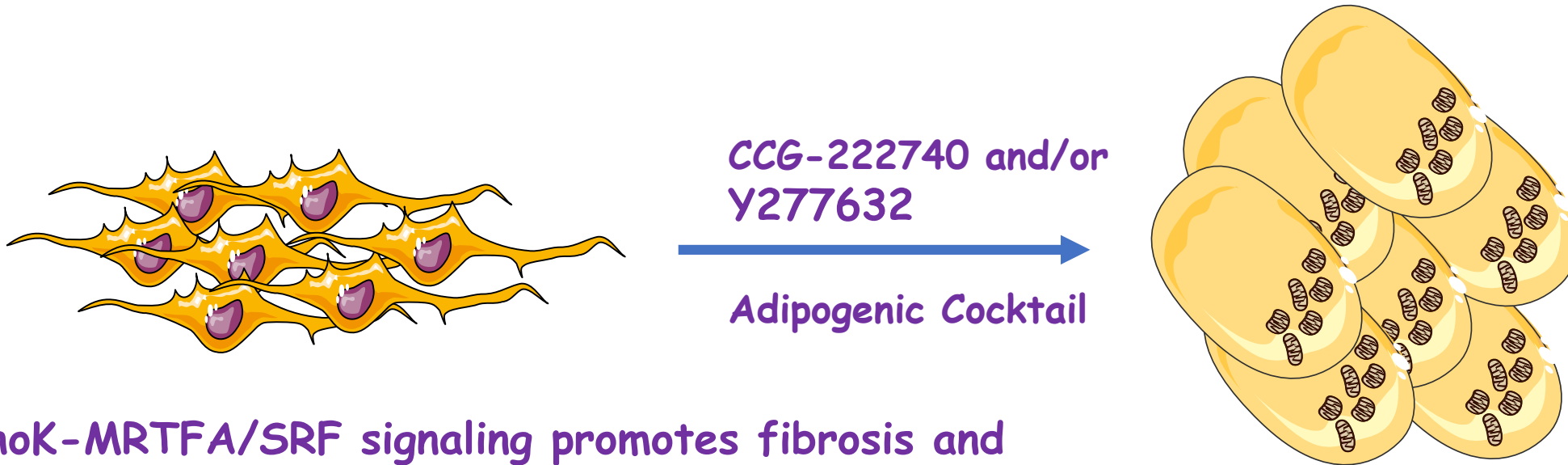
1. Browning of white adipose tissue with Roscovitine induces a distinct population of UCP1+ adipocytes Wang et al. *Cell Metabolism*, 24:835 (2016).



Roscovitine is a Cyclin dependent kinase (CDK) inhibitor.
CDKs block the browning activity of PPAR γ

Promote the differentiation of stromal cells into beige/brite adipocytes.

2. McDonald et al., (2015) Myocardin-related transcription factor A (MRTFA) regulates conversion of progenitors to beige adipocytes. *Cell*,160:105



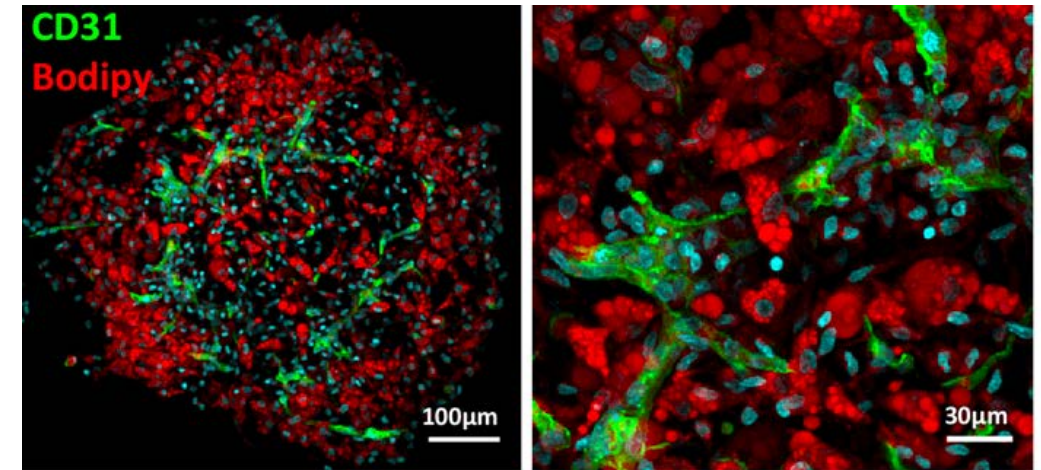
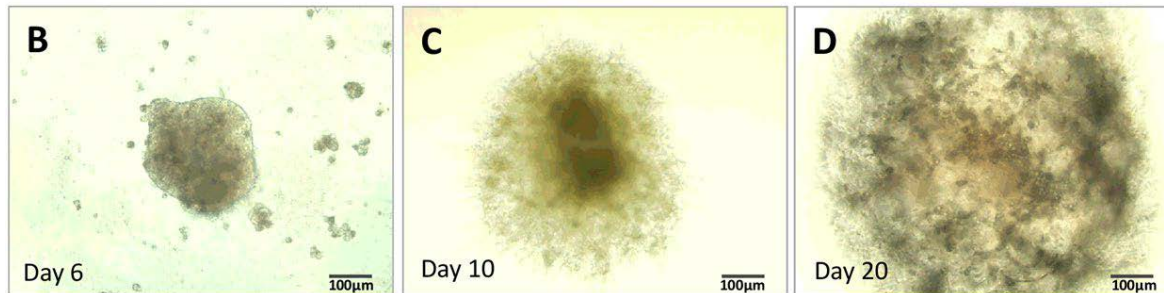
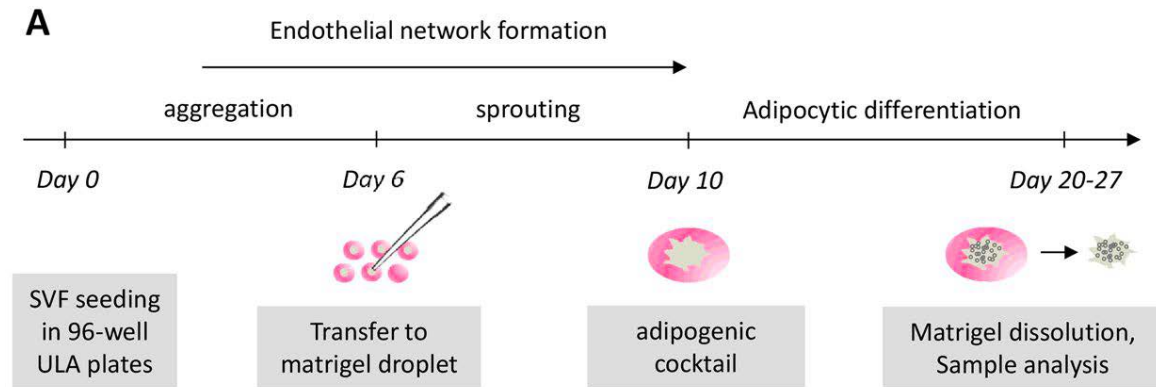
RhoK-MRTFA/SRF signaling promotes fibrosis and suppress beige adipogenesis.

Y222740 is a Rho kinase inhibitor

CCG222740 is a MRTF/SRF inhibitor

Formation of Vascularized Adipose Organoids

Mueller et al, Human adipose stromal-vascular fraction self-organizes to form vascularized adipose tissue in 3D cultures. Sci Rep. 9:7250, 2019



Future Procurements.

Adipose tissue from lean individuals

Adipose tissue from mammary of normal and breast cancer patients