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NAPOLI 19-20 FEBBRAIO 2026**

IL MANAGEMENT DELL'OBESITÀ

RESPONSABILE SCIENTIFICO
MAURIZIO DE LUCA



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EVENTO ACCREDITATO ECM 468736
12 CREDITI FORMATIVI

IL TESSUTO ADIPOSO. Fisiopatologia e recenti frontiere farmacologiche

GABRIELLA MILAN

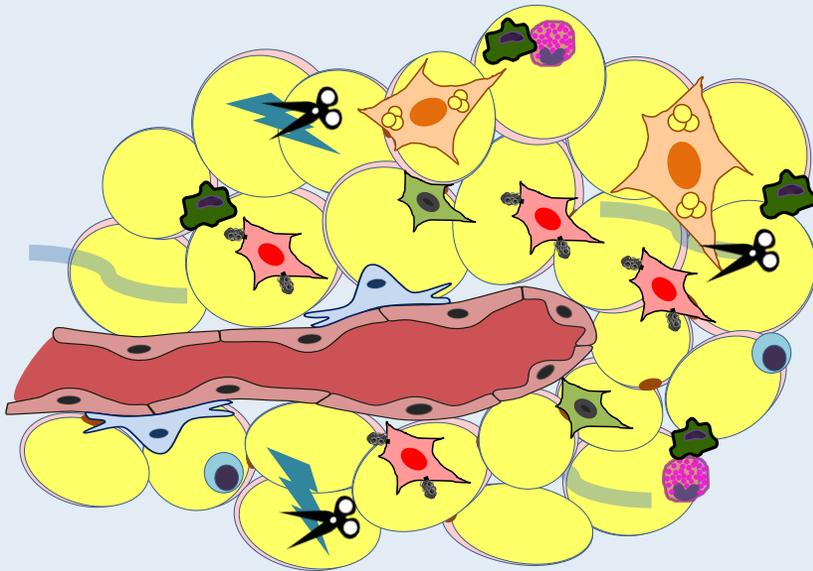
*Laboratorio Endocrino Metabolico
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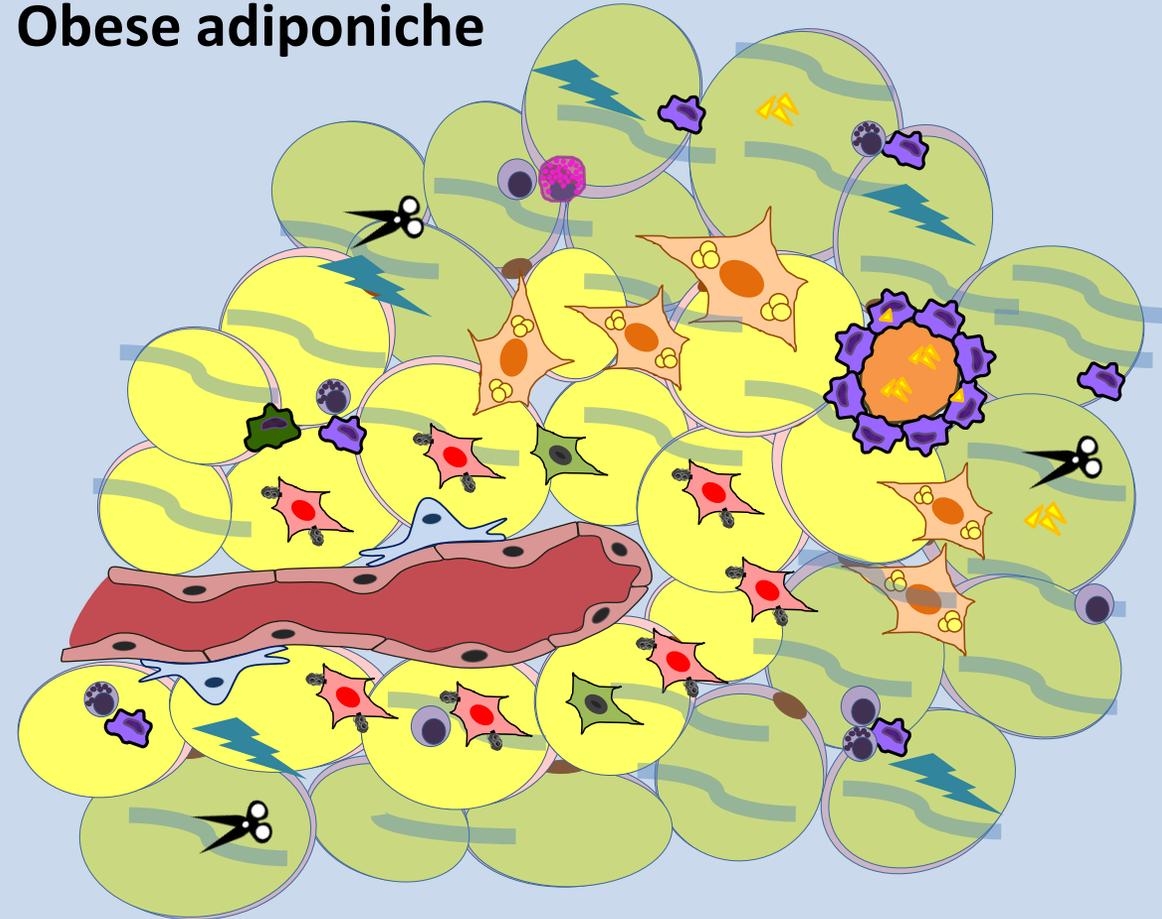
ASCs and their role in obesity and metabolic diseases

Gabriella Milan,^{1,2,*} Scilla Conci,^{1,2} Marta Sanna,^{1,2} Francesca Favaretto,^{1,2} Silvia Bettini,^{1,2} and Roberto Vettor^{1,2}

Lean adiponiche



Obese adiponiche





Adipose Stem Cell subpopulations



Differentiating preadipocyte



Pericyte/Mural cell



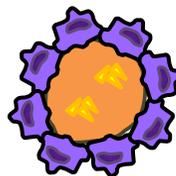
Endothelial and precursor cell



Antinflammatory cells



Proinflammatory cells



Crown-like structure



CD34



Lipid droplet



Eosinophil



M2 macrophage



T reg



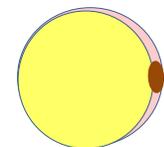
M1 macrophage



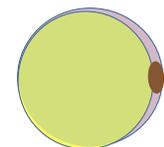
CD8 T cell



Th1 cell



Mature adipocyte



Hypoxic mature adipocyte



Extracellular matrix



Metalloproteinases



Cholesterol crystals



Normal oxygen tension



Hypoxia

Capillary density

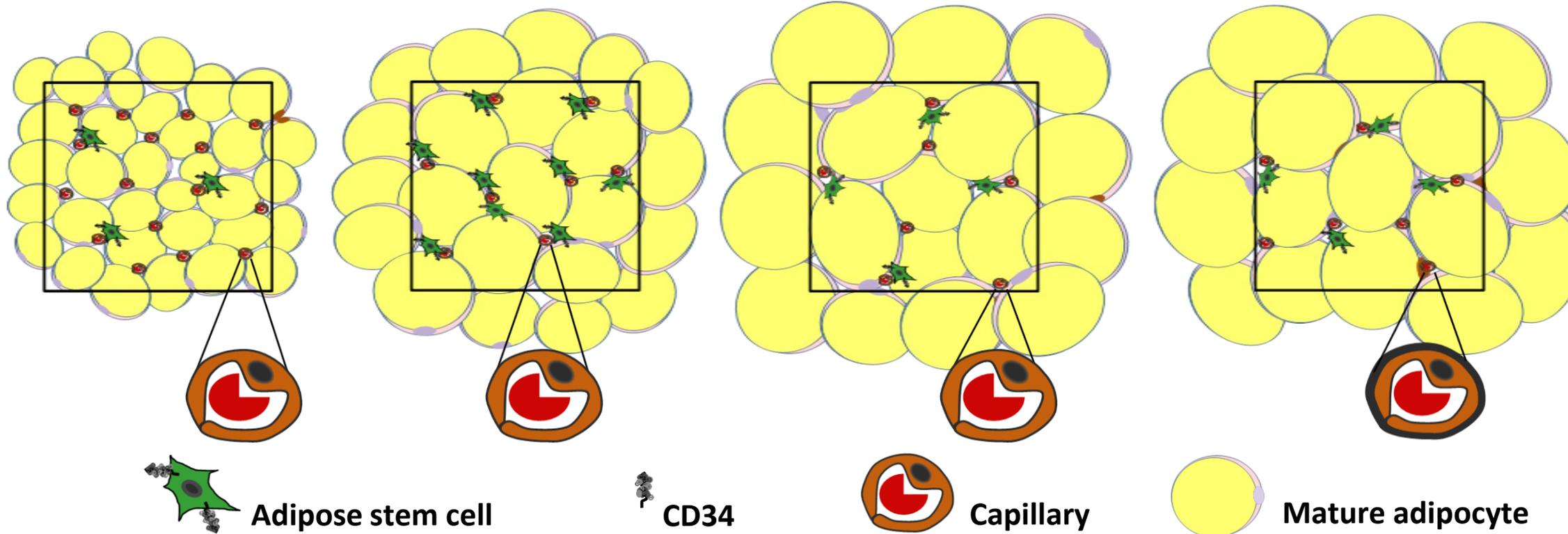
Adipocyte area

lean

ob N

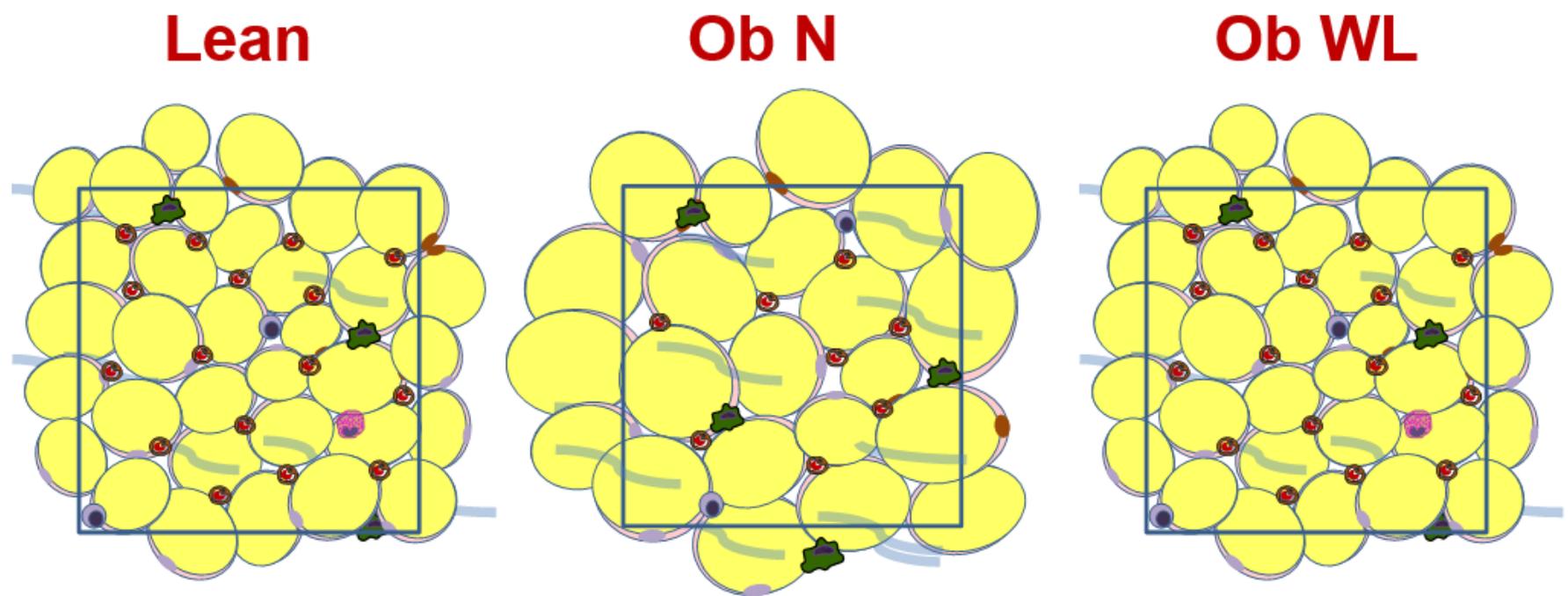
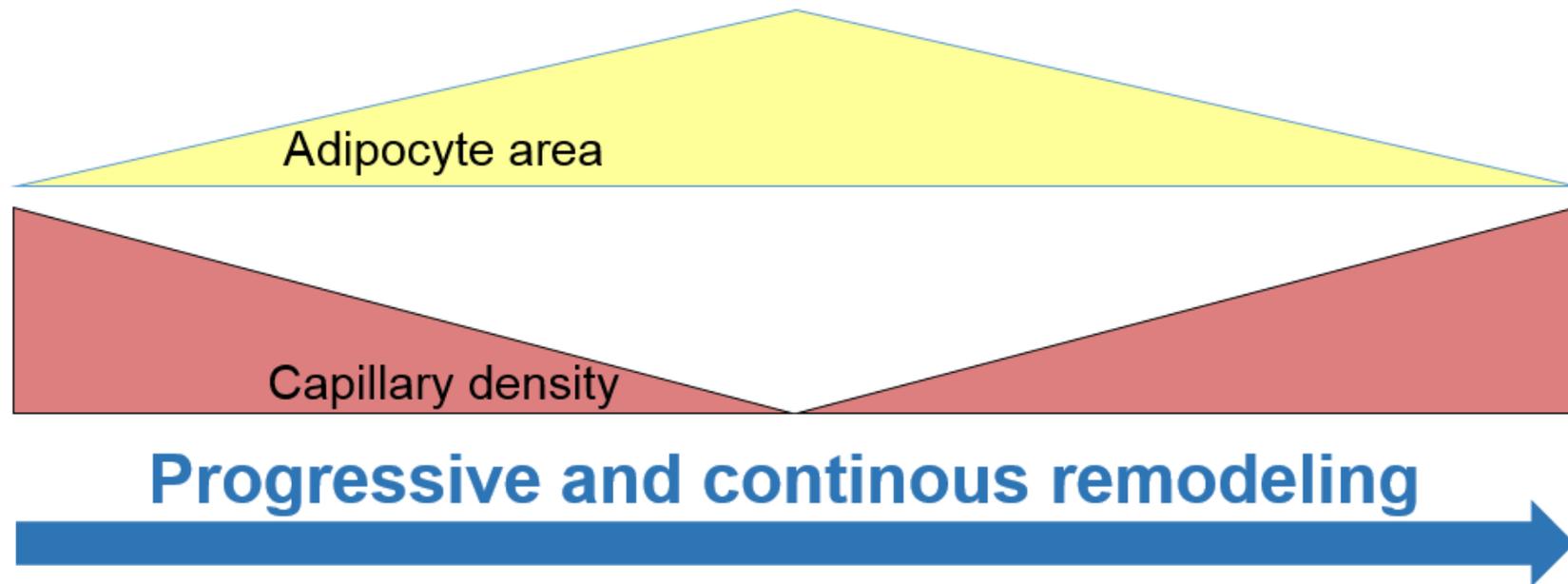
ob preDM

ob T2DM

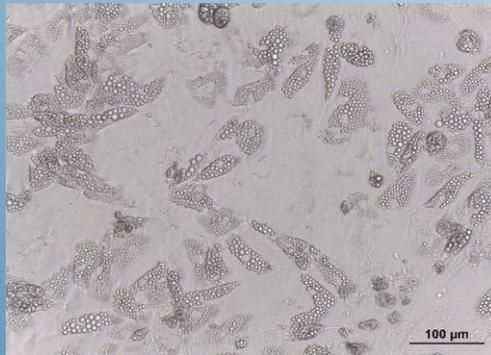
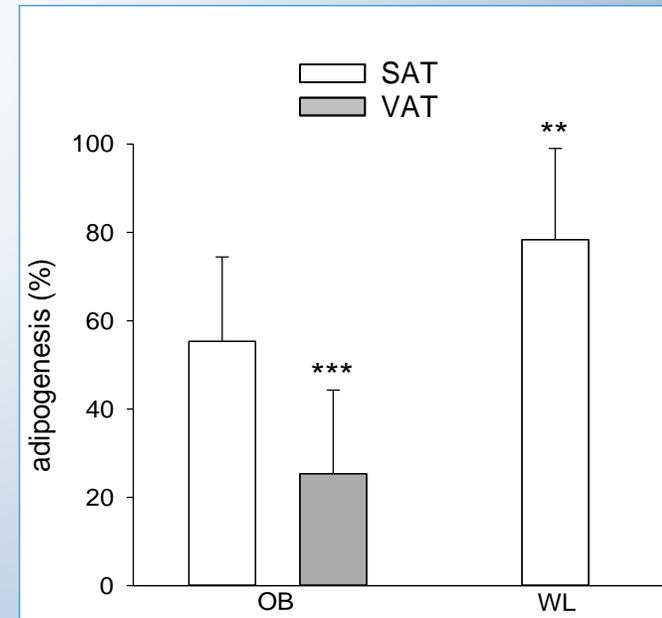
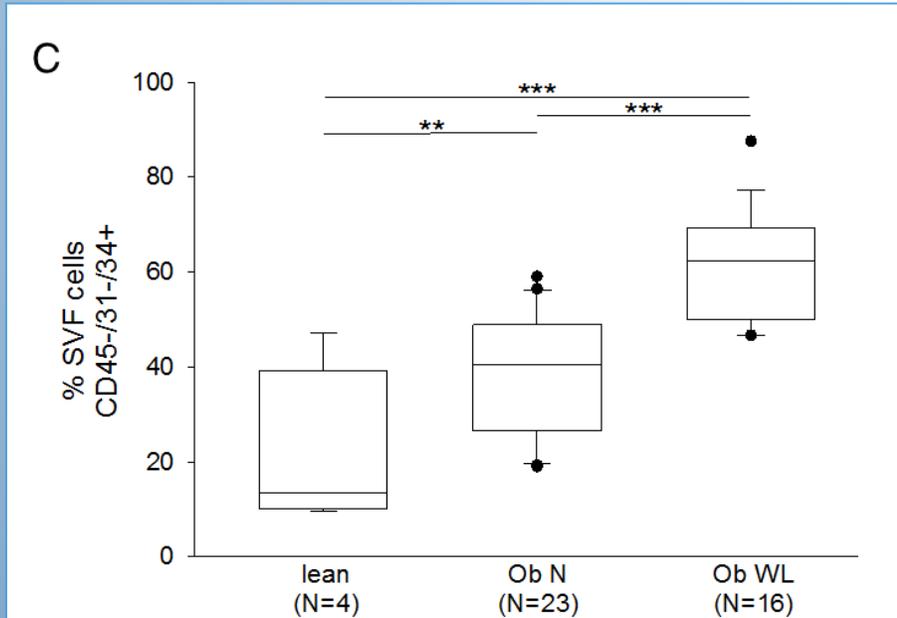


ADIPOSOPATHY

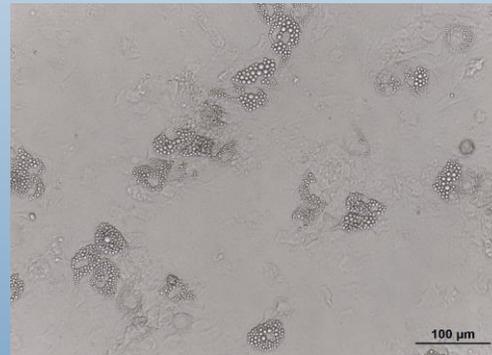
-  Mature adipocyte
-  Extracellular matrix
-  Capillary
-  Anti-inflammatory cells
-  Pro-inflammatory cells



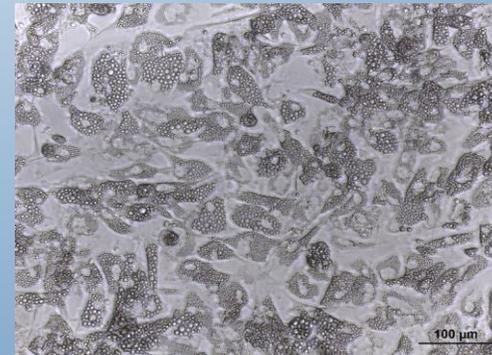
Adipose Stem Cells dopo calo ponderale (WL)



OB SAT



OB VAT



WL SAT

Safety profile of autologous adipose-derived stromal vascular fraction in clinical use: an exhaustive literature review

Review | [Open access](#) | Published: 30 January 2026

article number , (2026) [Cite this article](#)

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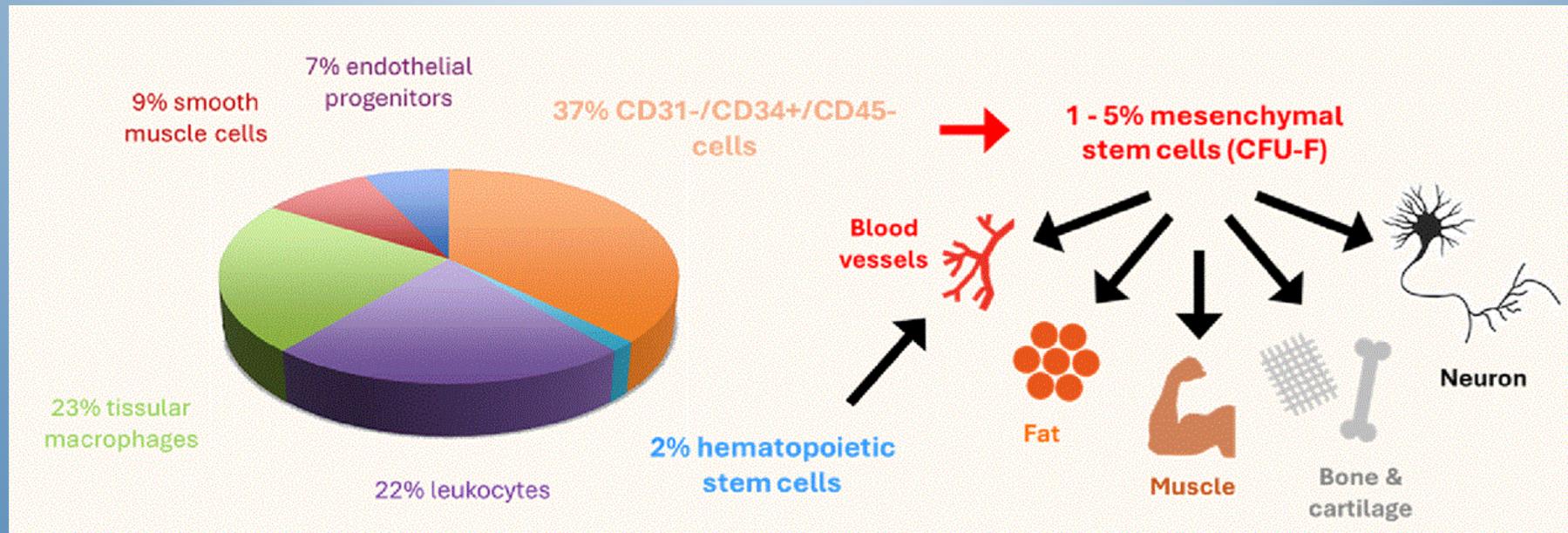
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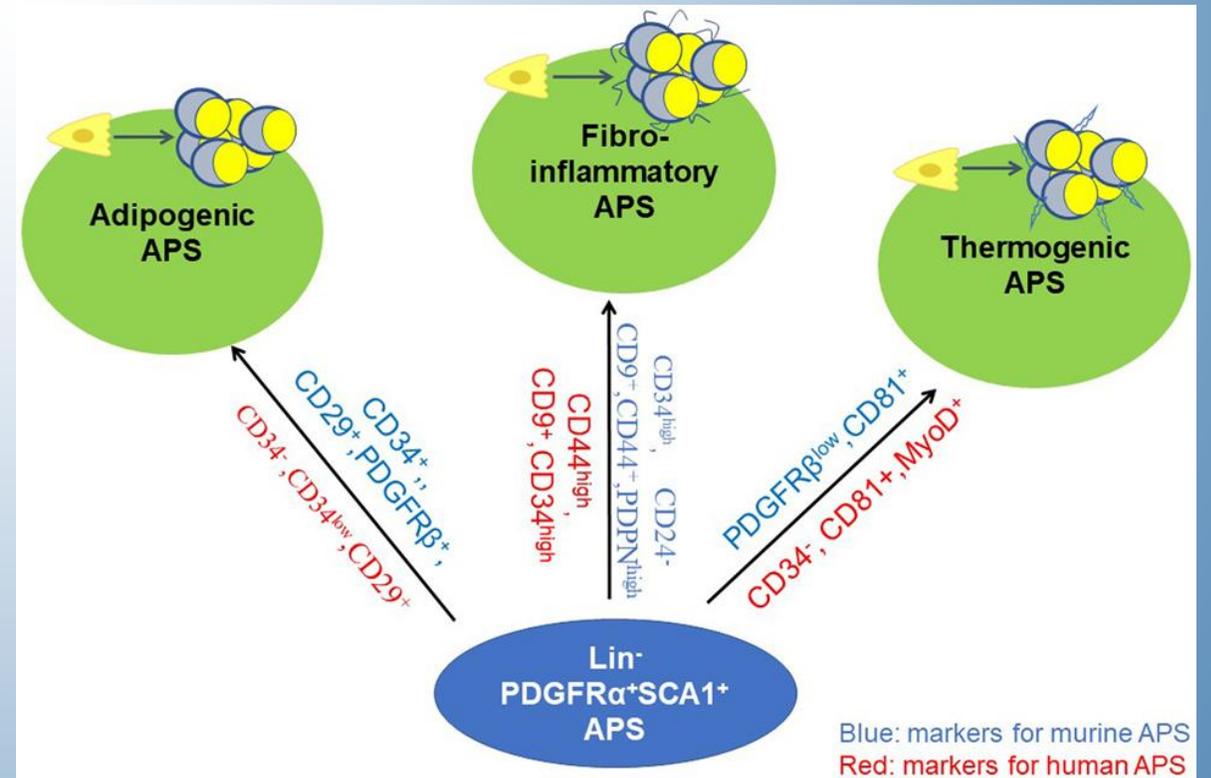
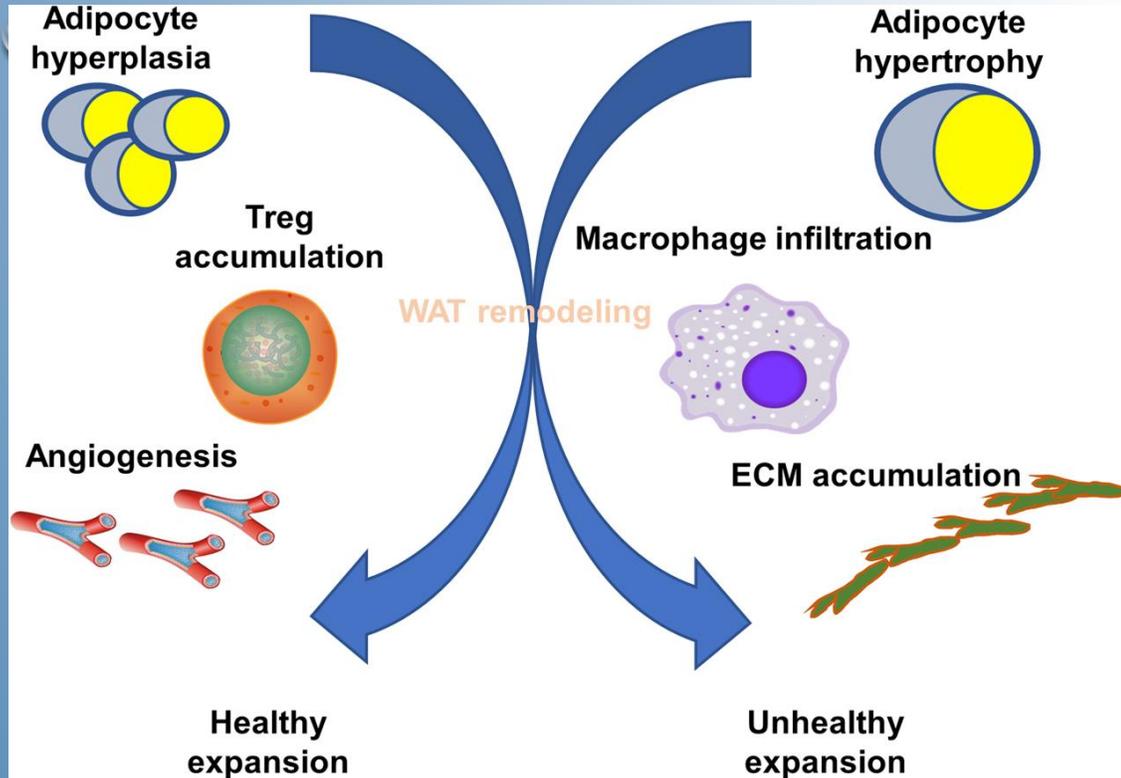


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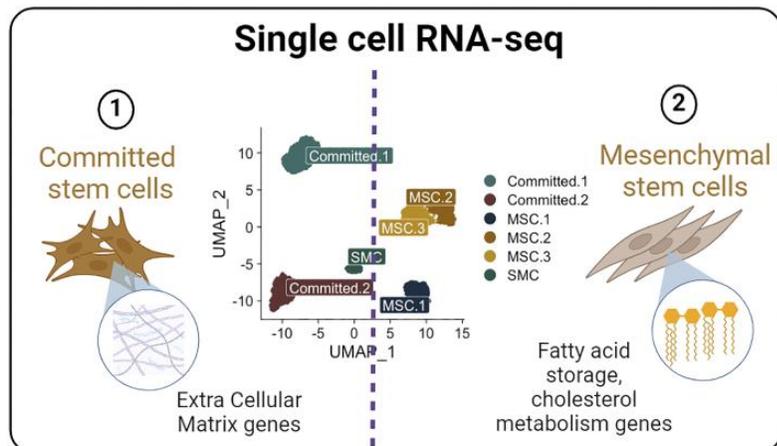
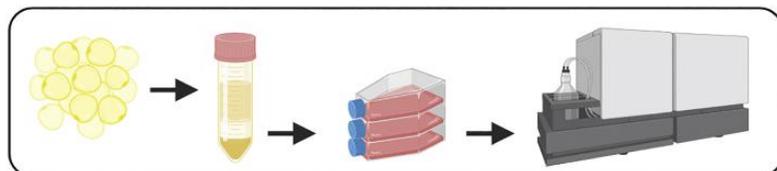
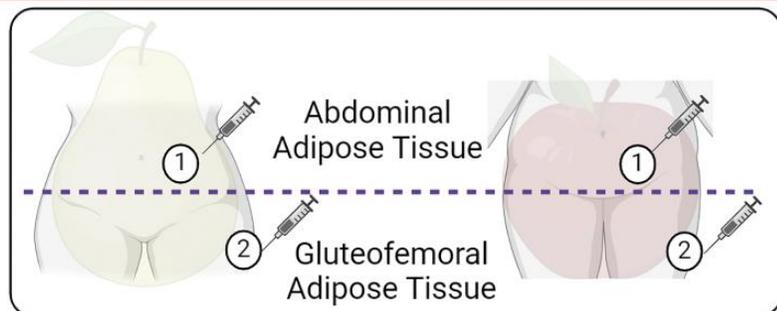
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Liu W, Li D, Cao H, Li H, Wang Y. **Expansion and inflammation of white adipose tissue - focusing on adipocyte progenitors.** *Biol Chem.* 2020 Oct 16;402(2):123-132.



Am J Physiol Cell Physiol 326: C1248–C1261, 2024.
First published March 4, 2024; doi:10.1152/ajpcell.00726.2023



AMERICAN JOURNAL OF PHYSIOLOGY
CELL PHYSIOLOGY

RESEARCH ARTICLE

Distinct subpopulations of human subcutaneous adipose tissue precursor cells revealed by single-cell RNA sequencing

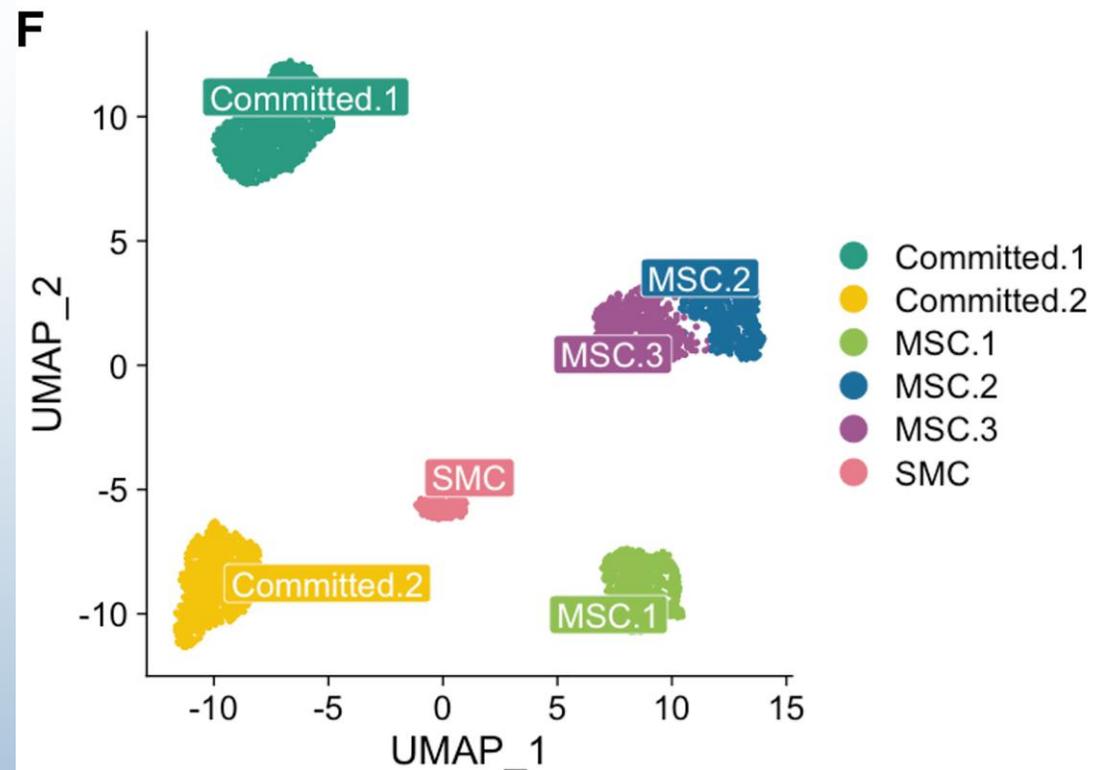
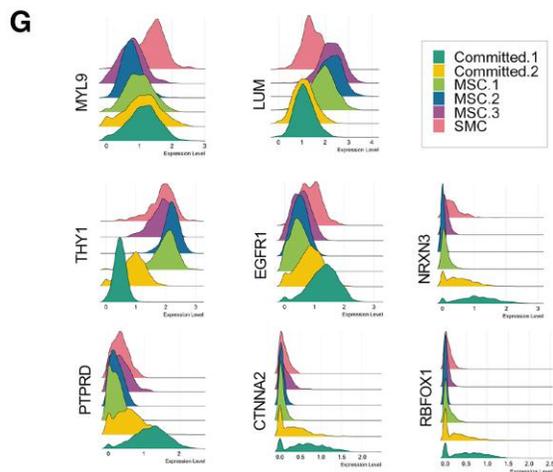
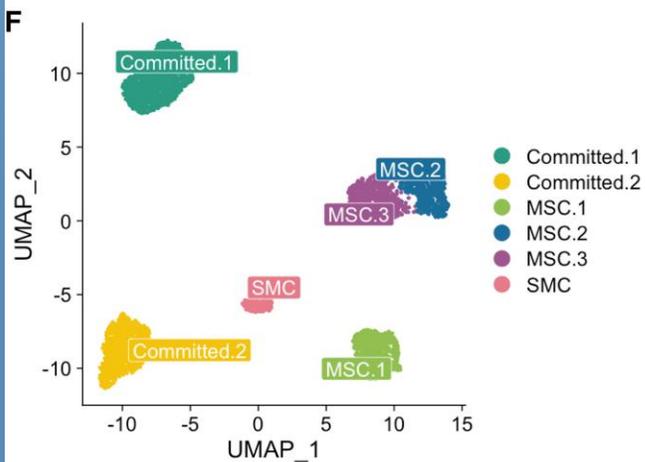
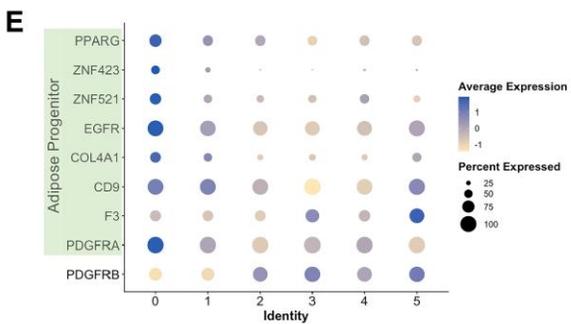
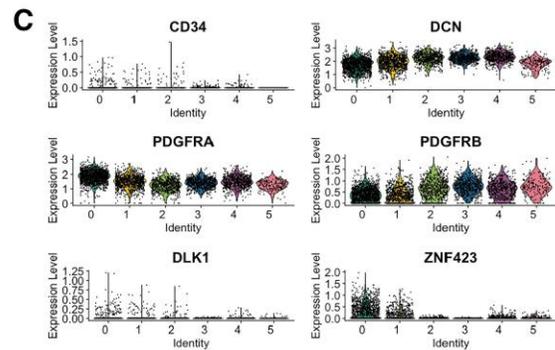
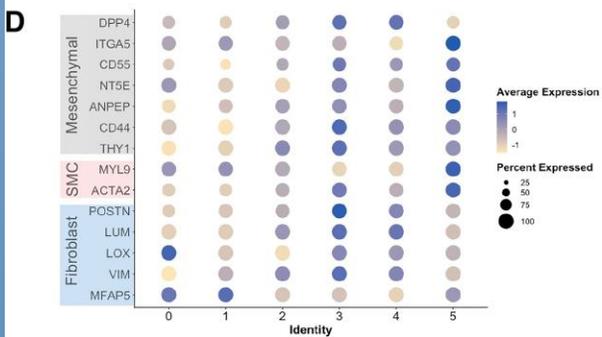
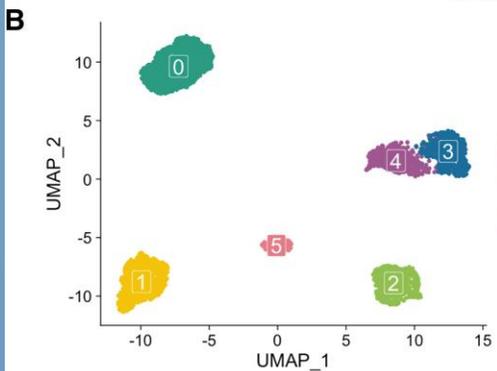
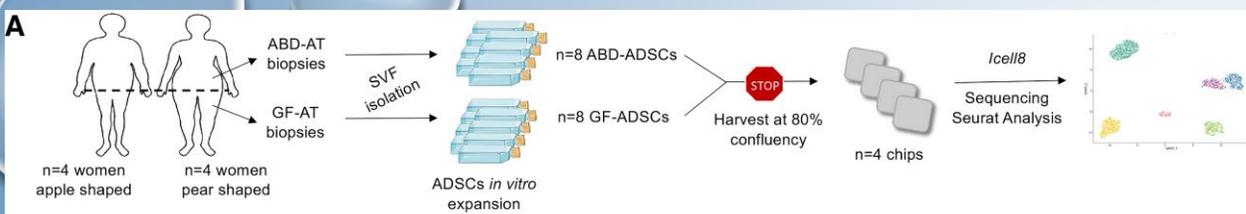
Adeline Divoux,^{1*} Katie L. Whytock,^{1*} Laszlo Halasz,^{2,3,4,5} Meghan E. Hopf,¹ Lauren M. Sparks,¹ Timothy F. Osborne,^{2,3,4,5} and Steven R. Smith¹

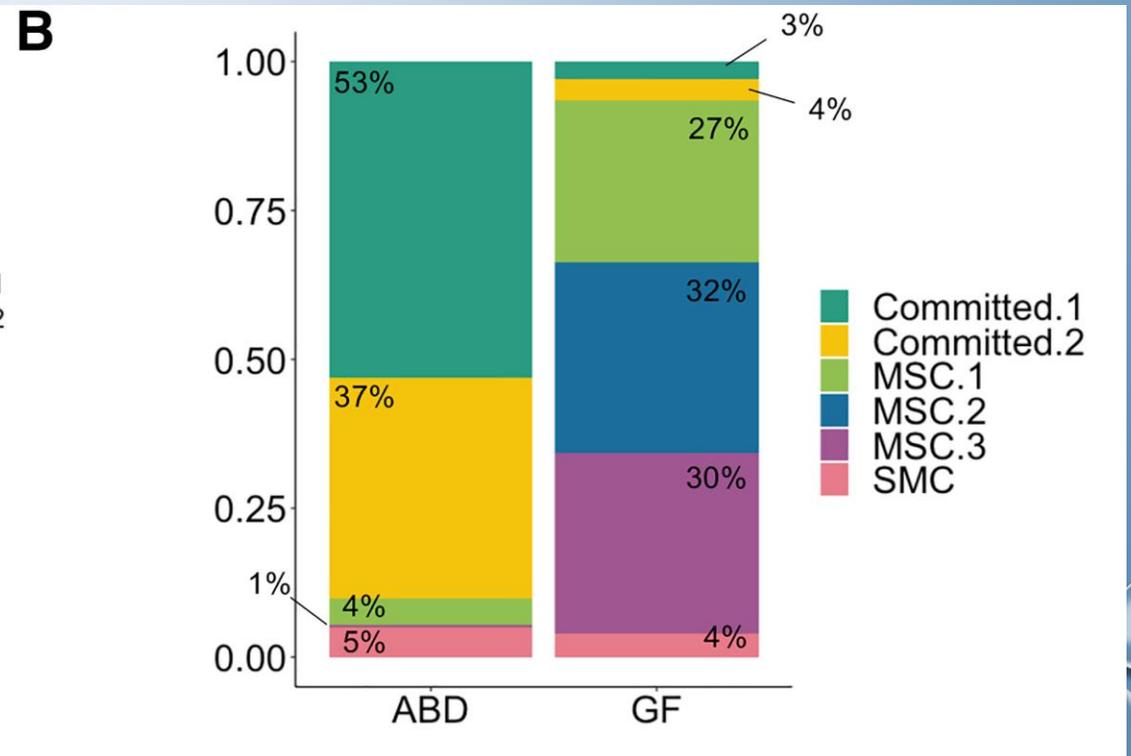
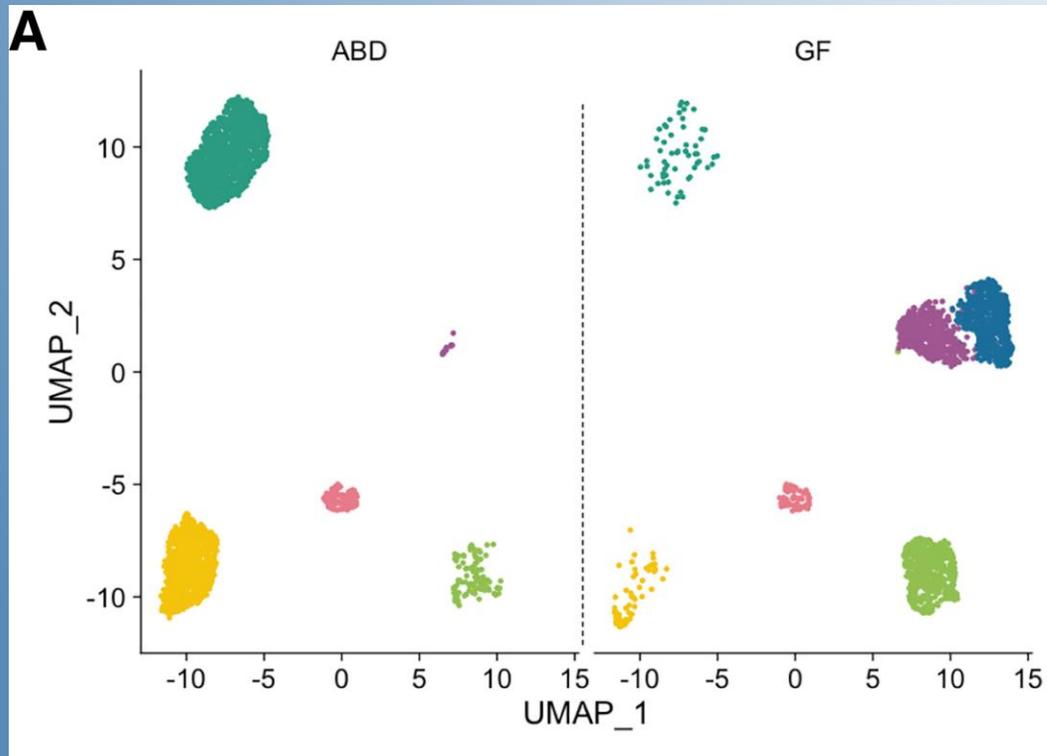
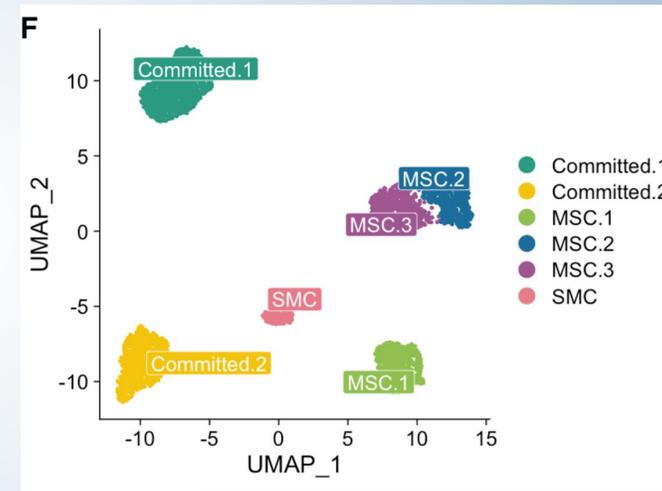
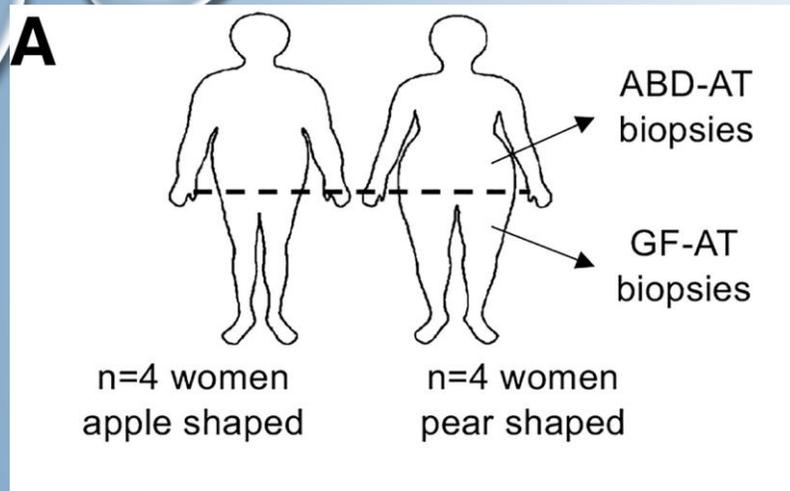
¹Translational Research Institute, AdventHealth, Orlando, Florida, United States; ²Division of Diabetes Endocrinology and Metabolism, Johns Hopkins University School of Medicine, Institute for Fundamental Biomedical Research, Johns Hopkins All Children's Hospital, St. Petersburg, Florida, United States; ³Department of Medicine, Johns Hopkins University School of Medicine, Institute for Fundamental Biomedical Research, Johns Hopkins All Children's Hospital, St. Petersburg, Florida, United States; ⁴Department of Biological Chemistry, Johns Hopkins University School of Medicine, Institute for Fundamental Biomedical Research, Johns Hopkins All Children's Hospital, St. Petersburg, Florida, United States; and ⁵Department of Pediatrics, Johns Hopkins University School of Medicine, Institute for Fundamental Biomedical Research, Johns Hopkins All Children's Hospital, St. Petersburg, Florida, United States

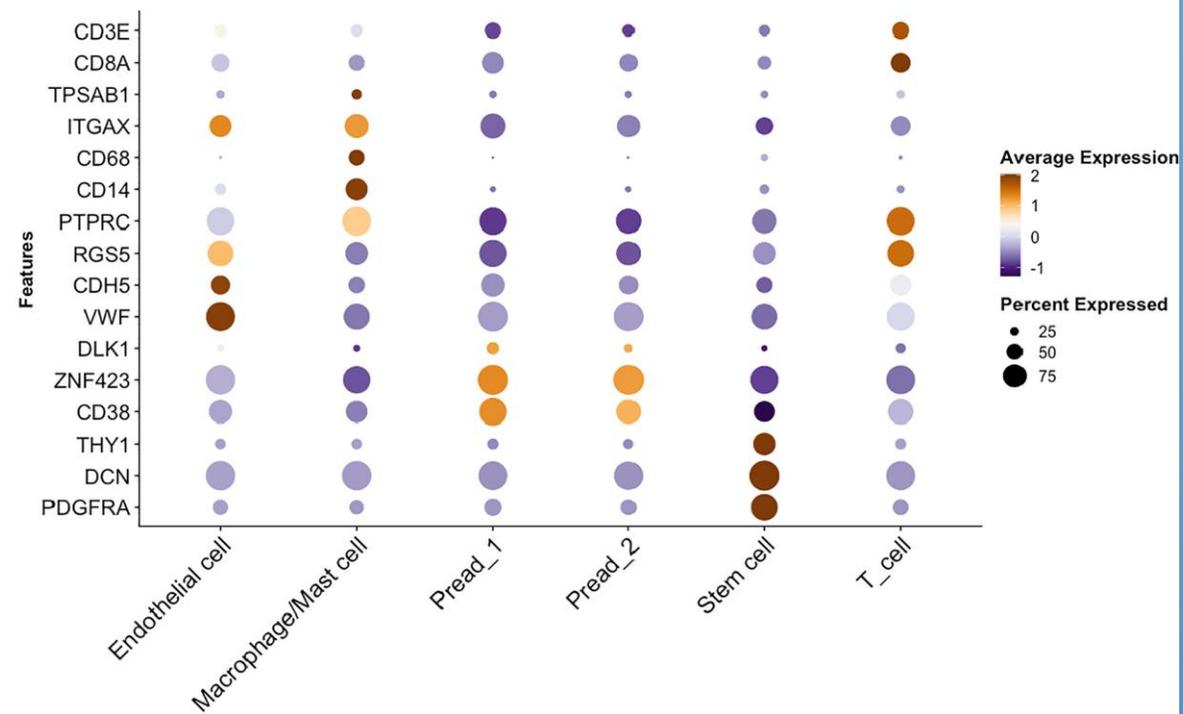
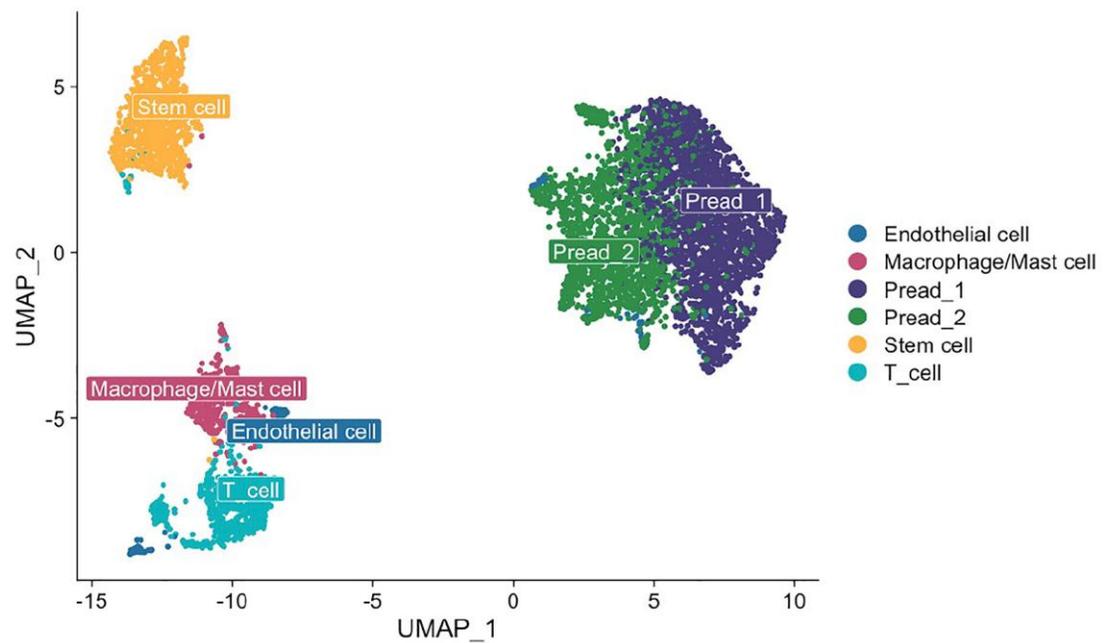
Abstract

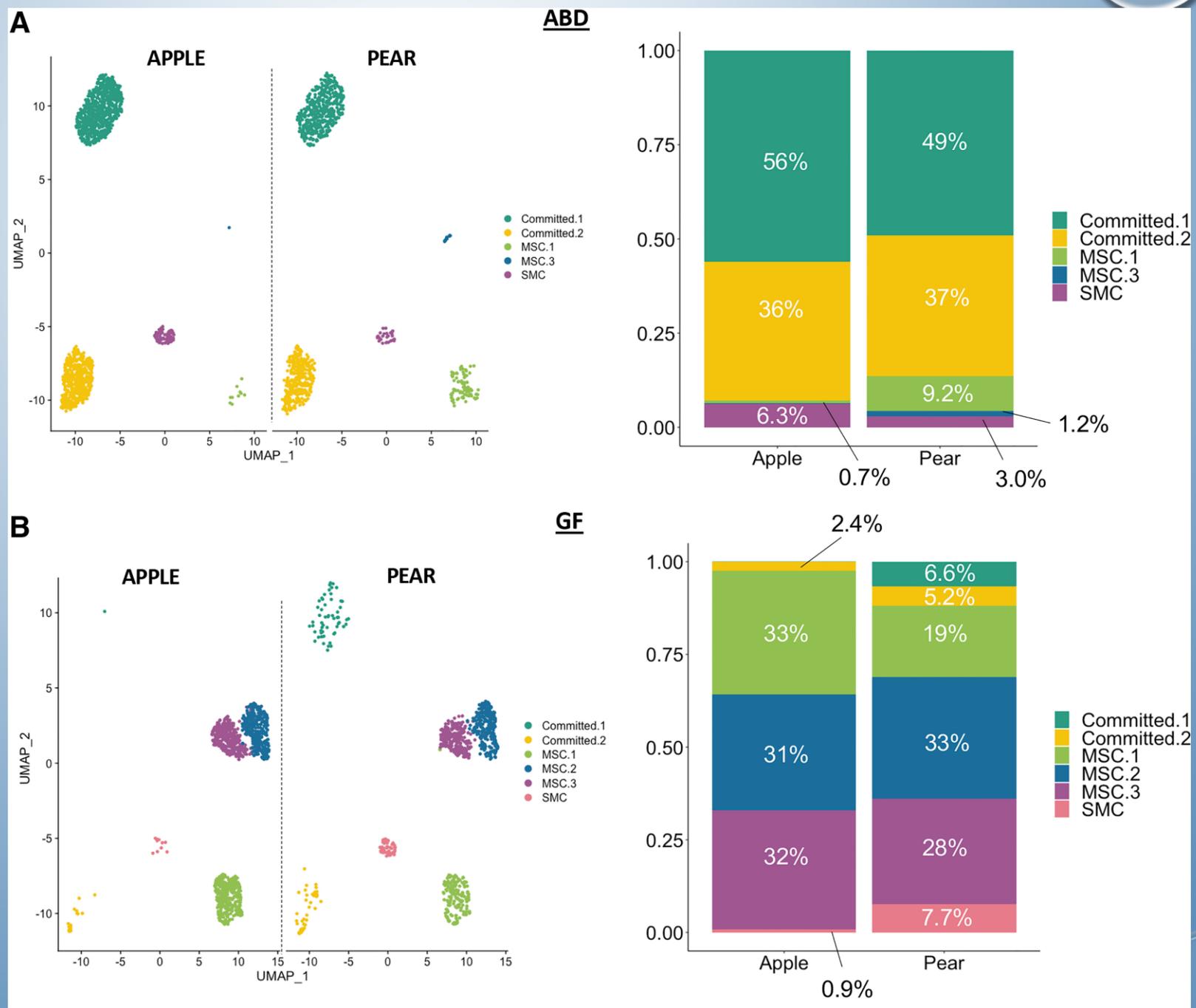
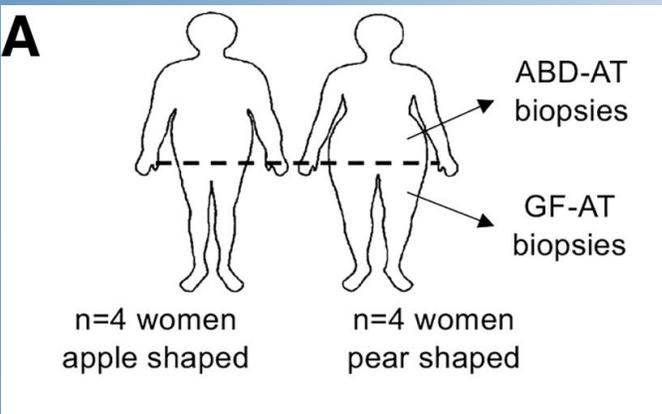
Adipose-derived stem cells (ADSCs) play an important role in the differential capacity for excess energy storage between upper body abdominal (ABD) adipose tissue (AT) and lower body gluteofemoral (GF) AT. We cultured ADSCs from subcutaneous ABD AT and GF AT isolated from eight women with differential body fat distribution and performed single-cell RNA sequencing. Six populations of ADSCs were identified and segregated according to their anatomical origin. The three ADSC subpopulations in GF AT were characterized by strong cholesterol/fatty acid (FA) storage and proliferation signatures. The two ABD subpopulations, differentiated by higher expression of committed preadipocyte marker genes, were set apart by differential expression of extracellular matrix and ribosomal genes. The last population, identified in both depots, was similar to smooth muscle cells and when individually isolated and cultured in vitro they differentiated less than the other subpopulations. This work provides important insight into the use of ADSC as an in vitro model of adipogenesis and suggests that specific subpopulations of GF-ADSCs contribute to the more robust capacity for GF-AT to expand and grow compared with ABD-AT in women.







A



Review

Adipose tissue-targeting nanomedicines for obesity pharmacotherapy

Lingling Wang¹, Qingyi Jia¹, Jinhan He^{1,*}, and Yanping Li^{1,*}

The increasing global prevalence of obesity presents a substantial challenge to public health. Current nutrient-stimulated hormone (NuSH)-based therapeutics are hindered by receptor desensitization, muscle loss, and weight regain. The adipose tissue, the primary organ responsible for energy storage and metabolic management, is a promising target for obesity treatment. Nanomedicine holds promise to precisely deliver medication to the adipose tissue to maximize therapeutic efficacy and minimize off-target effects; indeed, various adipose tissue-targeting nanomedicines have shown impressive anti-obesity effects by optimizing drug pharmacokinetic profiles and reducing nonspecific distribution in preclinical studies. Here we examine the current state of the art of adipose tissue-targeting nanomedicines, offering insights into recent advances, future possibilities, and the remaining challenges associated with their application in obesity treatment.

Adipose tissue-targeting nanomedicine is a promising alternative for obesity treatment

Obesity has become a global issue, with projections indicating that 1.02 billion adults will be obese by 2030 [1,2]. It also raises the risk of comorbidities such as type 2 diabetes, cardiovascular diseases, and metabolic dysfunction-associated steatotic liver disease, potentially shortening life expectancy by 5–20 years [3]. Therefore, obesity is a substantial health challenge that necessitates urgent intervention.

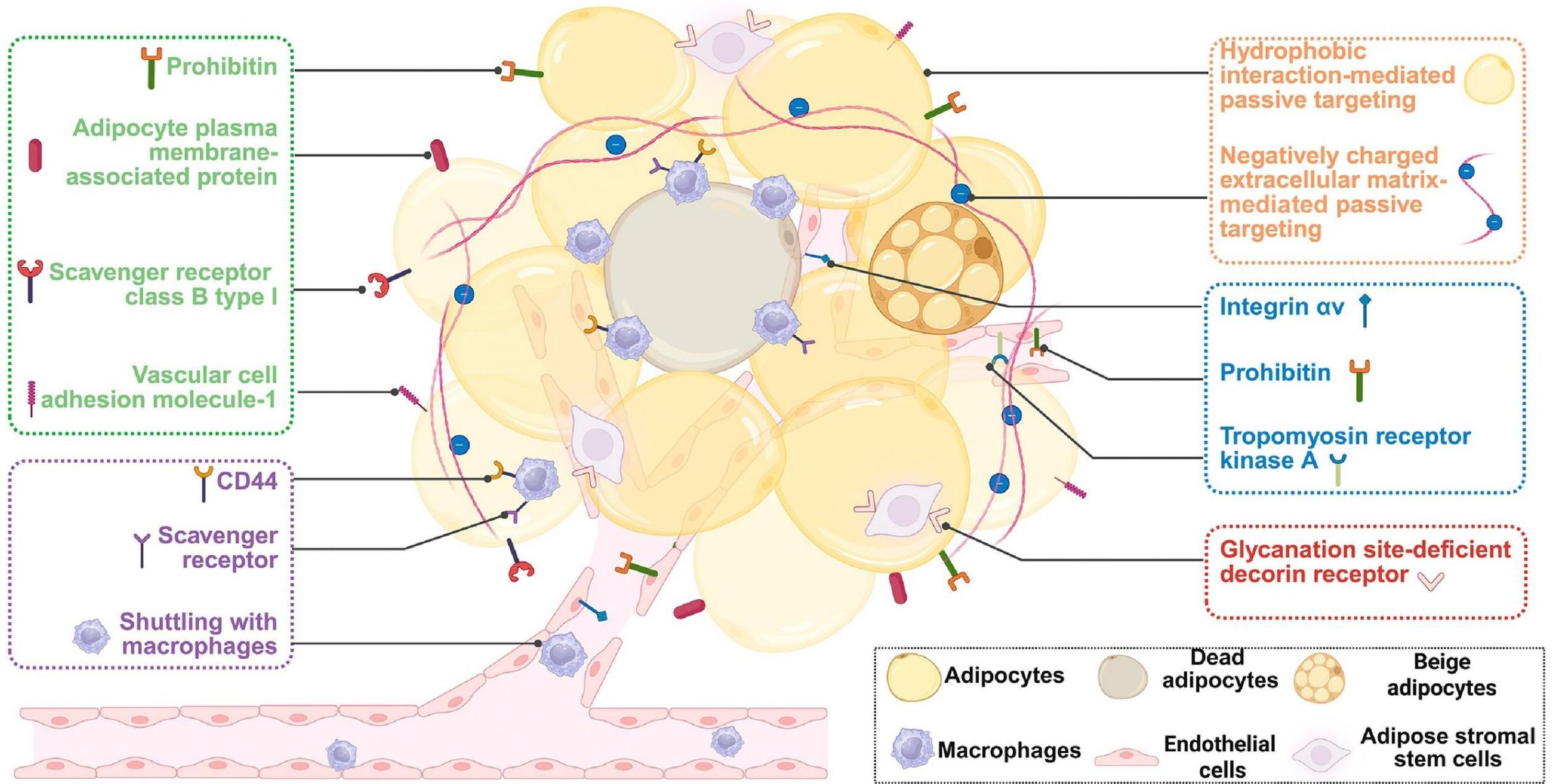
Highlights

The adipose tissue is the principal organ for energy storage and metabolic regulation, making it a promising target for obesity pharmacotherapy.

Adipose tissue-targeting nanomedicine holds promise in overcoming limitations arising from traditional obesity pharmacotherapy.

The distinct receptor profiles and physicochemical properties of the adipose tissue allow nanomedicines to target it through both active and passive strategies.

The principal approaches for adipose tissue-specific nanomedicine involve targeting adipocytes for energy balance, macrophages to reduce inflammation, and multiple cell types simultaneously to achieve synergistic effects.

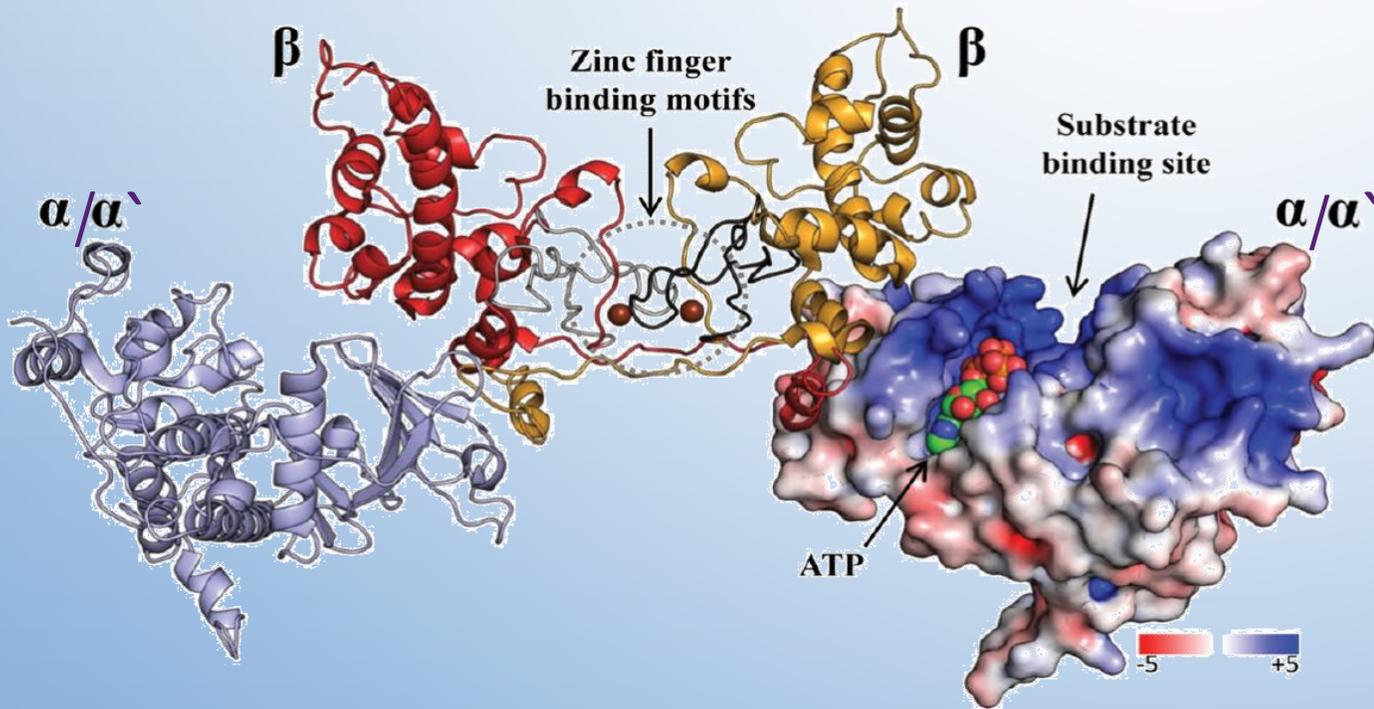


CK2

Ser/Thr chinasi ubiquitaria e costitutivamente attiva,
composta da 2 subunità catalitiche (α/α') e 2 regolatorie (β).

Fosforila più di 500 substrati.

Altamente espressa in tessuti proliferanti e tumori.



Potenzia numerosi pathways

la cui alterazione contribuisce allo sviluppo di
molteplici patologie



Cancro



Infezioni virali



Fibrosi Cistica



Malattie Neurologiche

Malattie Cardiovascolari

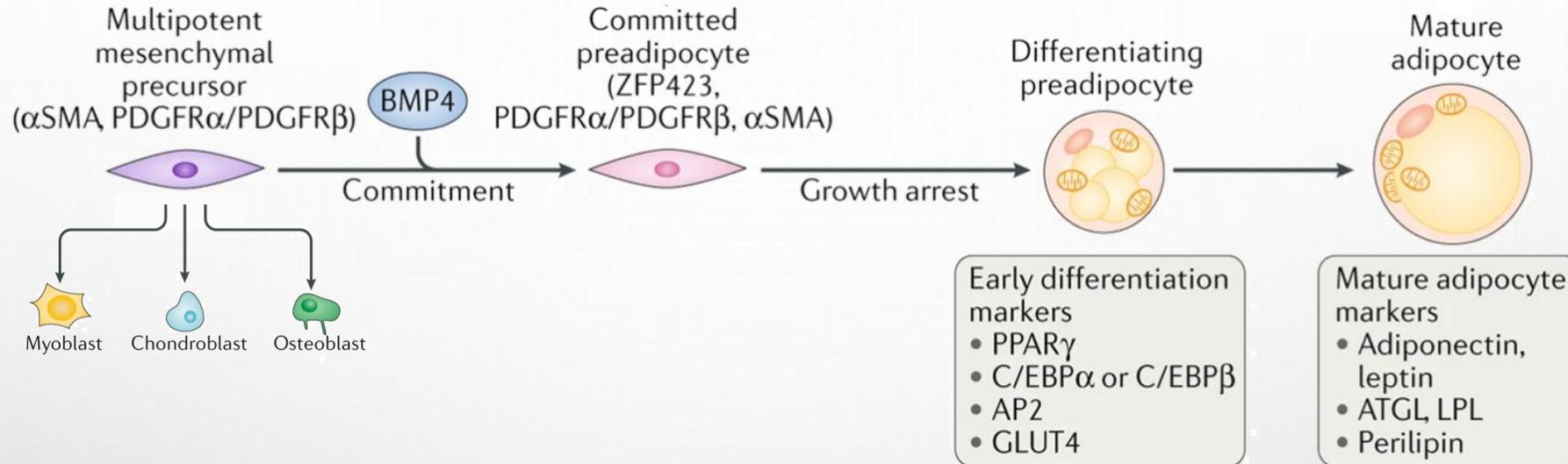


Infiammazione

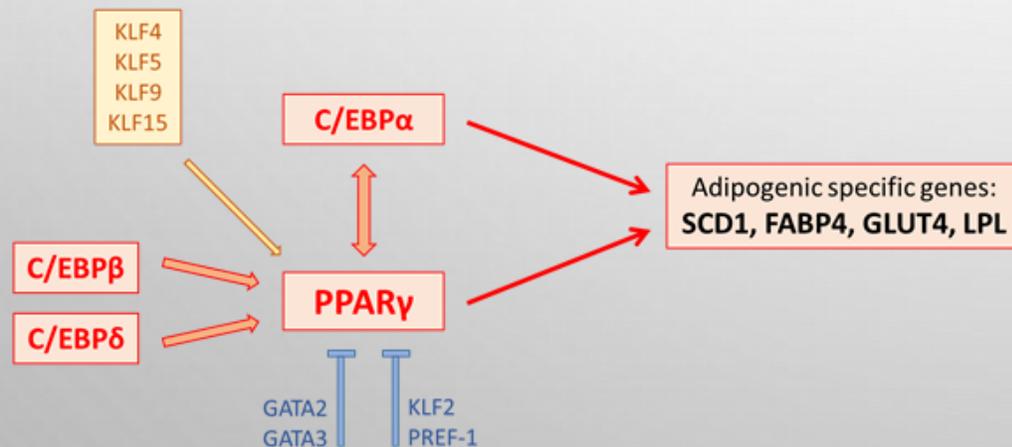
Obesità e malattie del
metabolismo



The Adipogenic Differentiation Process

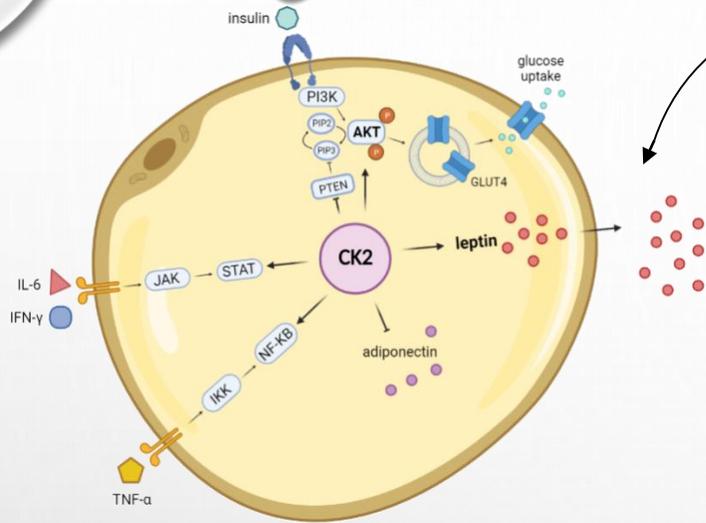


Ghaben, A. L. & Scherer, P. E. *Nat Rev Mol Cell Biol* **20**, 242–258 (2019)



C/EBP β , PPAR γ and C/EBP α are the master regulators of adipogenesis

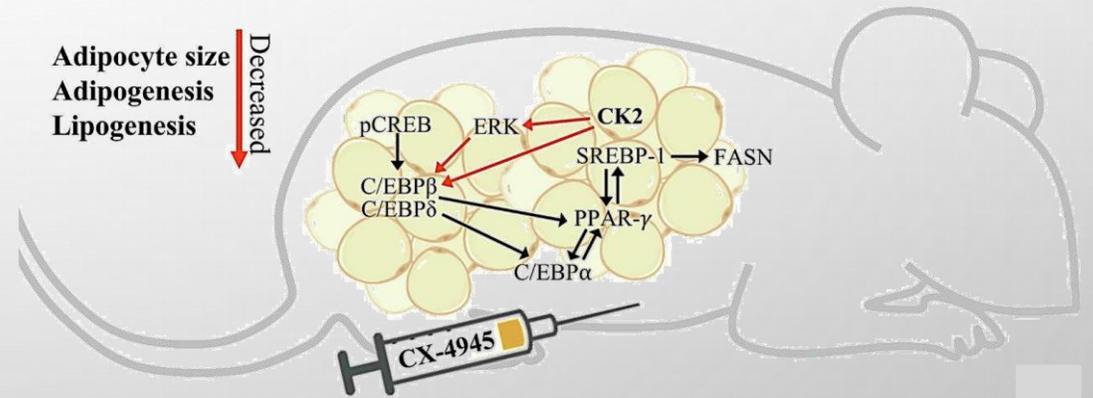
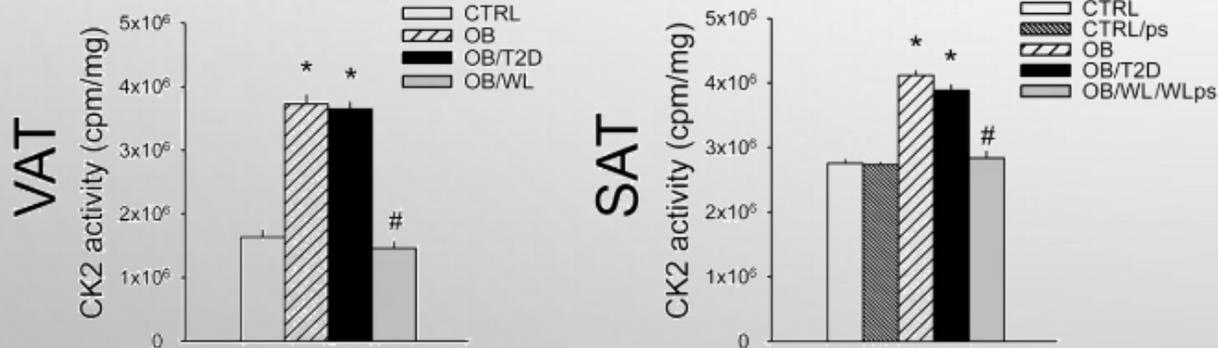
CK2 in OBESITY and METABOLIC DISEASES



CK2 inhibition decreases adipocyte size, adipogenesis and lipogenesis in vivo

High-Fat-Diet (HFD) fed mice injected with CK2-inhibitor (CX-4945) gain considerably less weight than control untreated group

CK2 stimulates insulin-dependent glucose uptake through PI3K/AKT PATHWAY, mediating GLUT4 translocation

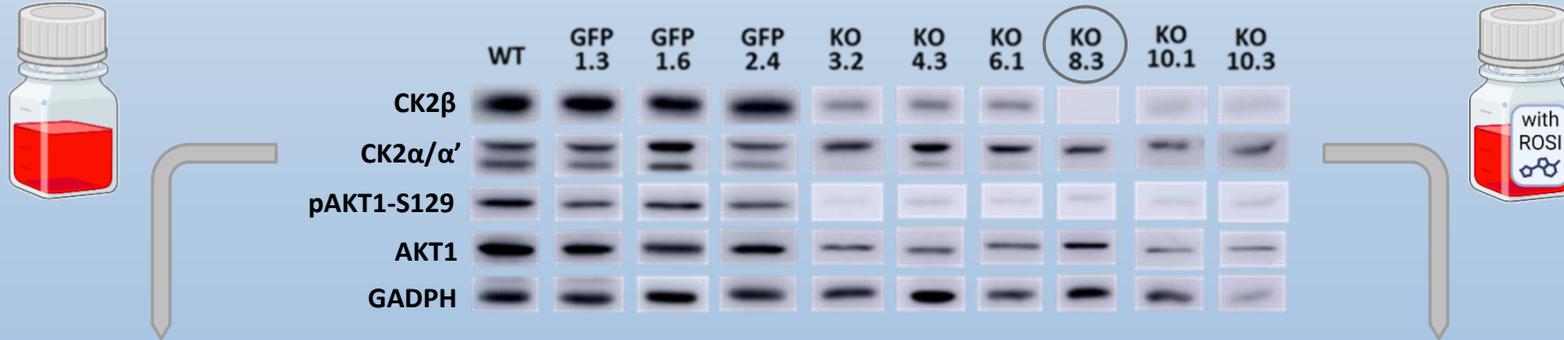


Buchwald, L. M. et al. *Metabolism* **162** (2025).

CK2 è upregolata in VAT e SAT di pazienti con obesità e diabete e ritorna a valori normali in seguito a perdita di peso

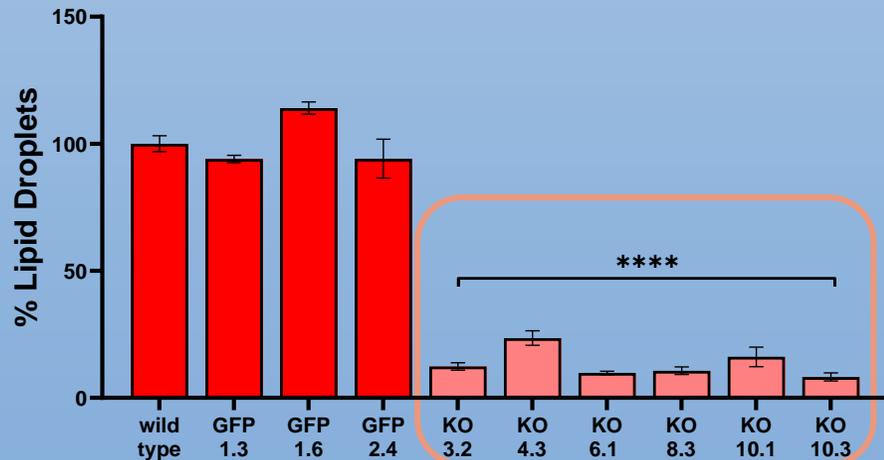
CK2 β knockout (KO) mediante CRISPR-Cas9

WB mostra un'ablazione quasi completa di CK2 β nei cloni KO



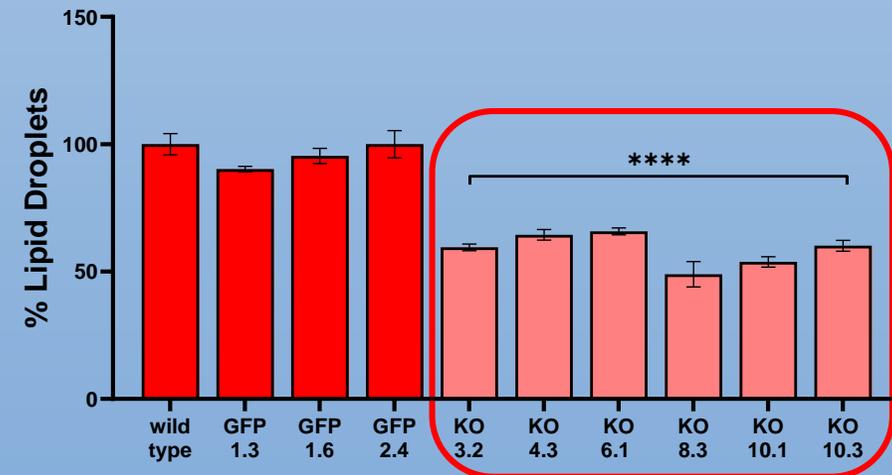
Induzione Adipogenica Standard

Minore quantità di adipociti maturi e vacuoli lipidici nei cloni CK2 β KO

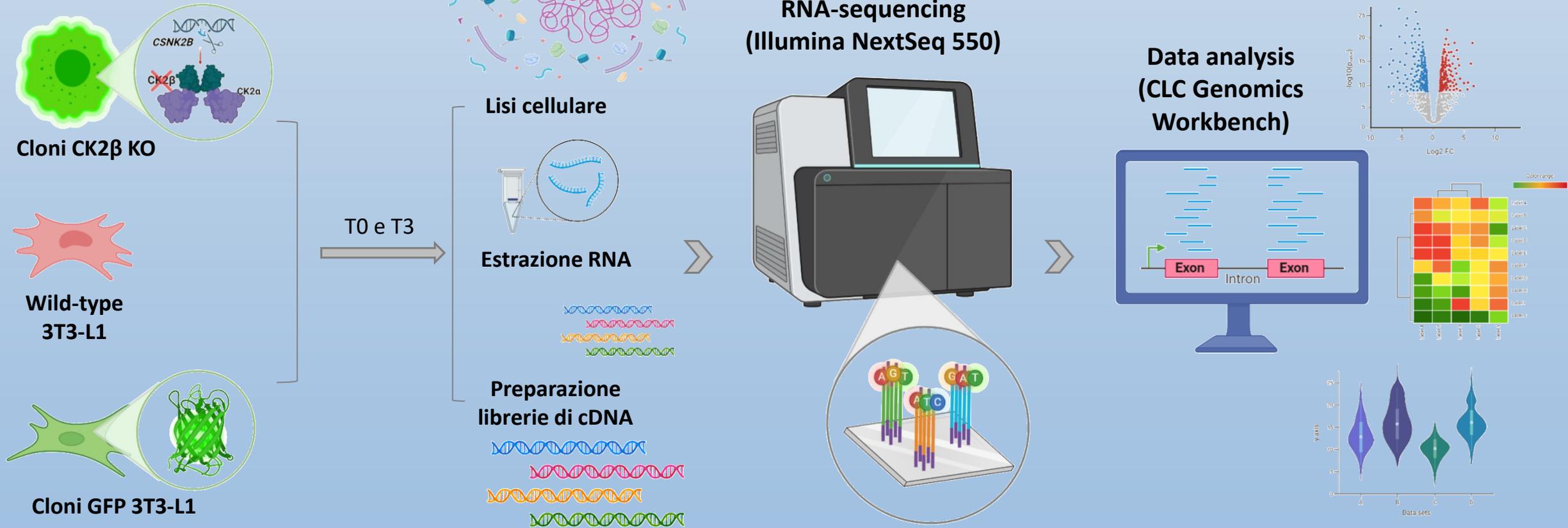


Induzione Adipogenica con Rosigitazione

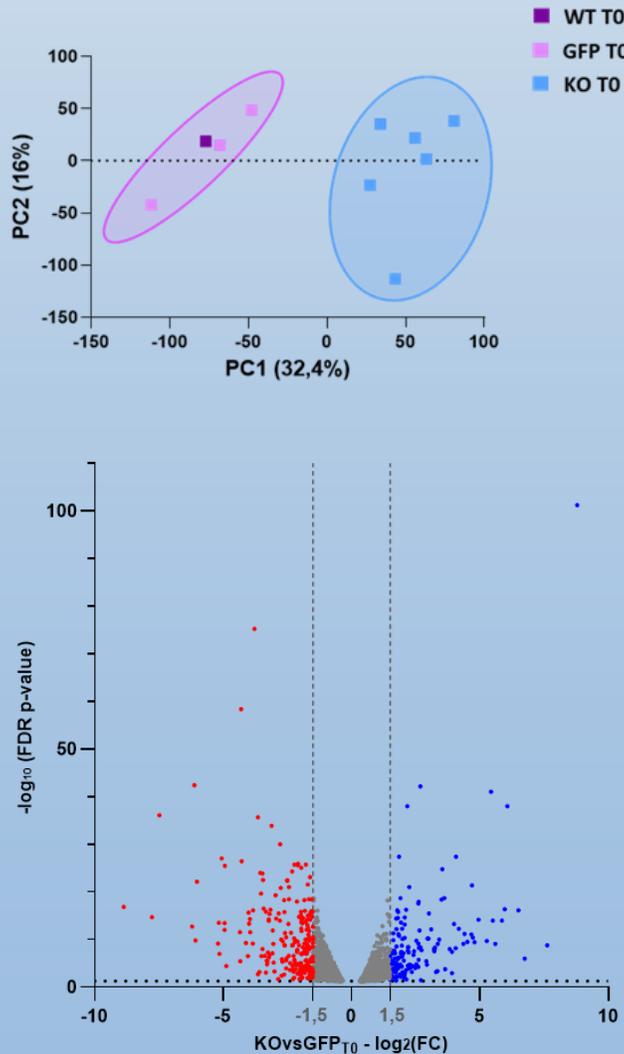
Cloni CK2 β KO e controlli presentano una ridotta differenza in termini di quantità di adipociti maturi e vacuoli lipidici



ANALISI TRASCRIPTOMICA nelle prime fasi di adipogenesi



Differenze di espressione genica tra CK2 β KO e controlli in condizioni basali (T0)



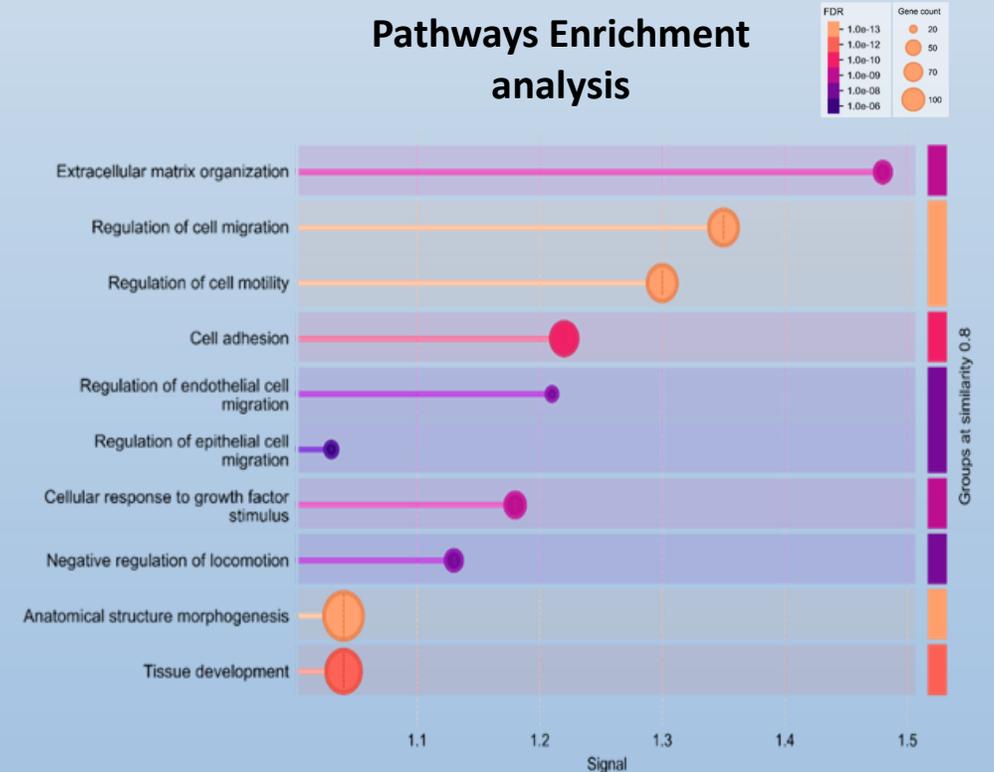
Analisi PCA al T0 indica che:

- Campioni WT e GFP costituiscono un singolo gruppo di controllo;
- Cloni CK2 β KO presentano fenotipi simili
- **I gruppi di controllo e cloni CK2 β KO sono ben separati, indicando che la perdita di CK2 β modifica il trascrittoma cellulare**

Il Volcano plot indica la presenza di:

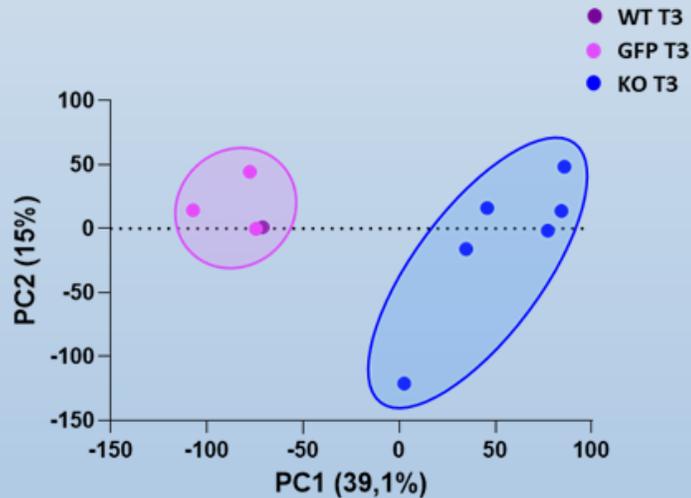
- **155 geni upregolati** ($\log_2 \text{FC} > +1.5$, punti blu);
- **227 geni downregolati** ($\log_2 \text{FC} < -1.5$, red dots)

Pathways Enrichment analysis



La perdita di CK2 β in condizioni basali produce effetti su organizzazione ECM, morfogenesi delle strutture cellulari e regolazione di migrazione e motilità cellulari

Differenze di espressione genica tra CK2 β KO e controlli a T3

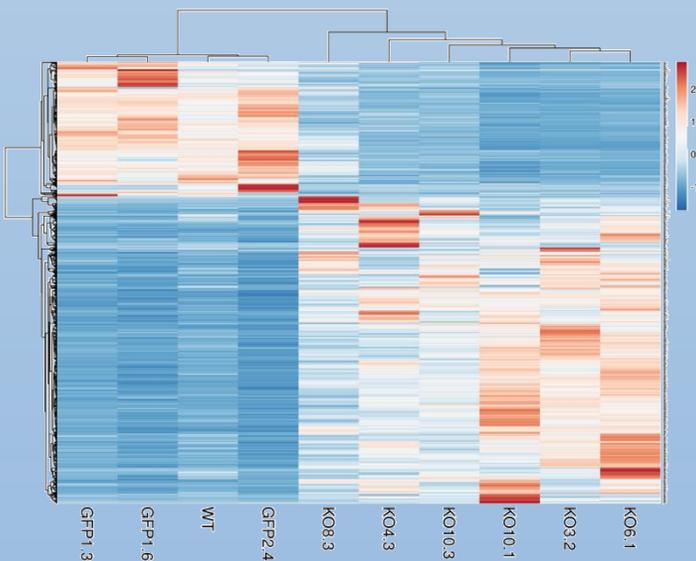


Analisi PCA analysis al T3 sostiene che:

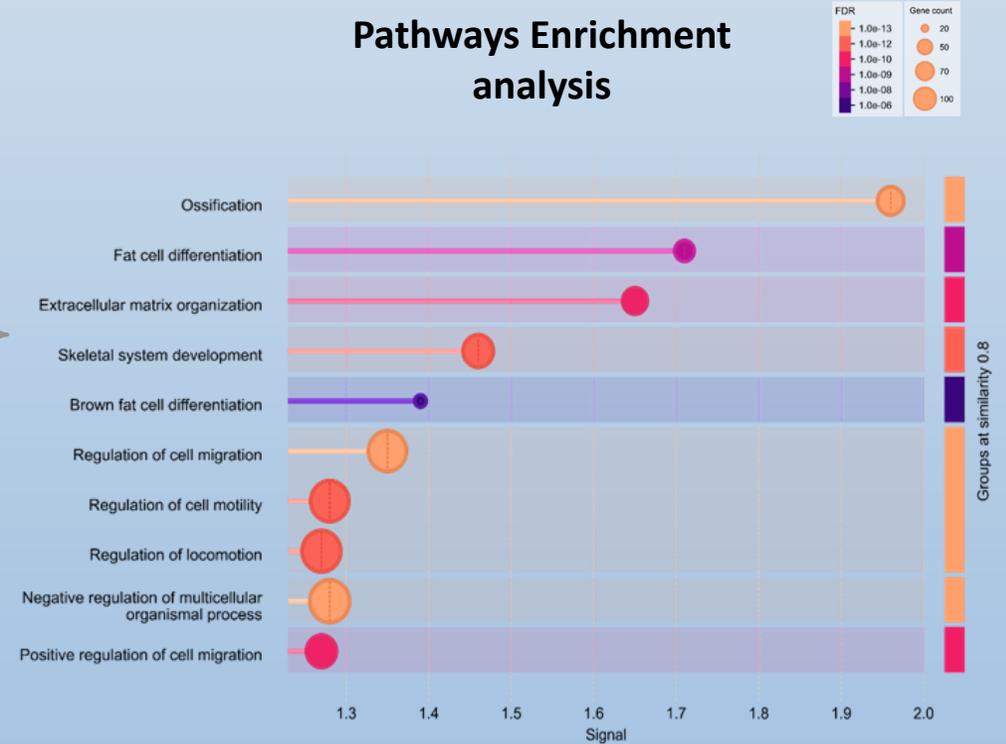
- Campioni WT e GFP samples formano un unico gruppo di controllo;
- Cloni CK2 β KO possono essere raggruppati assieme confermando il simile comportamento che presentano in corso di adipogenesi
- **Gruppi di controllo and CK2 β KO groups presentano profili trascrittomici differenti dopo 3 giorni di induzione adipogenica standard**

Heatmap evidenzia la presenza di:

- **620 geni upregolati** (colore rosso);
- **273 geni downregolati** (colore blu)

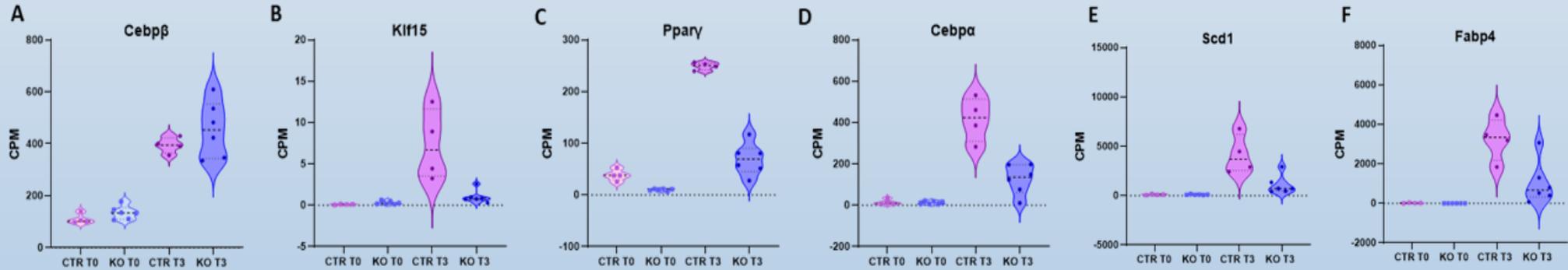


Pathways Enrichment analysis



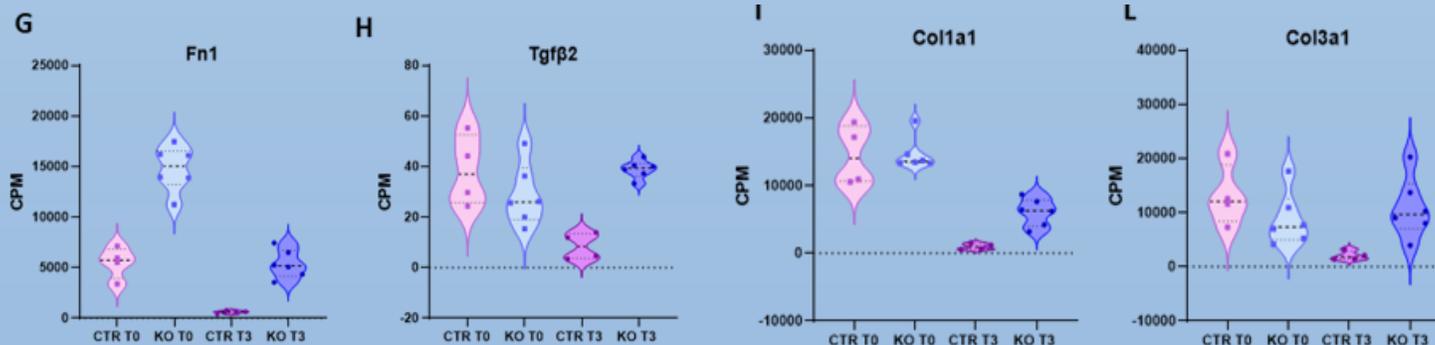
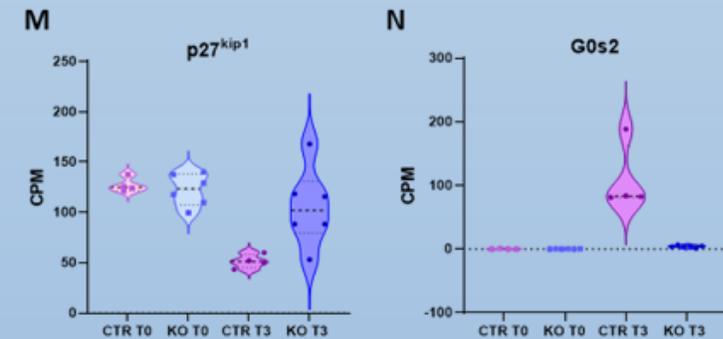
L'assenza di CK2 β durante l'adipogenesi influisce sui pathways riguardanti ossificazione, differenziamento cellule adipose, organizzazione ECM, regolazione della migrazione e della motilità cellulare

DEGs coinvolti in adipogenesi, ciclo cellulare e rimodellamento ECM



I cloni **CK2 β KO** presentano una **ridotta espressione** di master regulators e markers di **adipogenesi** (ad eccezione di *Cebpb*).
Il primo gene alterato nella cascata adipogenica è *Klf15*.

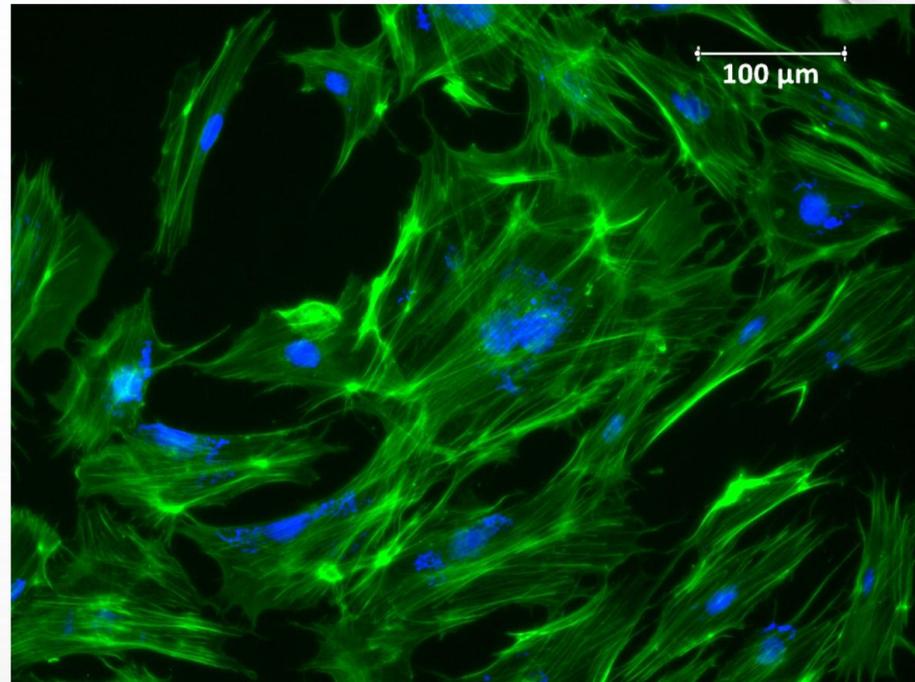
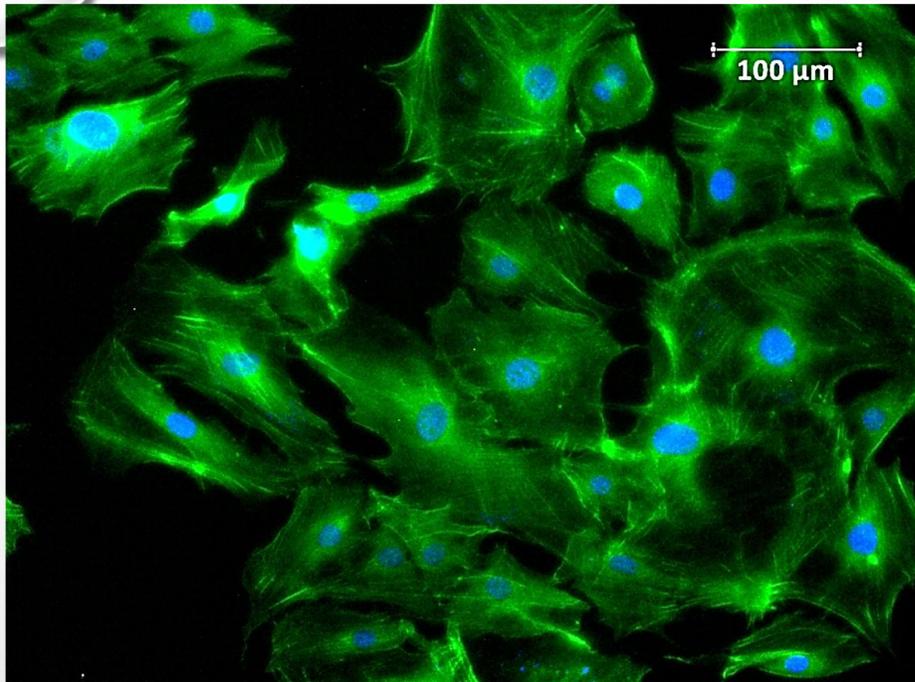
L'assenza di **CK2 β** modifica ciclo cellulare ed MCE, aumentando l'espressione di *p27^{kip1}* e riducendo l'espressione di *G0s2*



L'assenza di **CK2 β** , durante l'adipogenesi, produce una **ridotta diminuzione** dell'espressione di collageni e di geni coinvolti in rimodellamento ECM e fibrosi (*Fn1* e *Tgf β 2*)

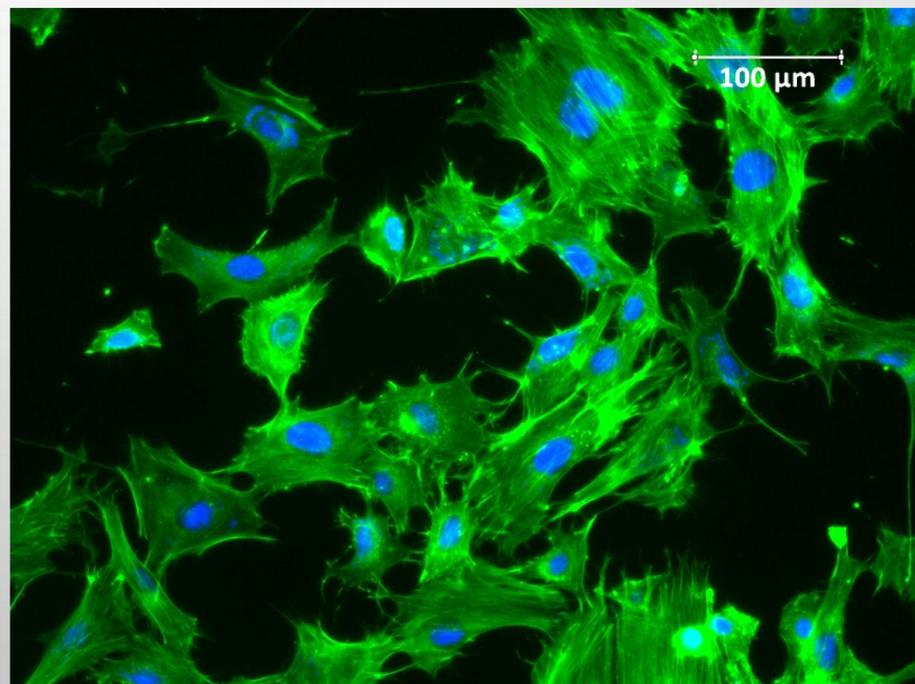
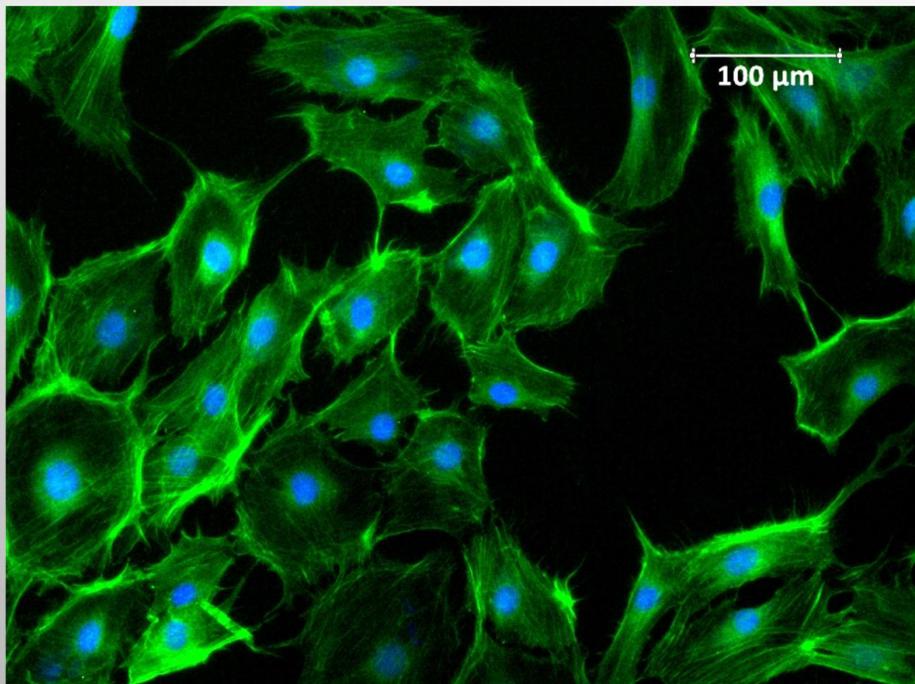
Phalloidin-488 (actin) HOESCHT Leica CTR6500 (20X magn)

WT



KO 3.2

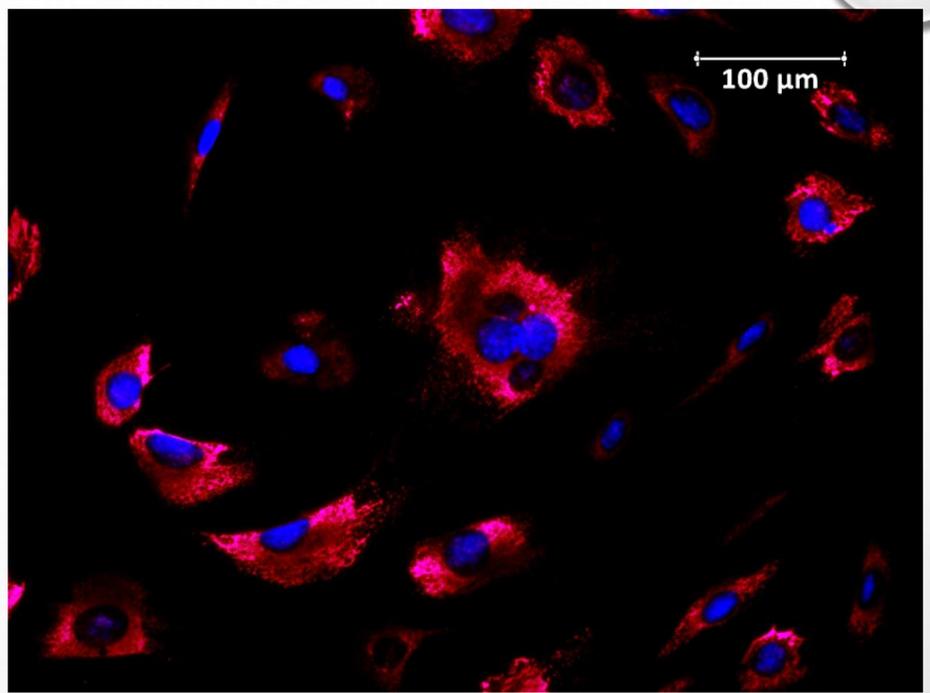
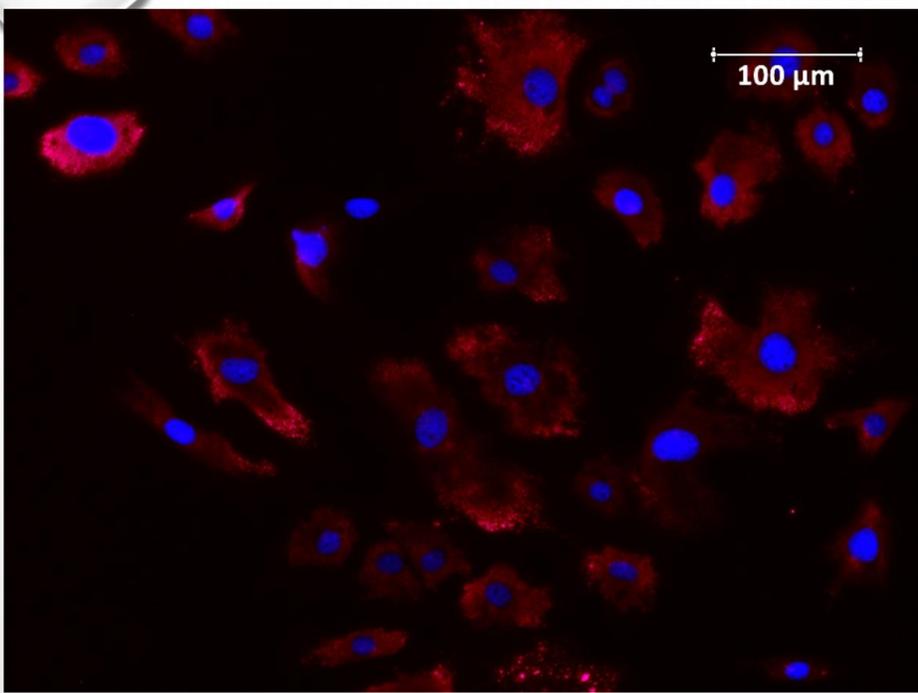
GFP 1.3



KO 8.3

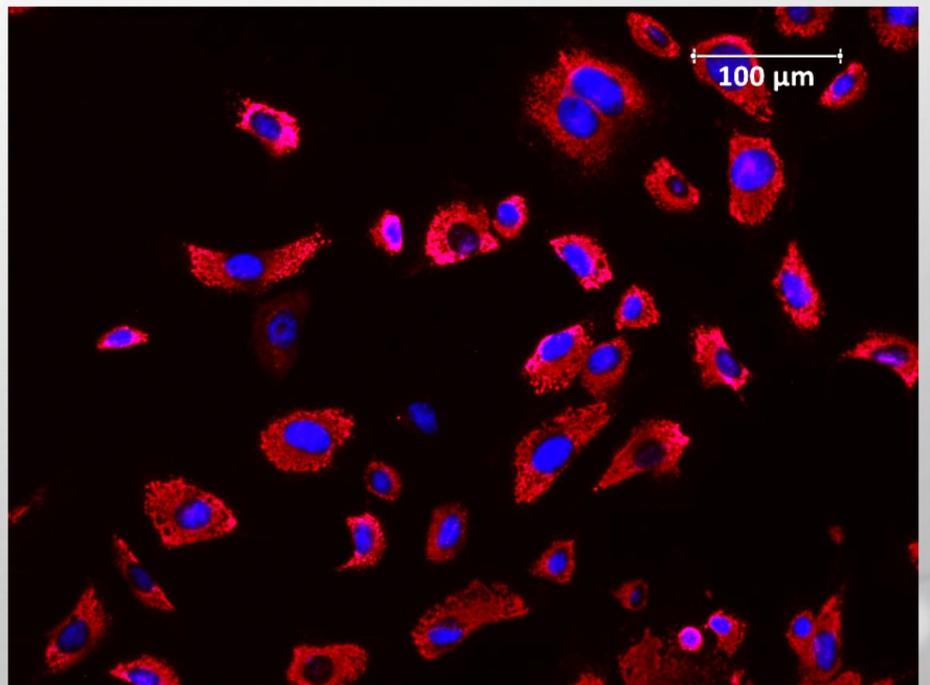
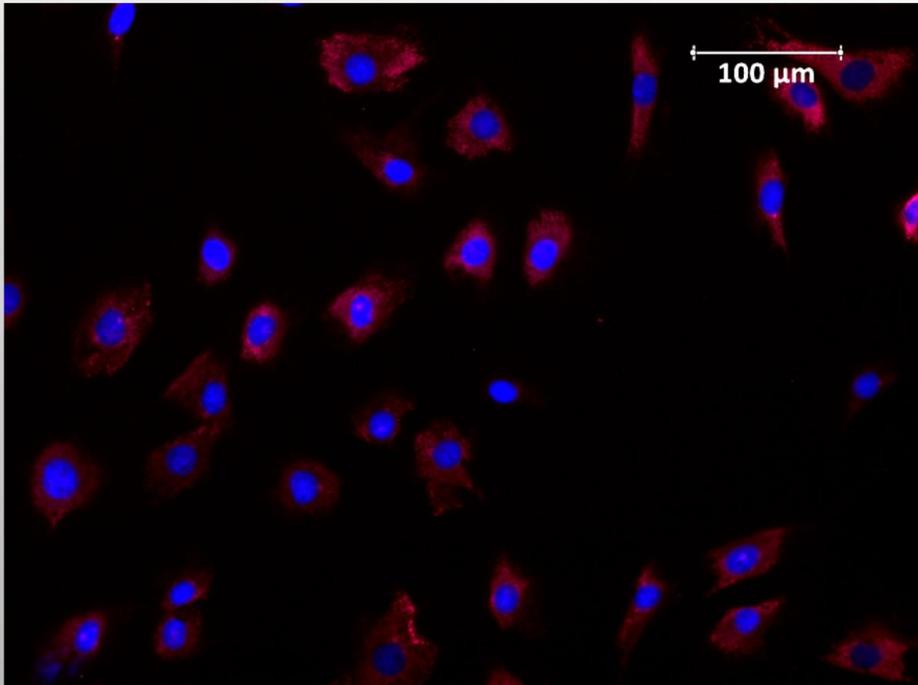
COL1A1-594 HOESCHT Leica CTR6500 (20X magnification)

WT

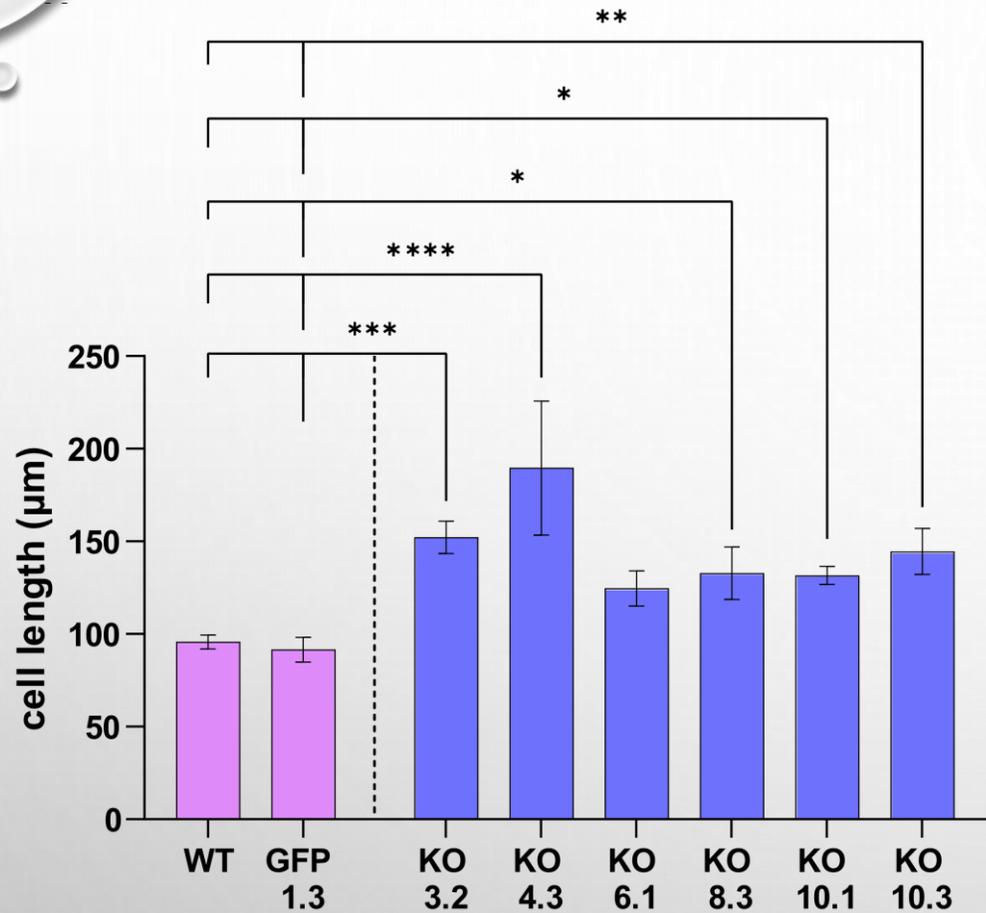


KO 3.2

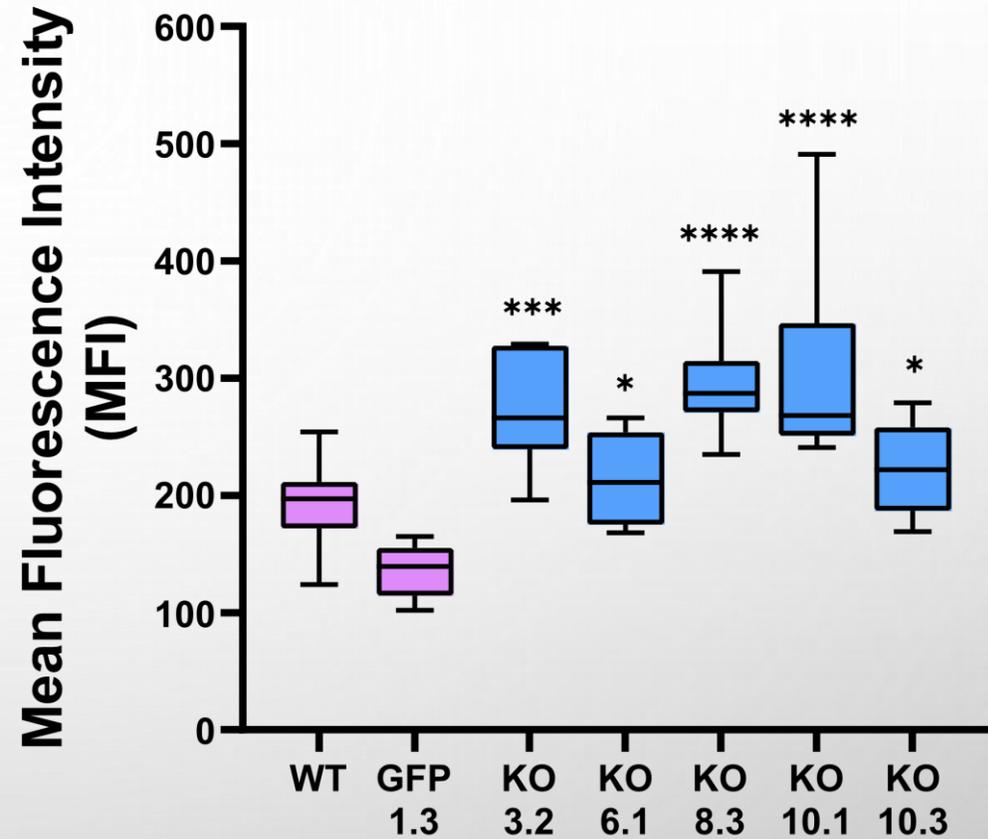
GFP 1.3



KO 8.3

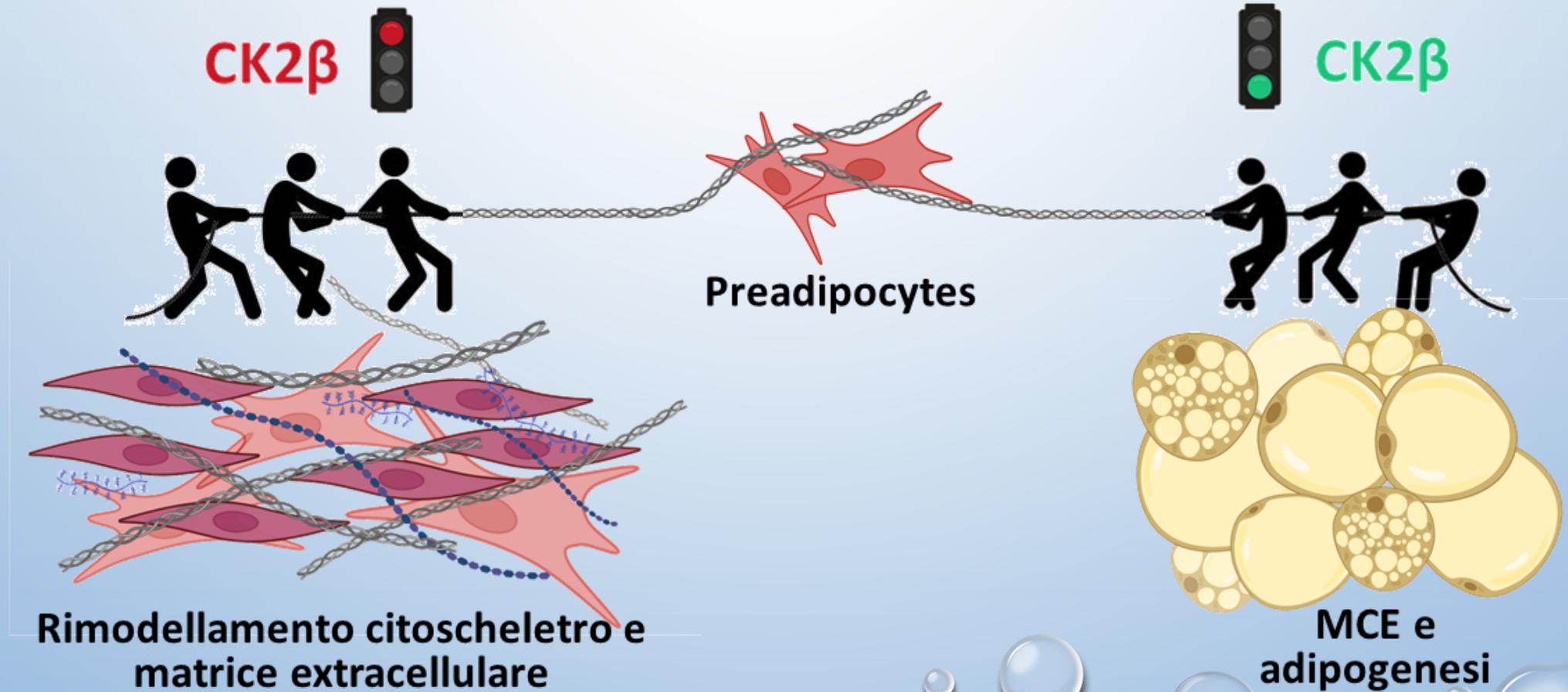


Histogram shows the cell length of control (violet bars) and CK2β KO (blue bars) clones. Values have been reported as mean \pm SEM. Statistical analysis has been performed using One-way ANOVA, $n=10$. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$; ****: $p < 0.0001$.



Boxplot shows the Mean Intensity Fluorescence (MFI) of control (violet boxes) and CK2β KO (blue boxes) clones. Statistical analysis has been performed using One-way ANOVA, $n=12$. *: $p < 0.05$; ***: $p < 0.001$; ****: $p < 0.0001$.

- ✓ **CK2 β** gioca un ruolo chiave nelle **prime fasi dell'adipogenesi**: l'agonista del PPAR γ (Rosiglitazone) produce un rescue parziale del differenziamento nei cloni CK2 β KO attraverso soli 3 giorni di trattamento
- ✓ **Assenza di CK2 β** previene il differenziamento adipogenico alterando l'espressione di geni coinvolti in insulin signaling e adipogenesi, ciclo cellulare, rimodellamento di citoscheletro ed ECM (pathways di fibrosi)





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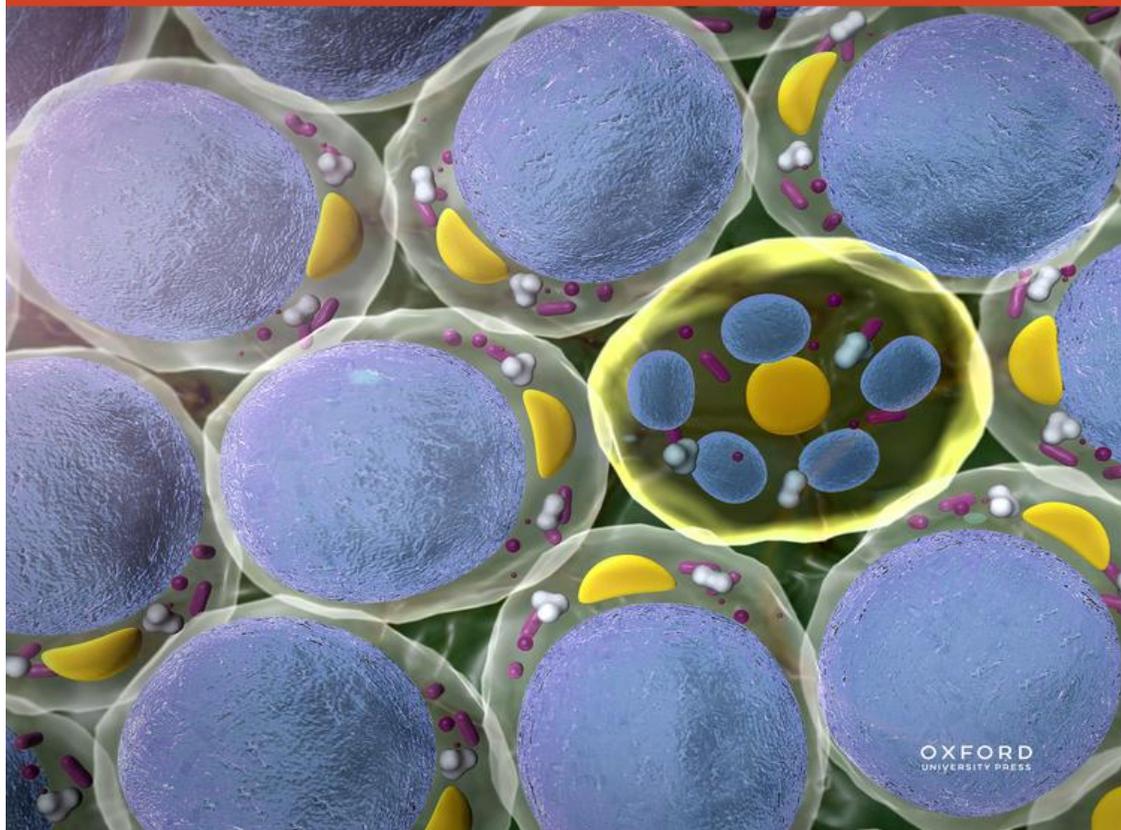
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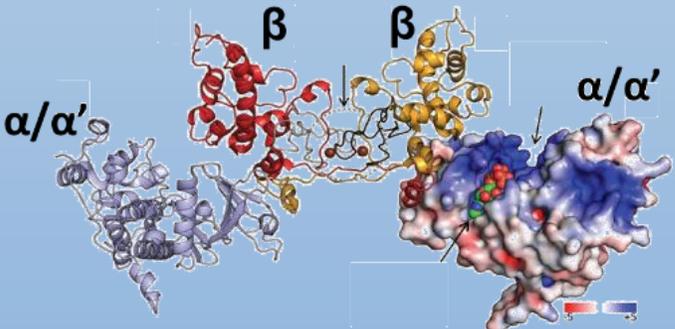
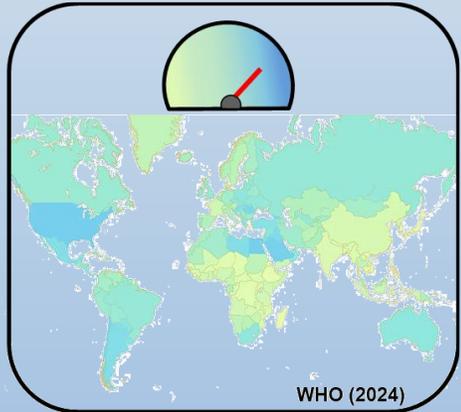
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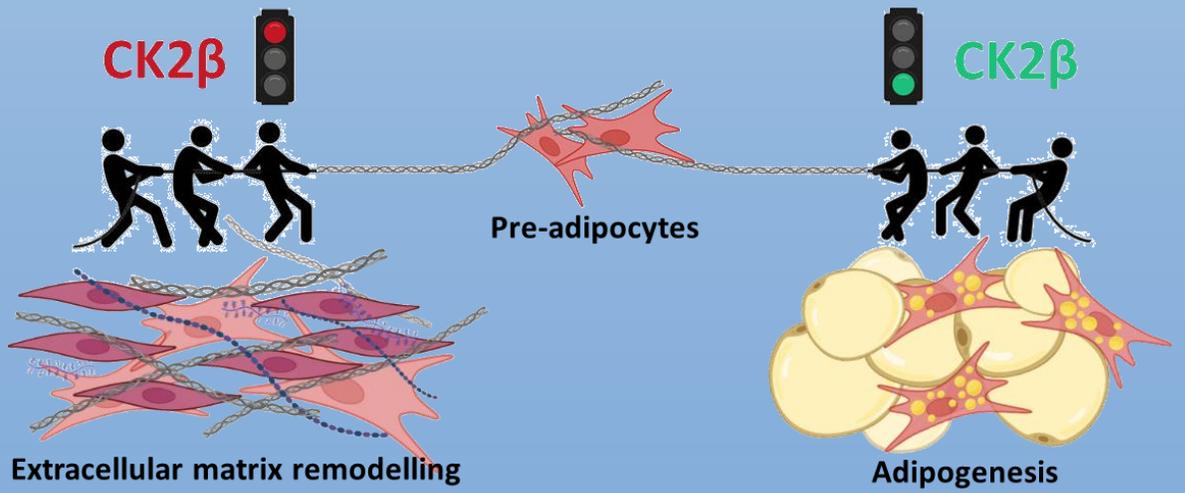
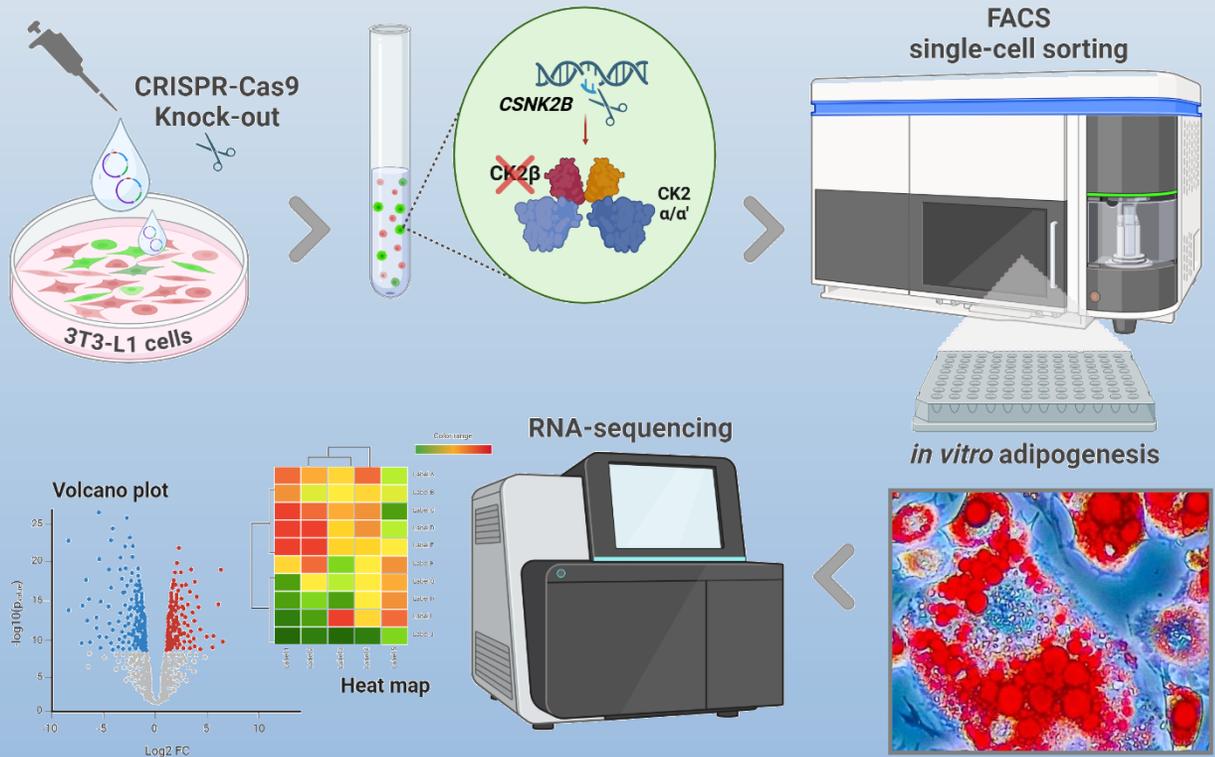
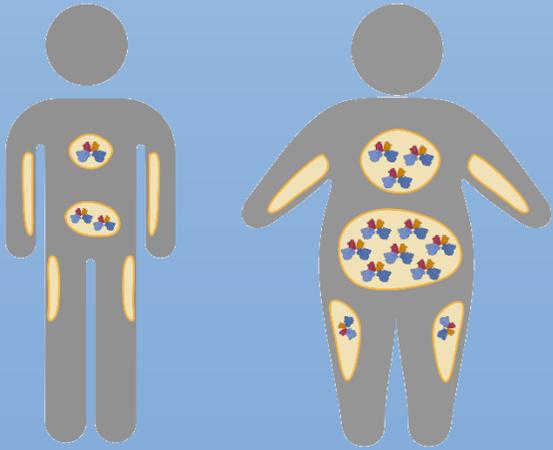


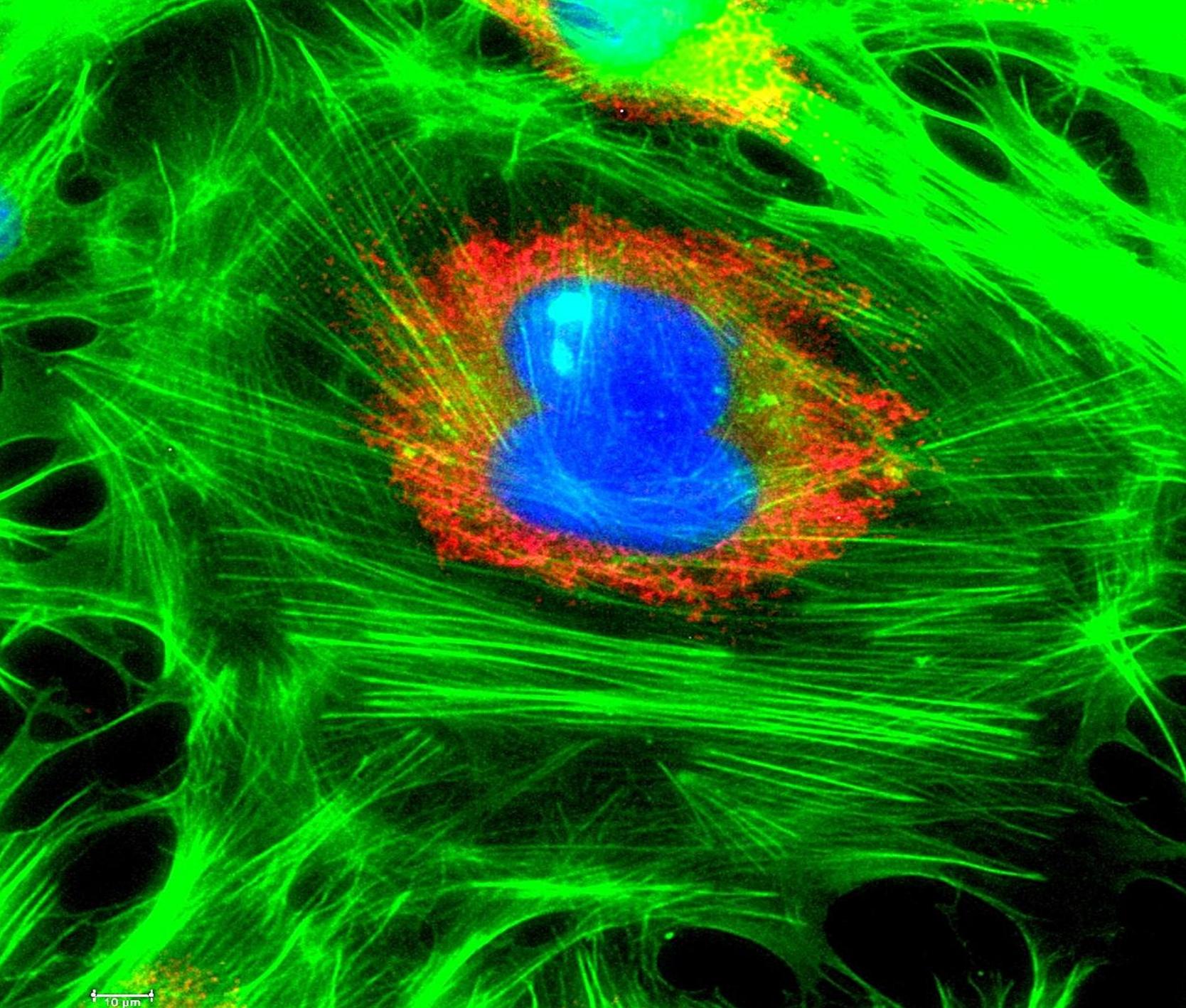
OBSESITY

Multifactorial chronic, relapsing and progressive disease



health \leftarrow CK2 \Rightarrow obesity





*Immunofluorescenza di
COL1A1, **ACTINA** e **nuclei**
di cloni di
preadipociti murini
3T3-L1 KO per CK2 β*