



The 75th EAAP Annual Meeting

1/5 September 2024 - Florence, Italy



Differential Cold Adaptation Mechanisms: Adipose Tissue Subpopulation Variances in Tibetan and Bama Pigs

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Sep 1, 2024

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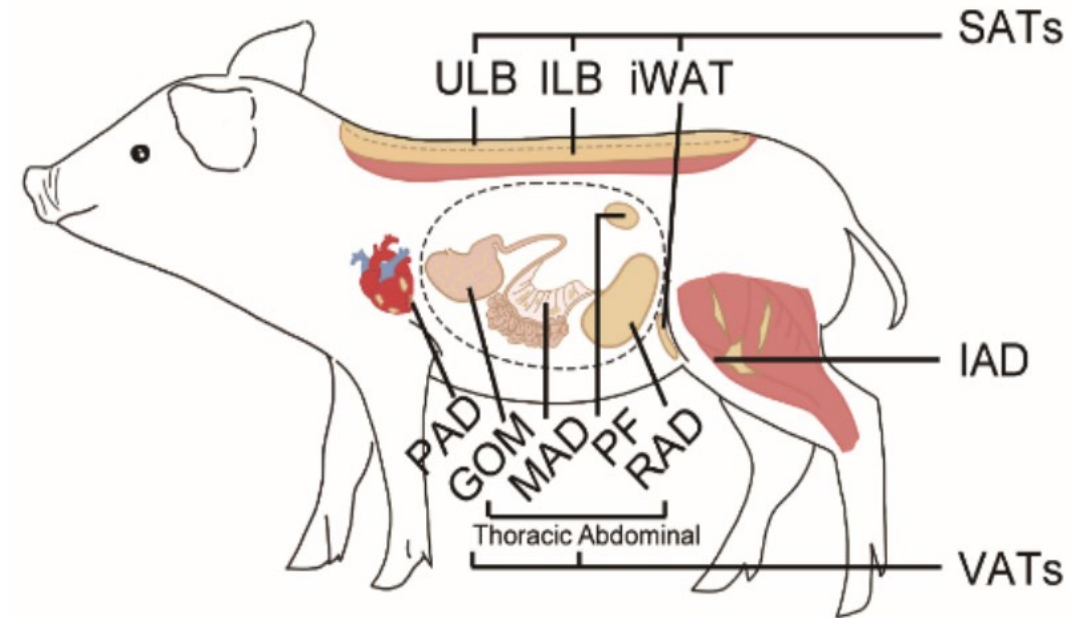


Fat deposition affects economic traits in pigs

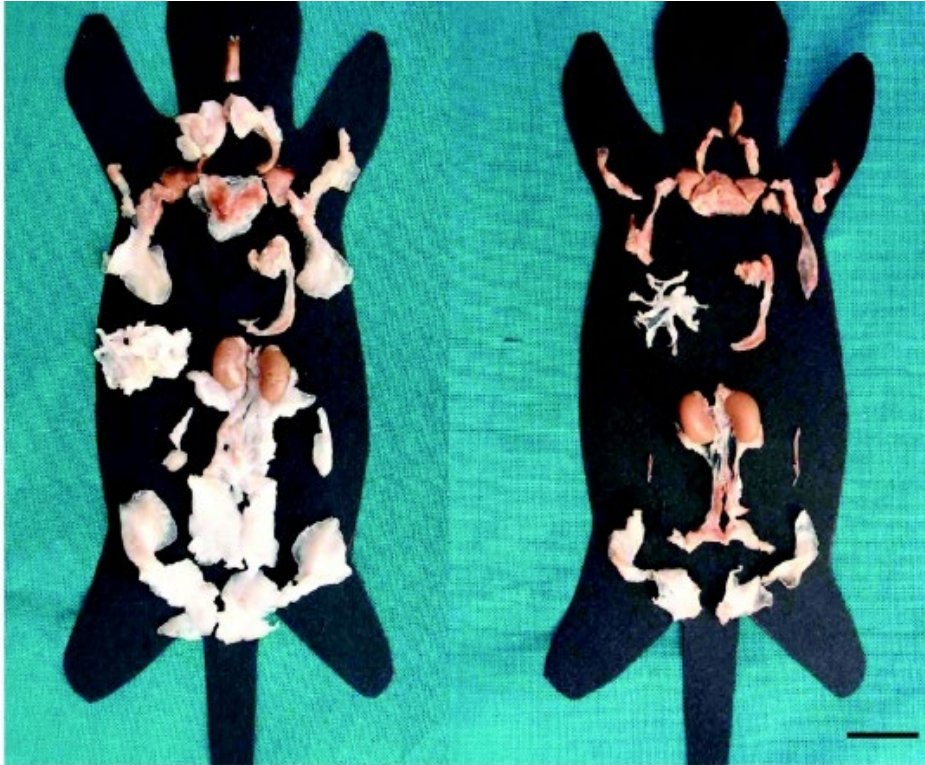
Production



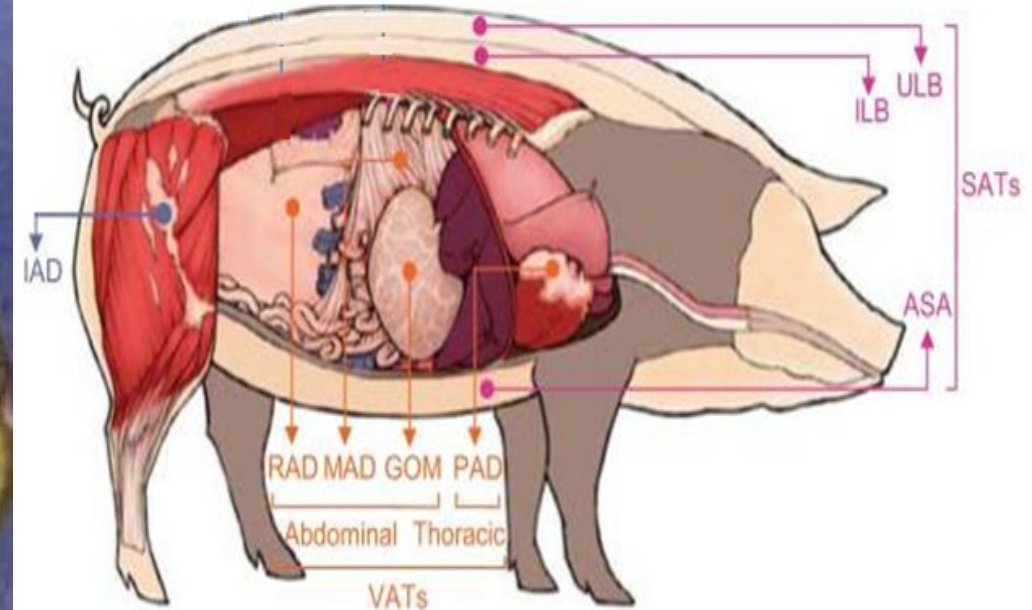
Meat quality



Pigs reflect human metabolism better than mice

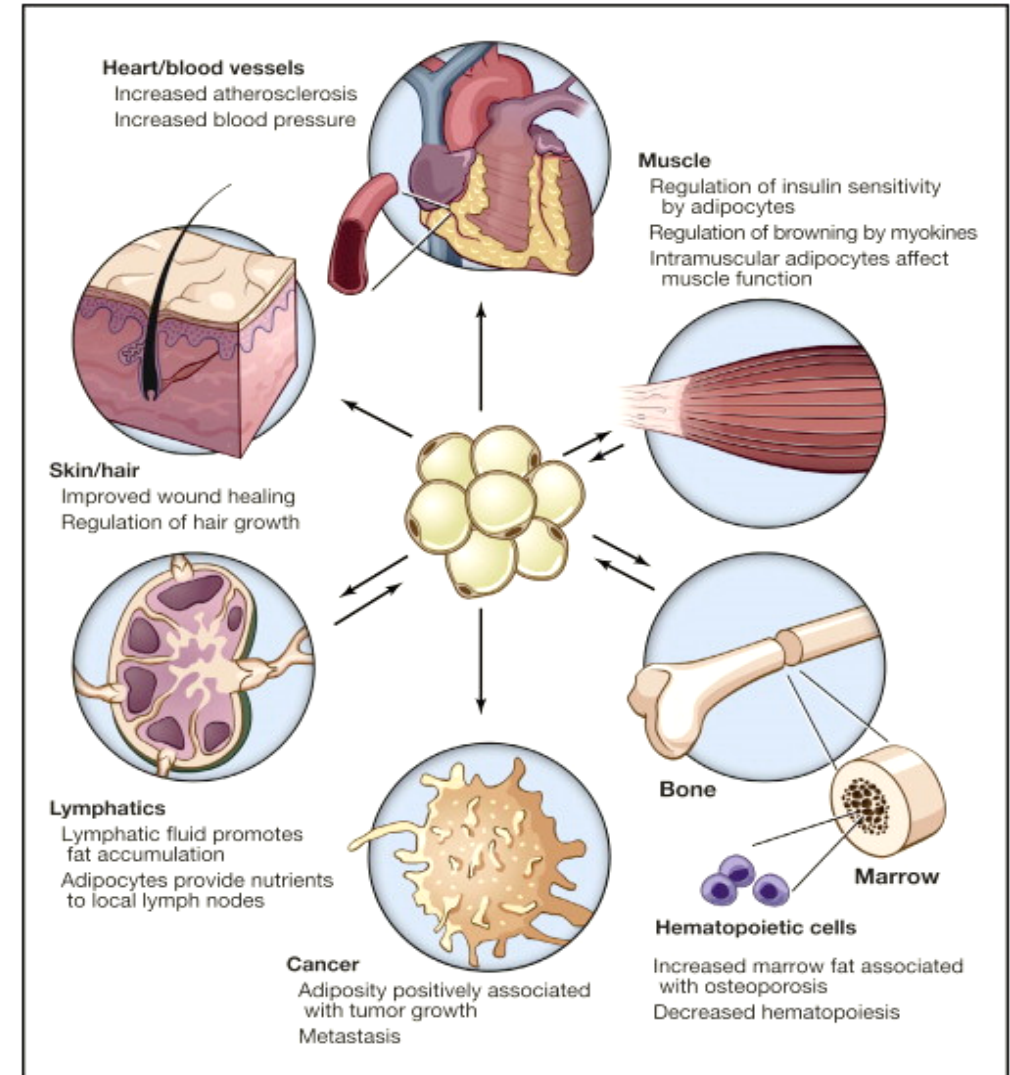
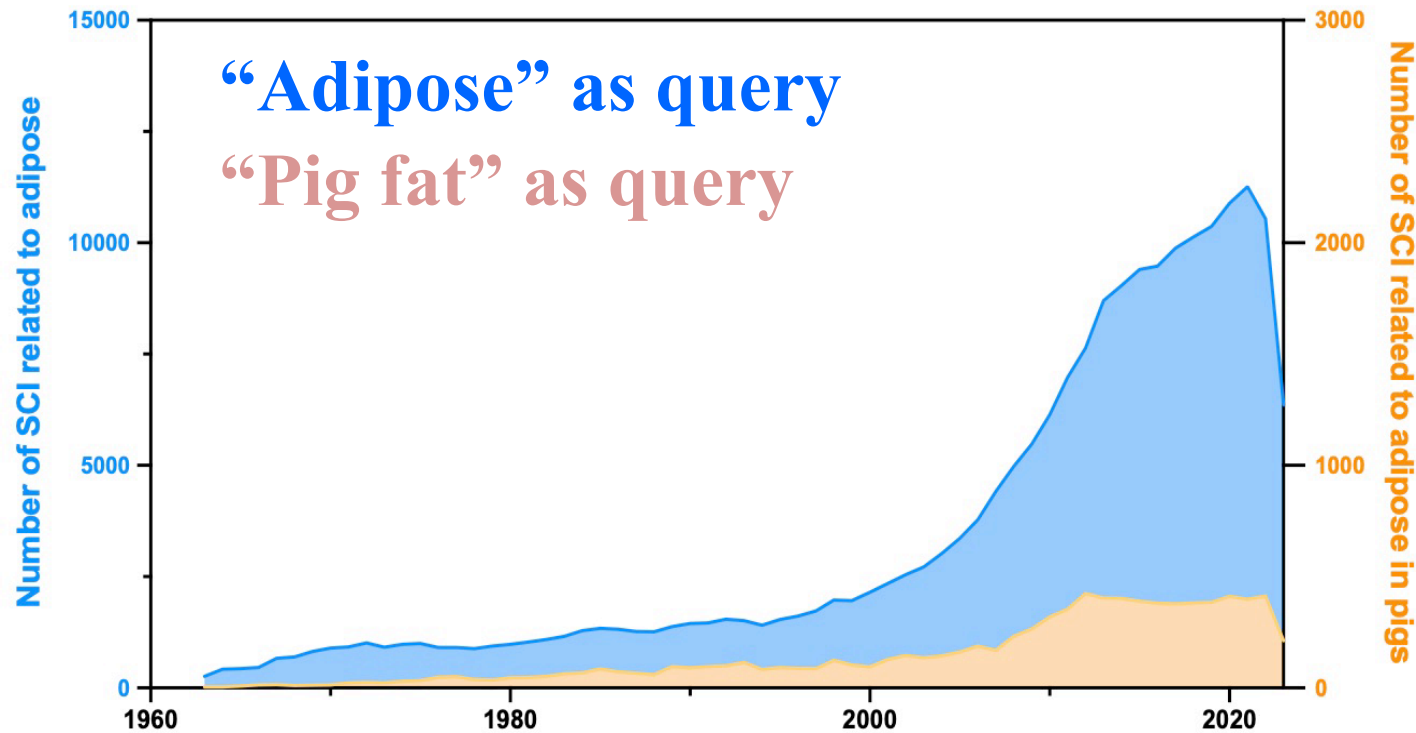


Murano et al., J Anatomy 2009



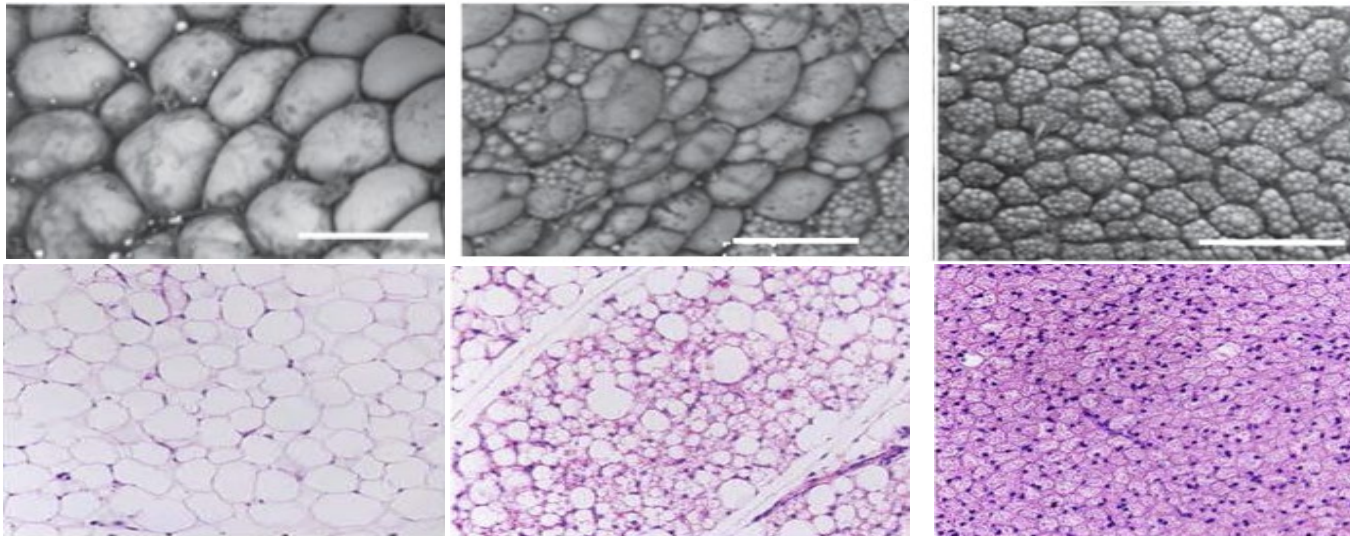
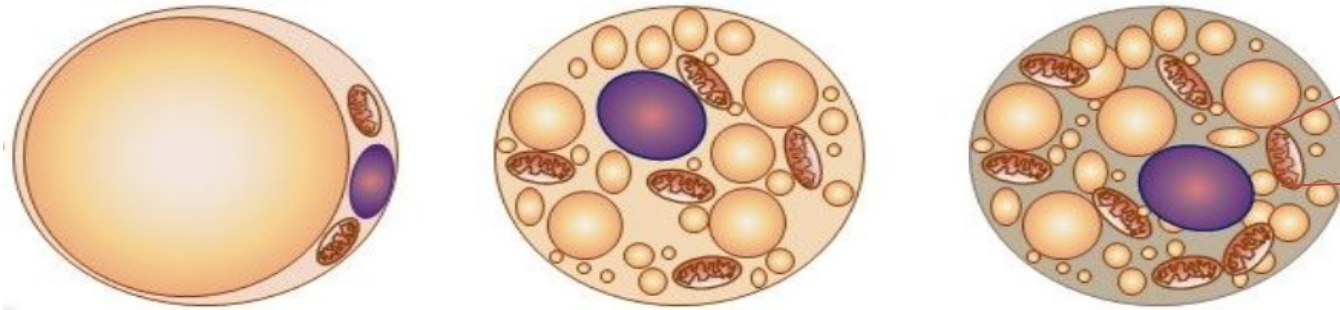
Adipose tissue is a central metabolic organ in the regulation of whole-body energy homeostasis

Adipose Biology



Characterizations of adipocytes

Thermogenic capacity

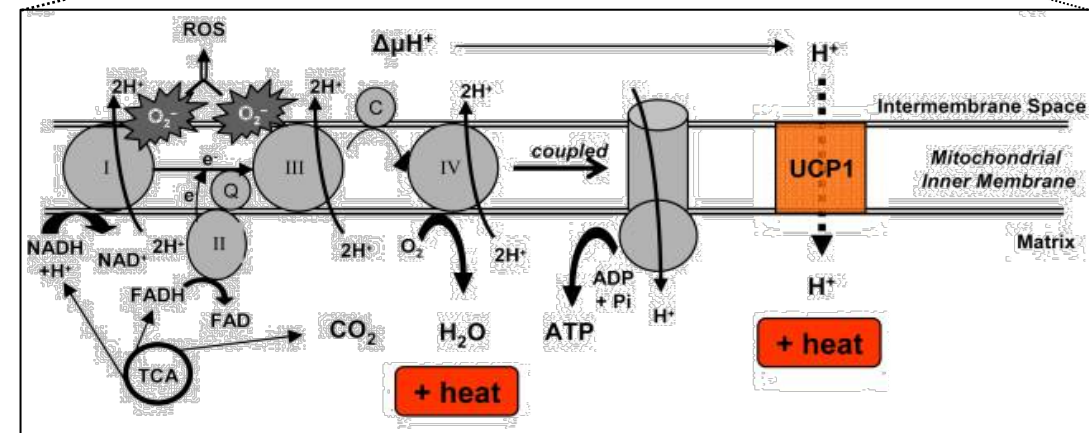
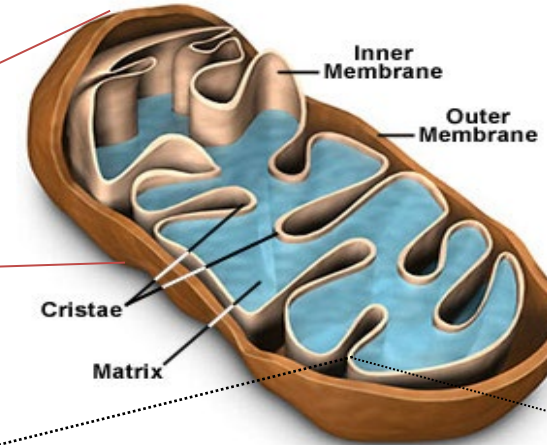


WAT
LEP, RETN

Beige
CD137

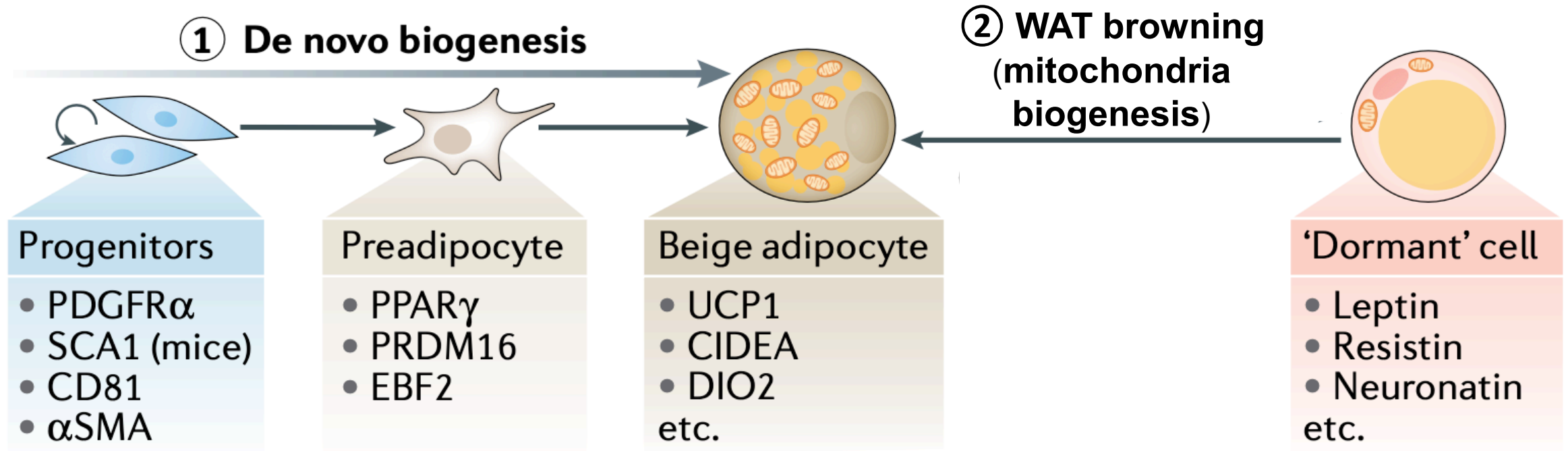
Brown
UCP1

Mitochondria Structural Features



**UCP1: Thermoregulation;
Fat deposition**

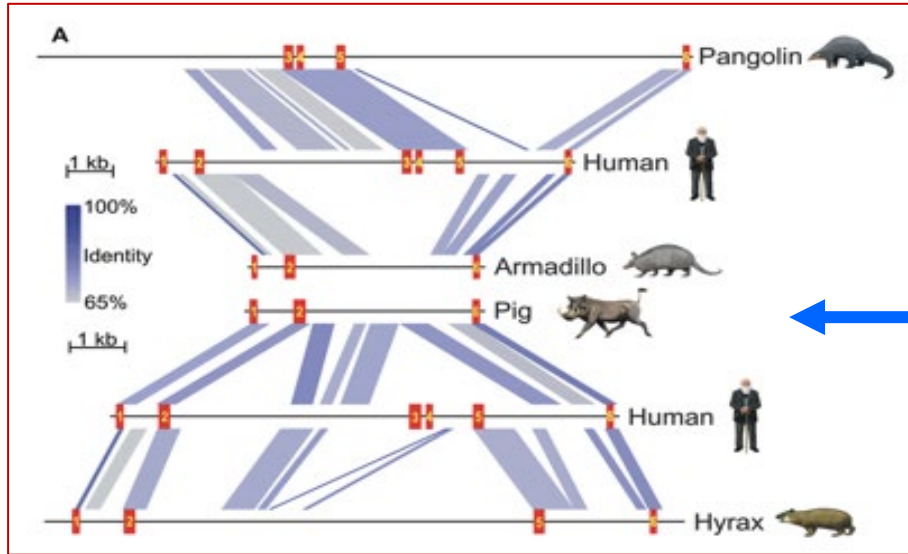
Beige was originated by de novo biogenesis and WAT browning



Revised from COHEN and KAJIMURA, 2021

Neither functional UCP1 nor BAT is present in pigs

Exon 3-5 of UCP1 was evolutionally lost



Gaudry et al. *Sci Adv* 2017

McGaugh S and Schwartz TS, *Biol Lett.* 2017

BAT is not present in the pigs

Can J Physiol Pharmacol. 1989 Dec;67(12):1480-5.

Evidence from immunoblotting studies on uncoupling protein that brown adipose tissue is not present in the domestic pig.

Trayhurn P¹, Temple NJ, Van Aerde J.

⊕ Author information

**Piglets are sensitive to cold environment;
Poor thermoregulation leads to neonatal mortality**



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PLoS GENETICS

The Uncoupling Protein 1 Gene (*UCP1*) Is Disrupted in the Pig Lineage: A Genetic Explanation for Poor Thermoregulation in Piglets

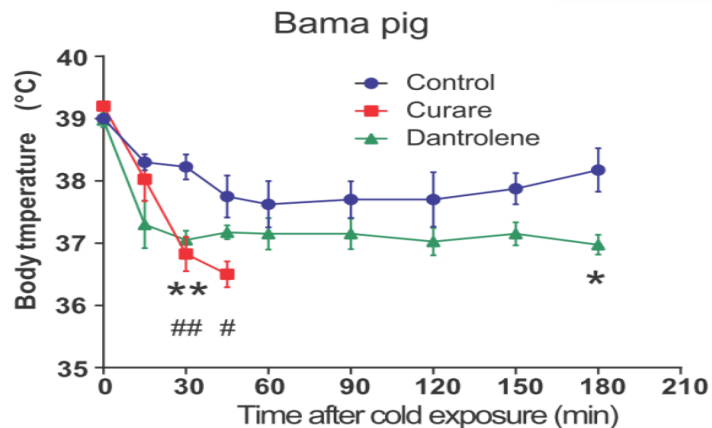
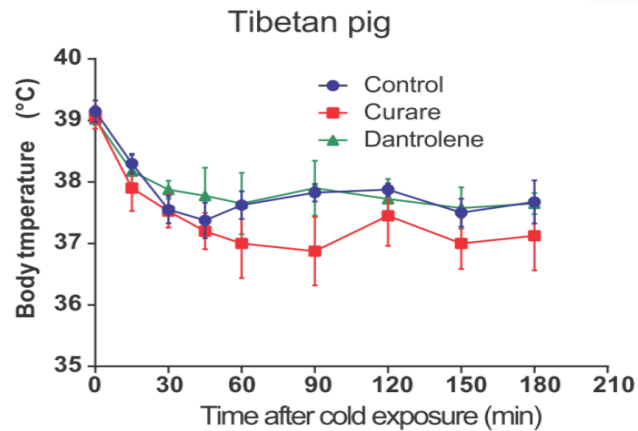
Frida Berg¹, Ulla Gustafson², Leif Andersson^{1,2*}

¹ Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, Sweden, ² Department of Animal Breeding and Genetics, Swedish University of Agricultural Sciences, Uppsala, Sweden

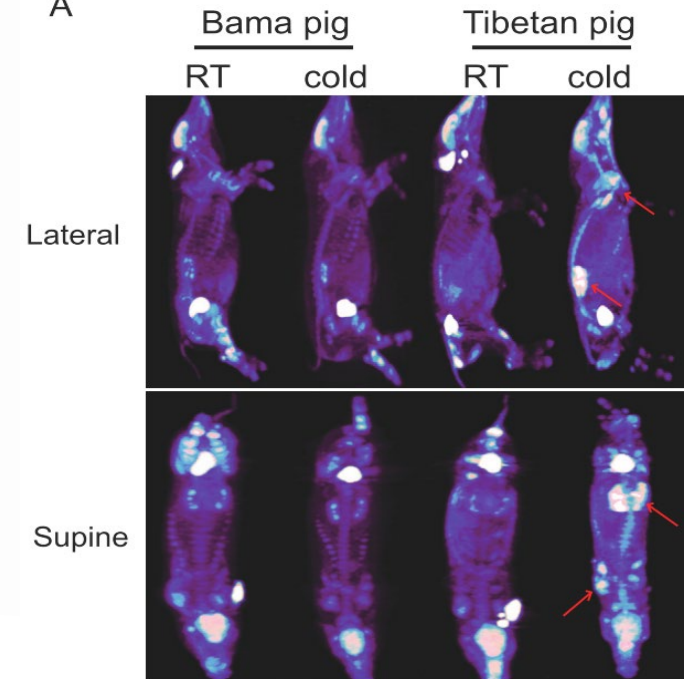
Tibetan pigs have an alternative pathway to maintain body temperature independent of muscle-mediated thermogenesis



Cold 4 °C, 3 hours

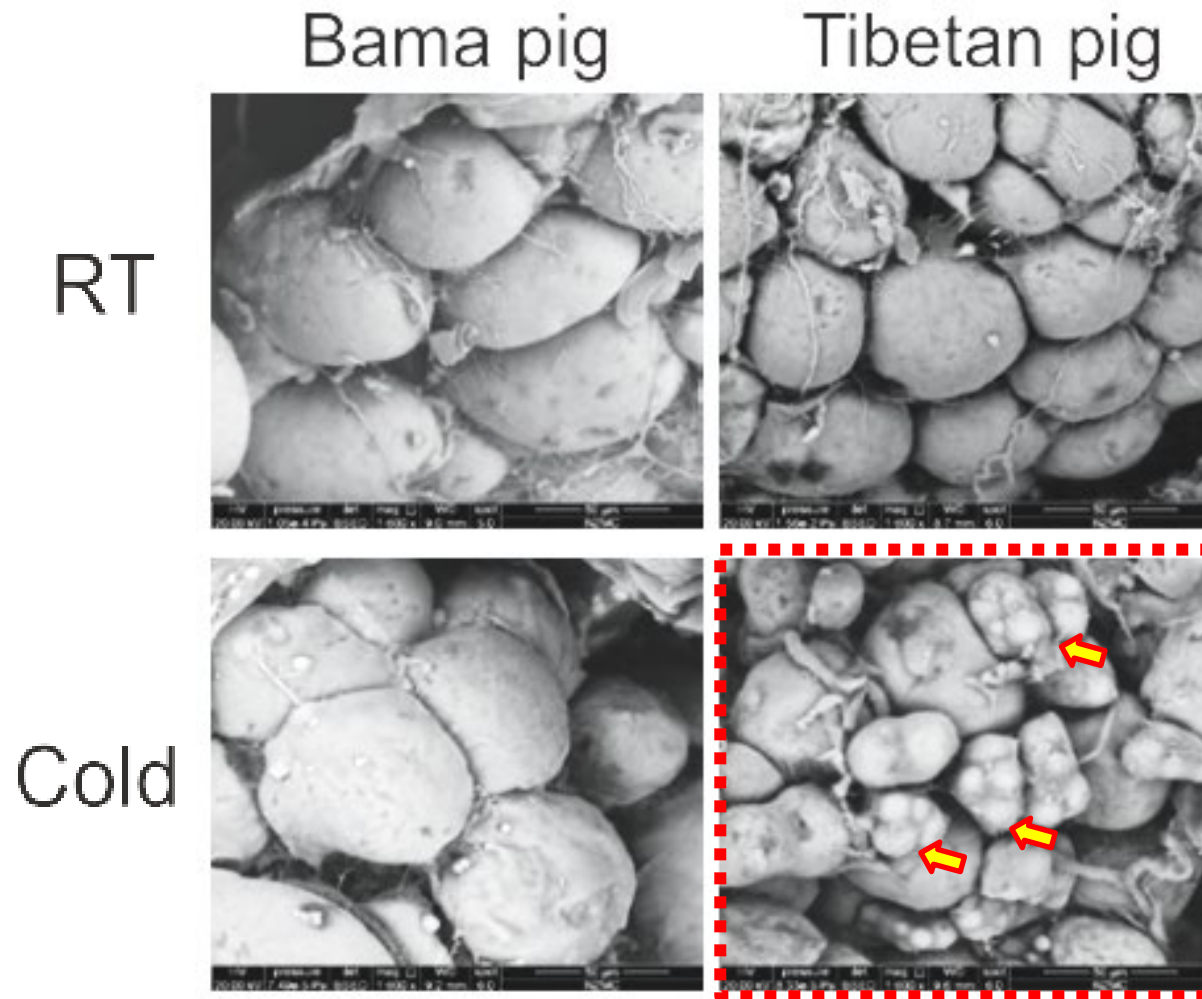


A



Lin et al, *J Mol Cell Biol*, 2017

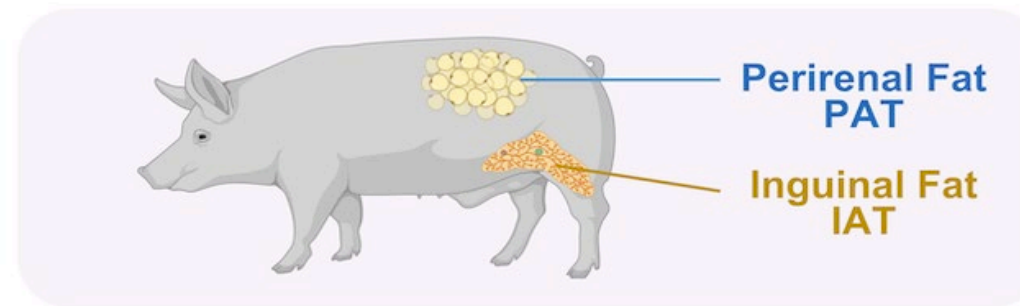
Cold adaption of Tibetan pigs relies on beige adipogenesis



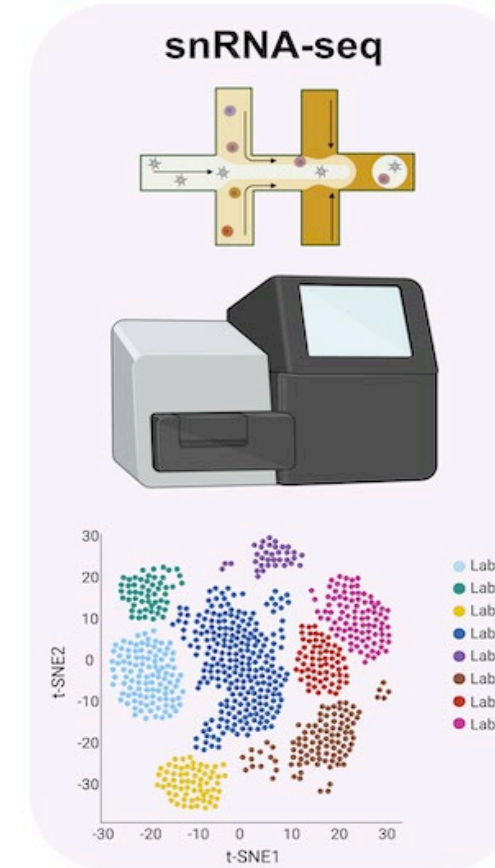
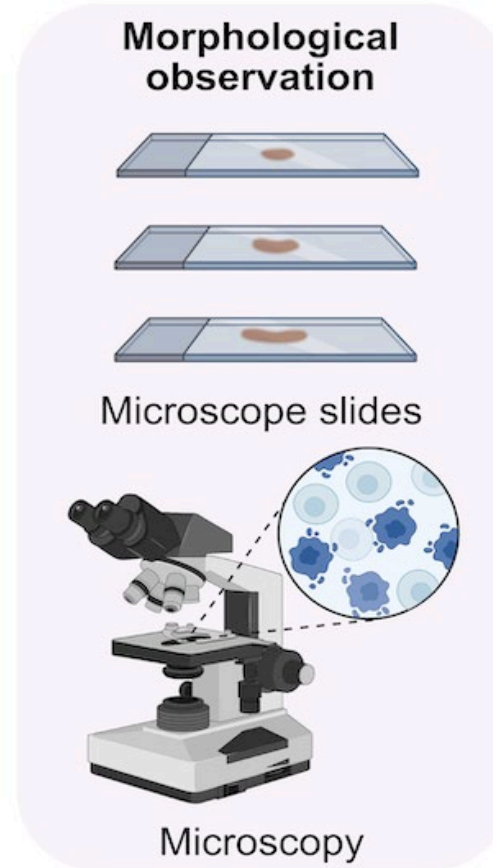
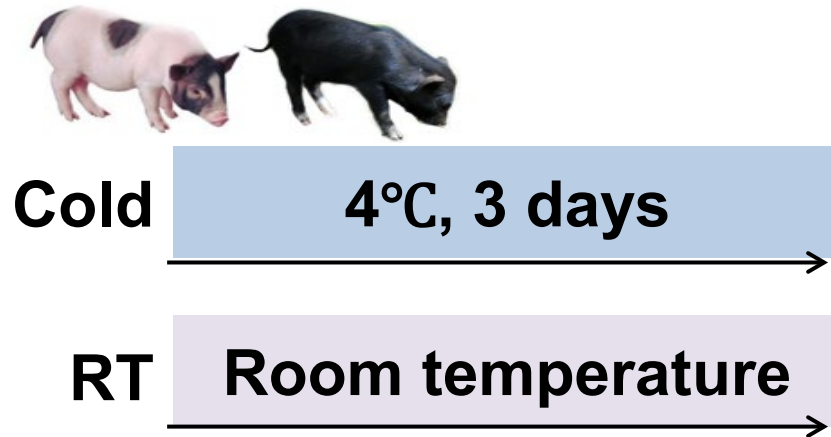
Biological Questions

1. Cellular mechanisms of cold-induced Beige formation in Tibetan pigs?
2. Can beige adipocytes be induced in Bama pigs when they are exposed to a prolonged cold environment?

Tissue collection

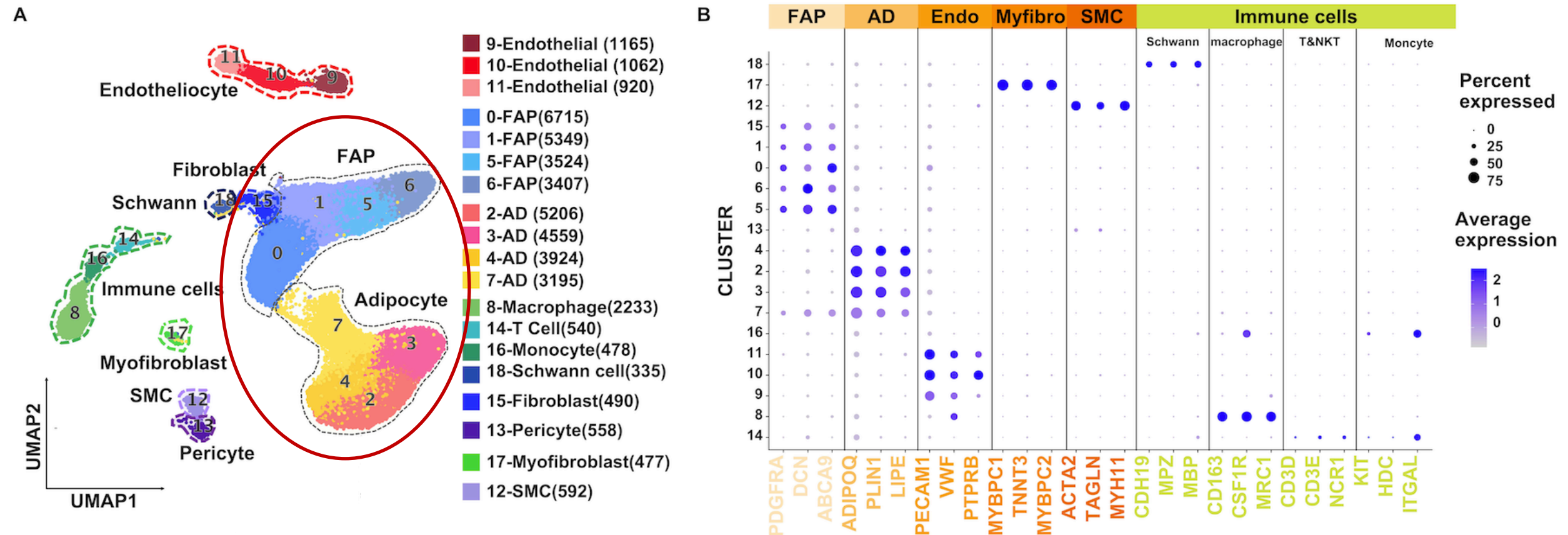


Tissue Analysis



Unpublished

SnRNA-sequencing defines the cell populations from eight adipose tissues of both pig breeds

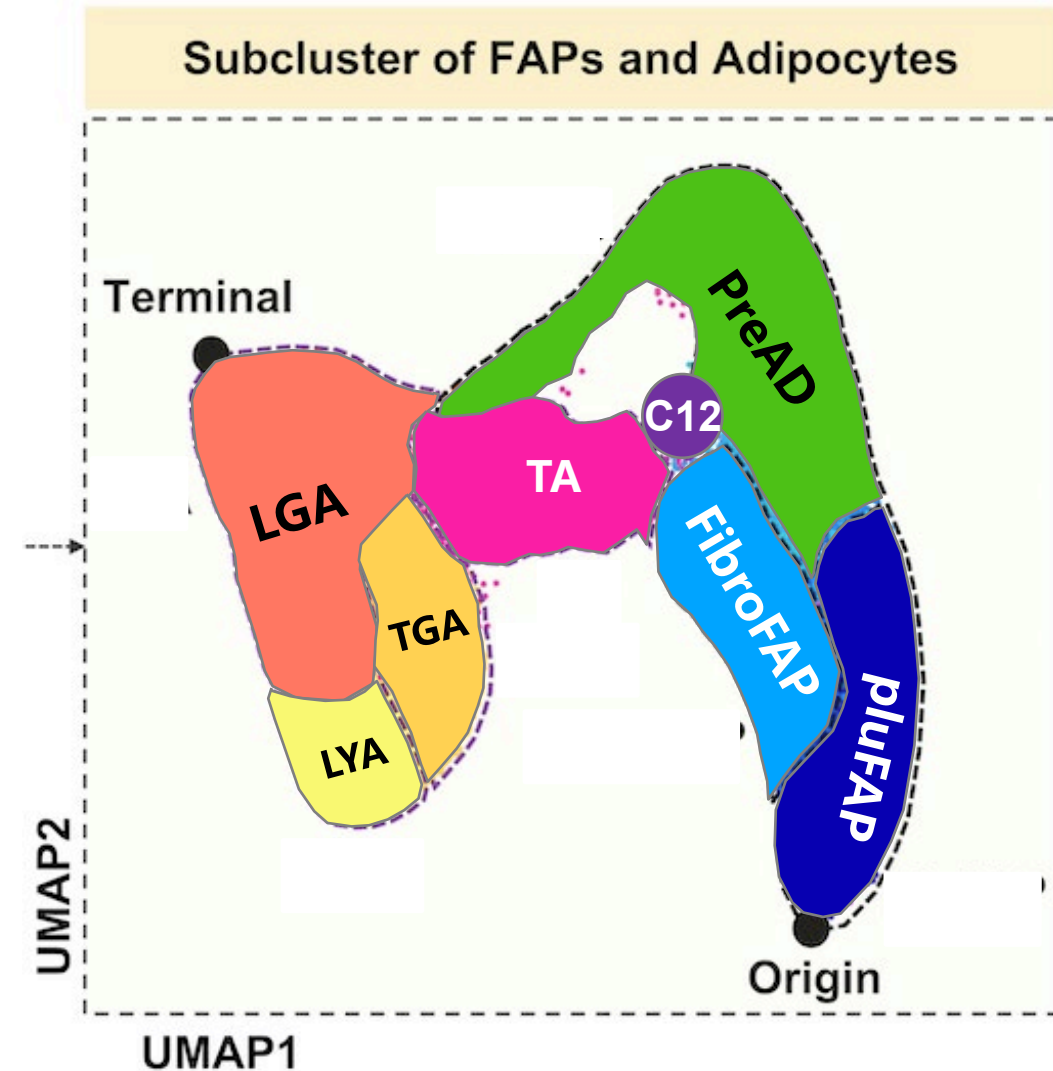
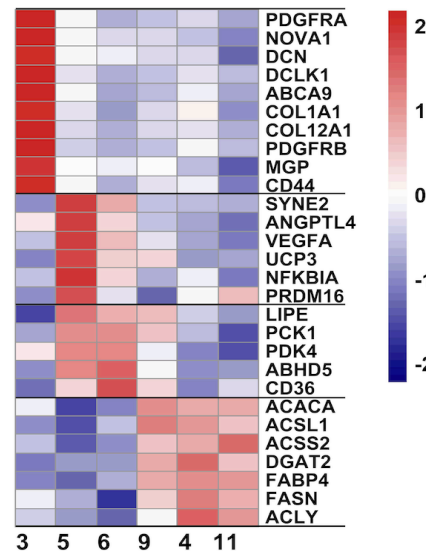
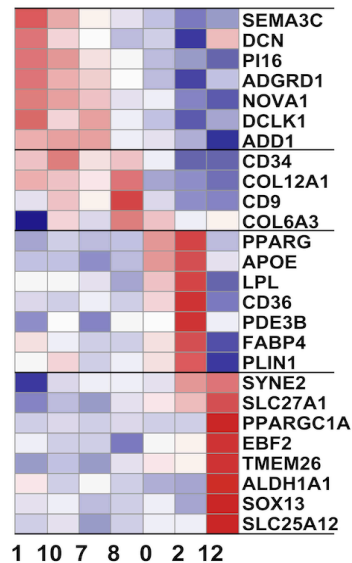
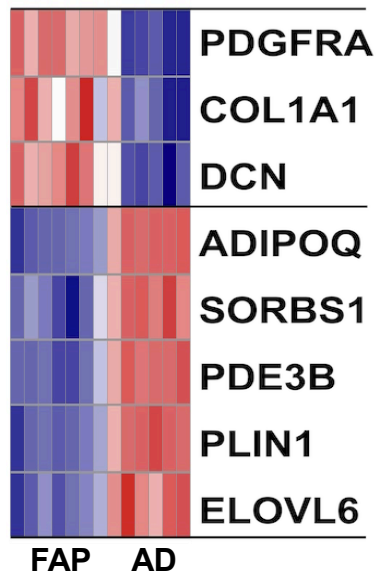
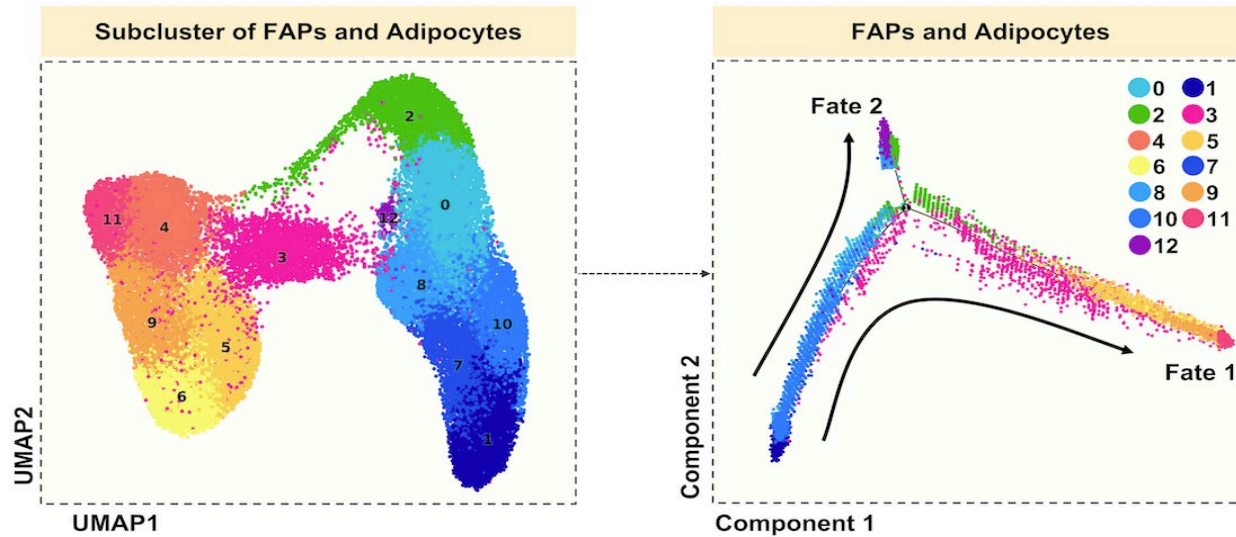


FAP: Fibro/adipogenic progenitors 43.24%

AD: Adipocyte, 37.75%

Unpublished data

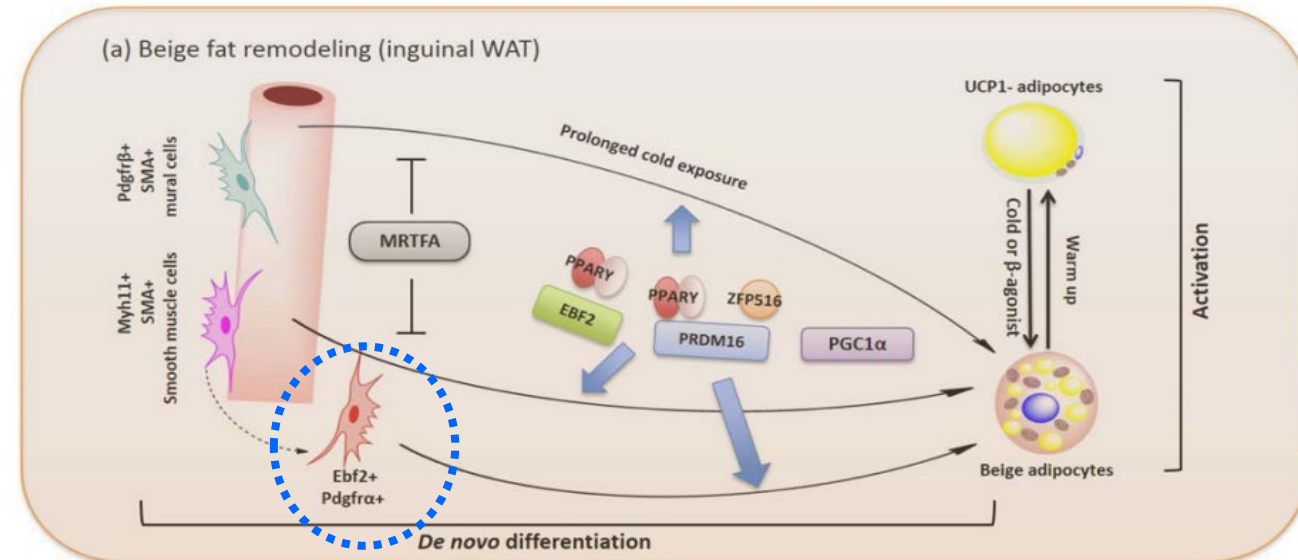
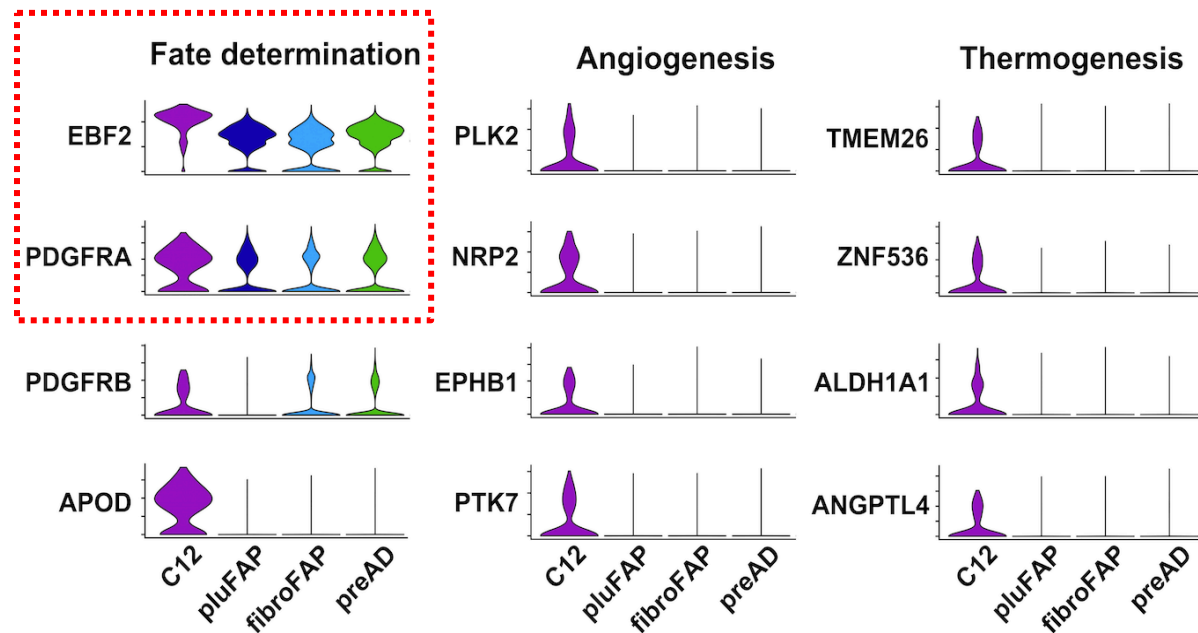
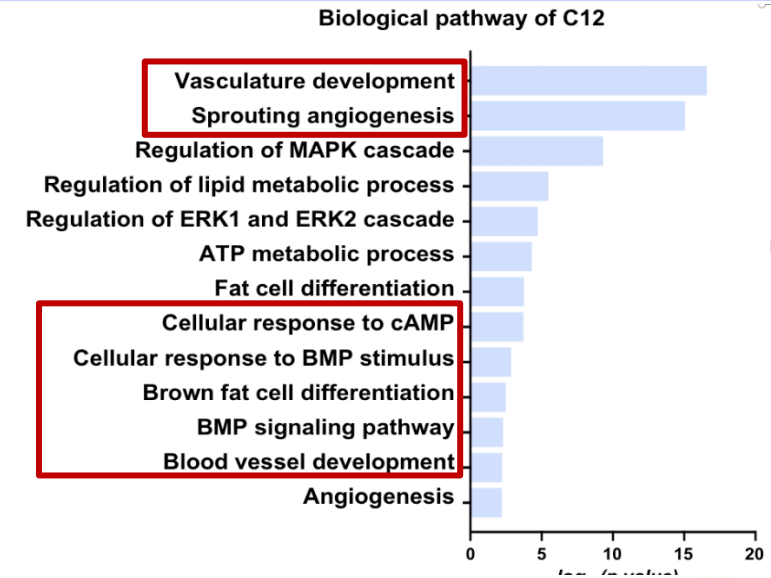
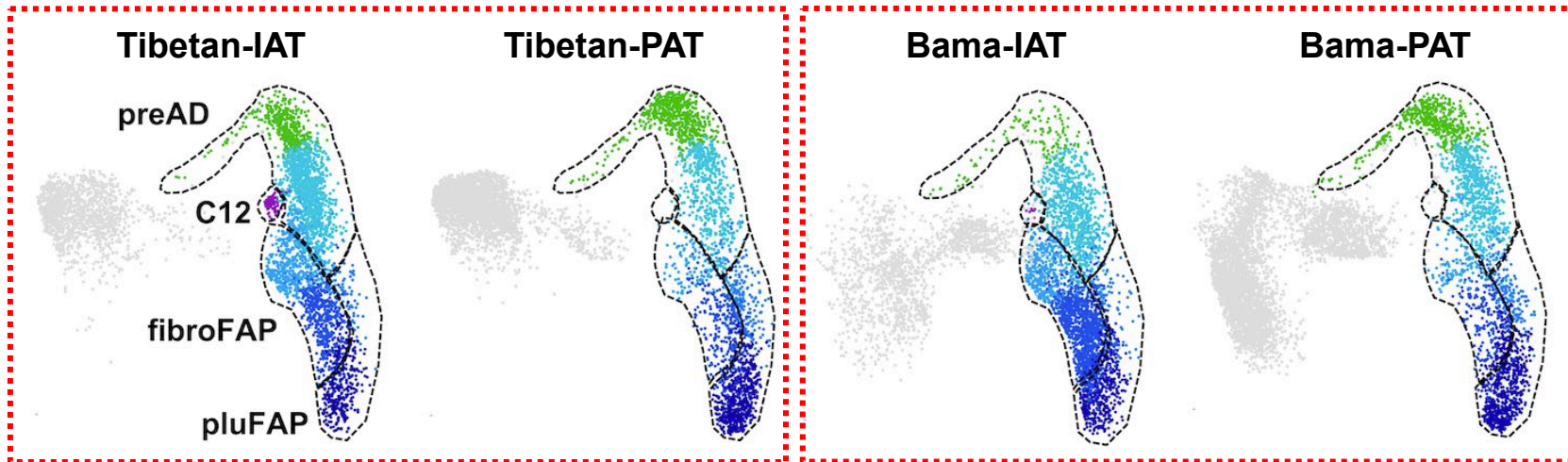
Functional annotation of FAP and AD



Unpublished data

Breed-specific features of FAP and AD subpopulations in Bama and Tibetan pigs

C12 cells (*PDGFRA*⁺ *EBF2*^{High}) are the potential beige precursors in IAT of Tibetan pigs



C11 (*ADIPOQ*⁺*HIF1A*^{high}) is present in Tibetan pigs specifically

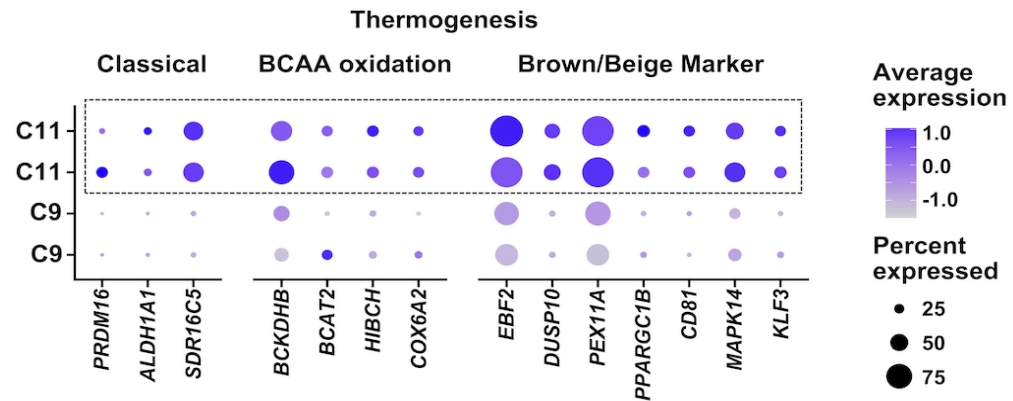
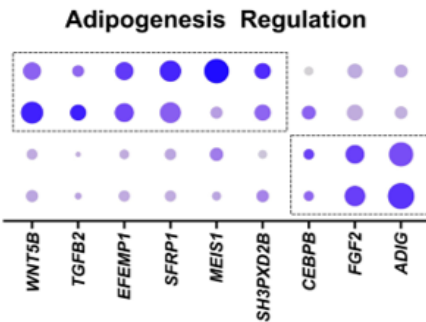
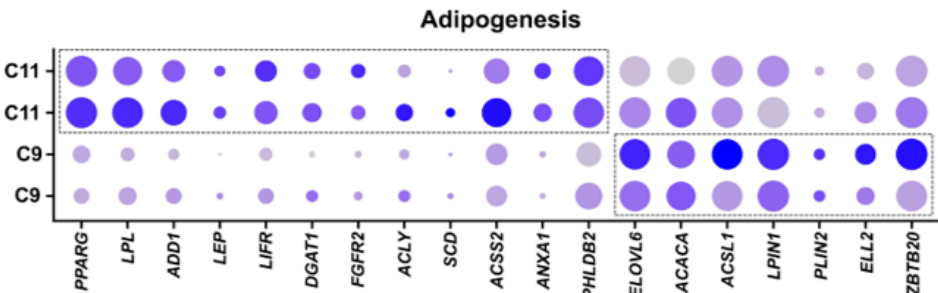
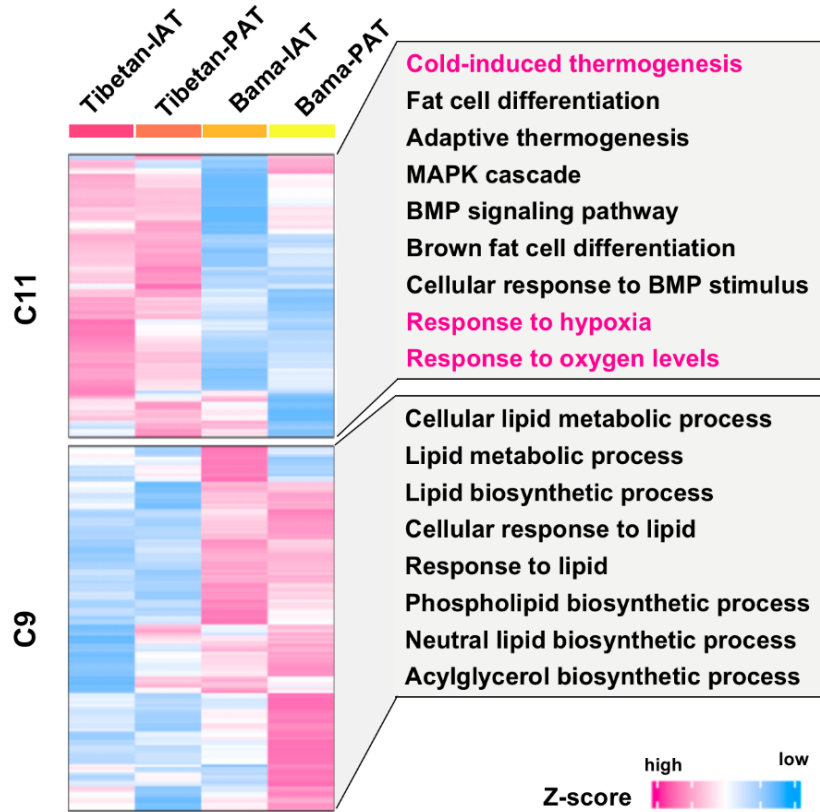
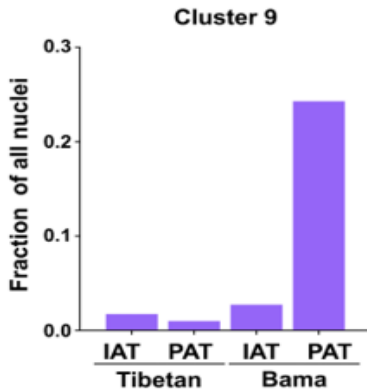
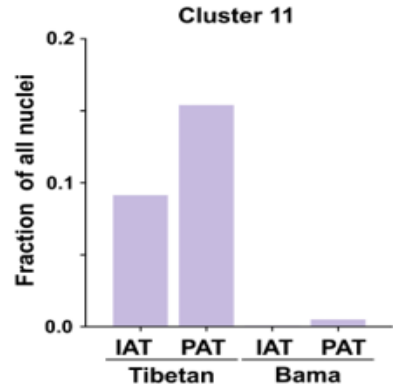
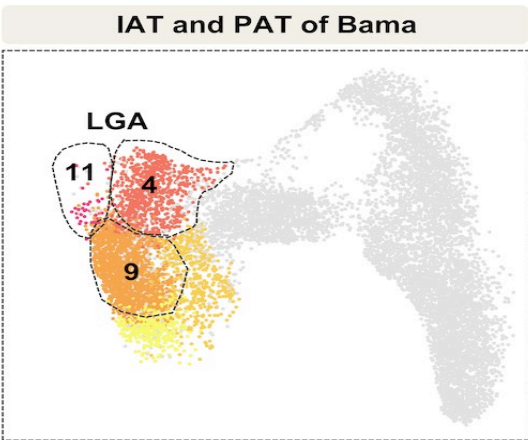
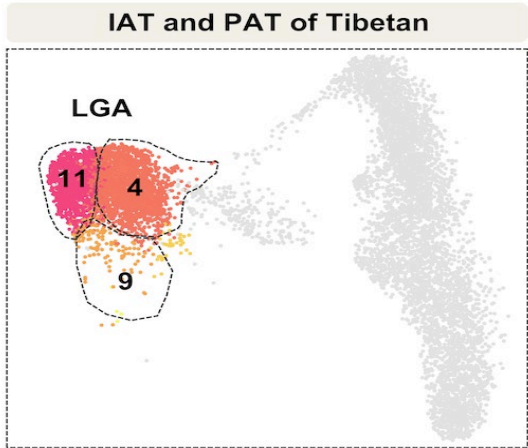
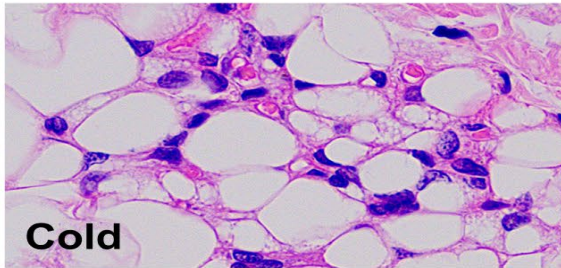
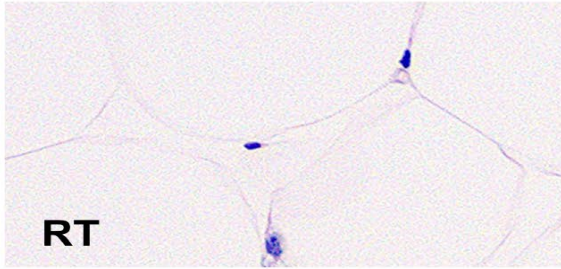


Figure 3 is a dot plot titled "PSGs identified in the Tibetan pigs genomes". The y-axis lists the cell lines: C11, C11, C9, and C9. The x-axis lists the genes: *NPR1*, *IGF1*, *GRIA2*, *PSPH*, *DGAT1*, *EEA1*, *TMTC4*, *PANK3*, *HIF1A*, *MMP11*, *GP2*, *TTC13*, *MAPK8IP3*, and *FBXO30*. A dashed box encloses the first two rows (C11, C11). To the right, there are two legends: "Average expression" with a color scale from -1.0 (light purple) to 1.0 (dark purple), and "Percent expressed" with dot sizes corresponding to 20, 40, and 60%.

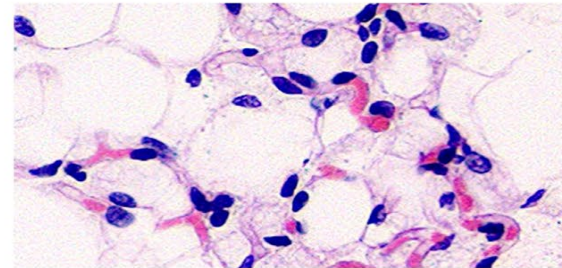
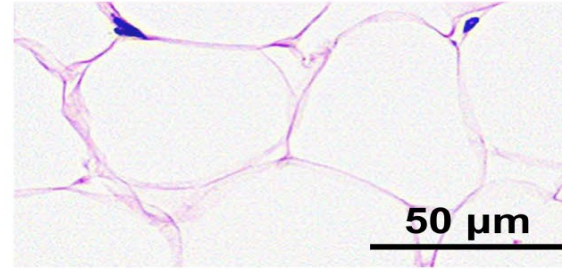
Cold-induced cellular responses in adipose tissues from Tibetan and Bama pigs

Beige formation was observed in short time cold-treated both pigs

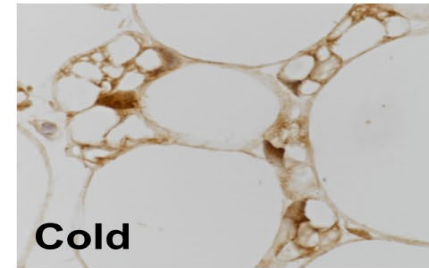
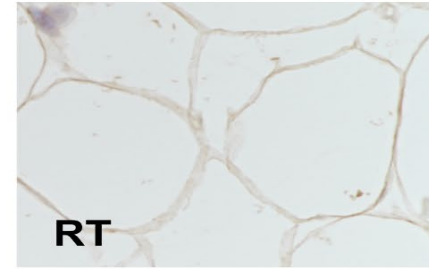
Tibetan-IAT



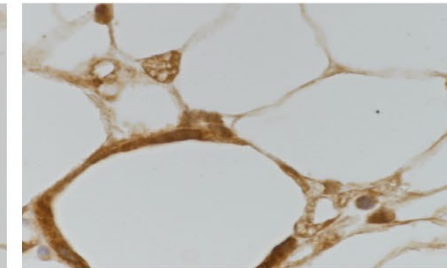
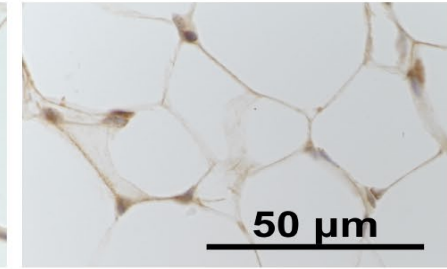
Tibetan-PAT



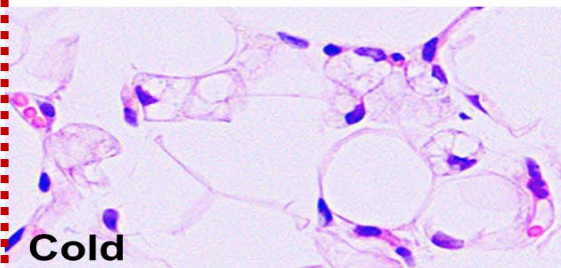
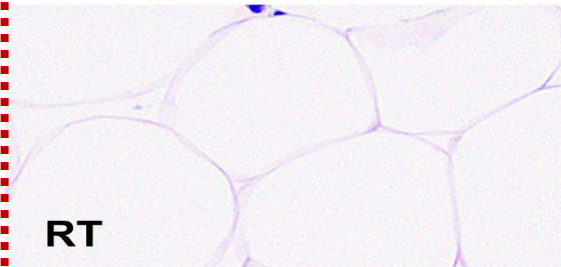
Tibetan-IAT



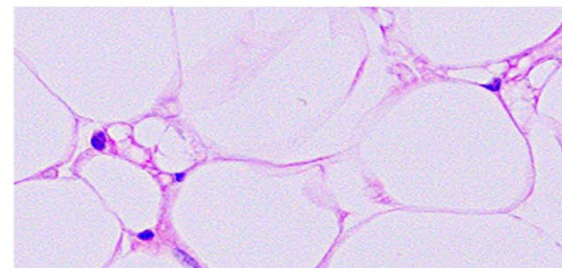
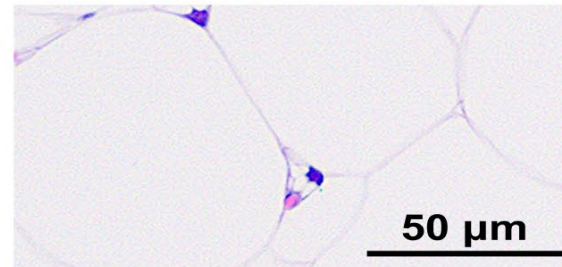
Tibetan-PAT



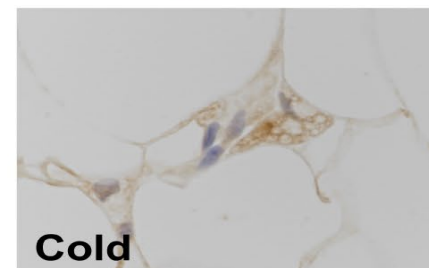
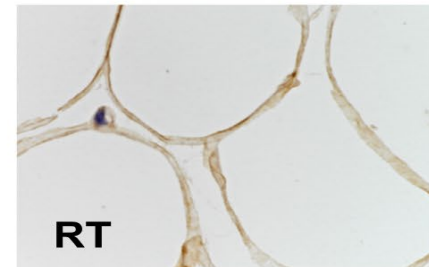
Bama-IAT



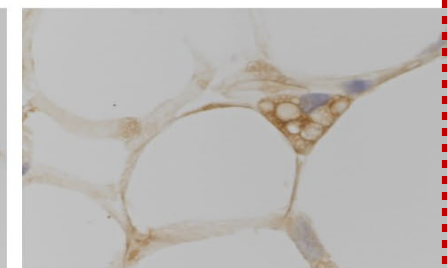
Bama-PAT



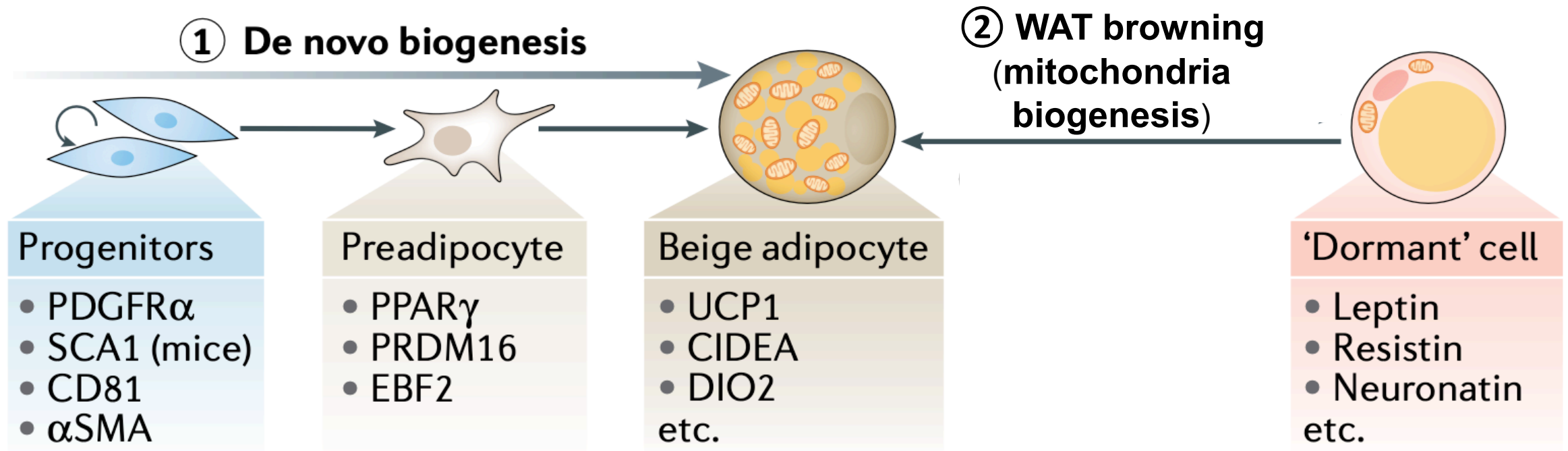
Bama-IAT



Bama-PAT



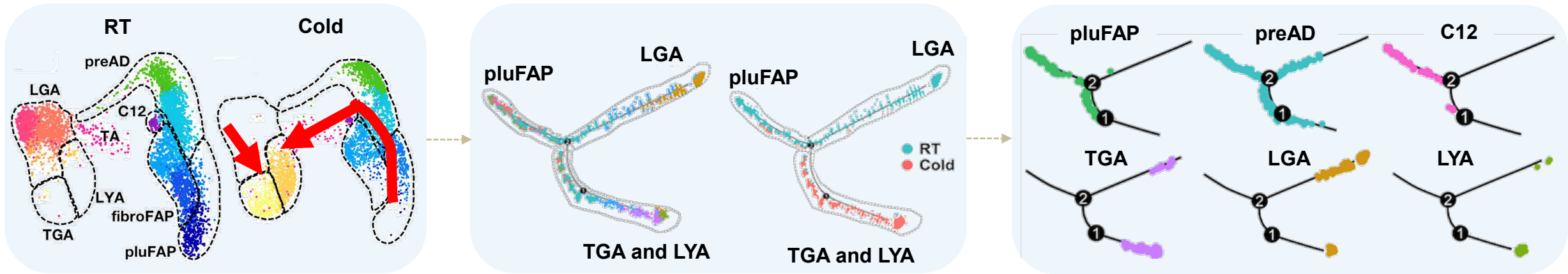
Beige was originated by de novo biogenesis and WAT browning



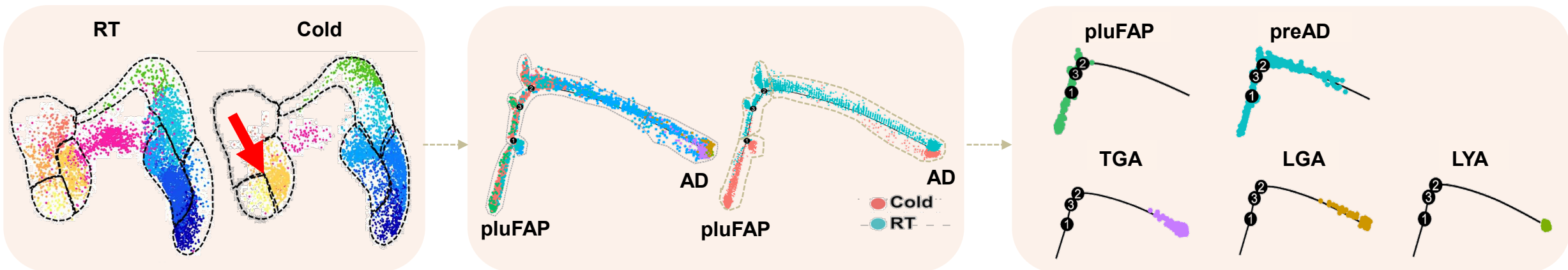
Revised from COHEN and KAJIMURA, 2021

Cold induced-beige *de novo* biogenesis was only found in Tibetan pigs

Tibetan-IAT : Cold induces a new cell fate from pluFAP to TGA and LYA

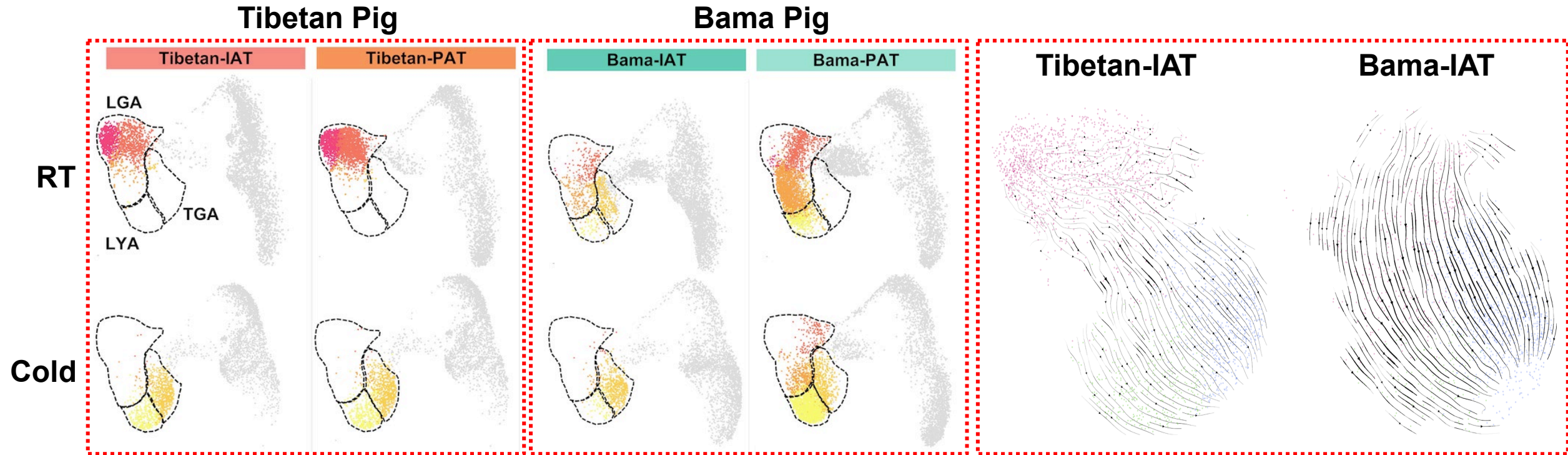


Bama-IAT



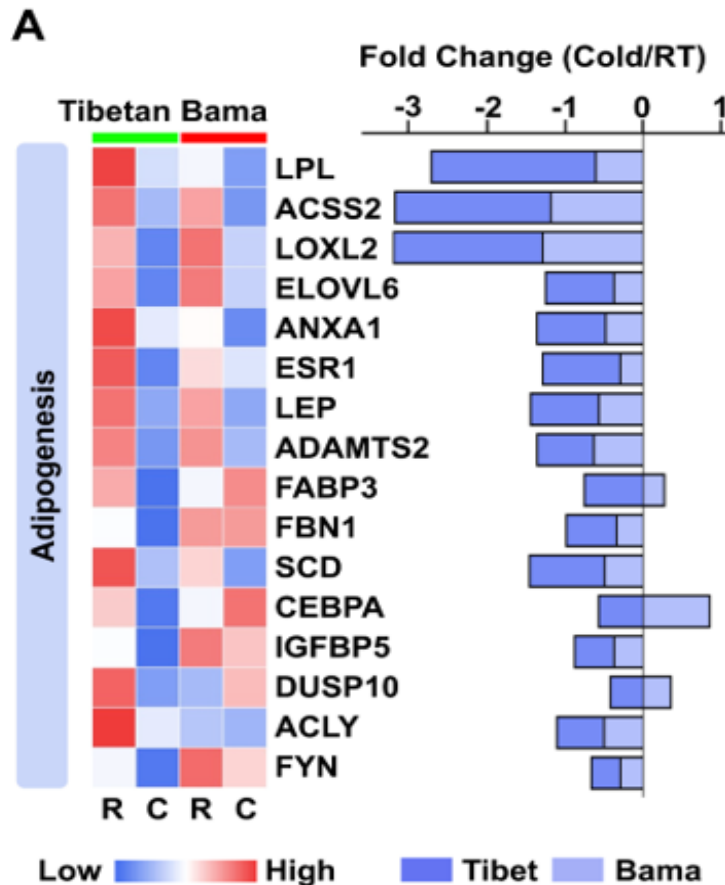
Cold induces WAT browning in both pigs

Cold induces a stronger cellular remodeling in the adipose tissues of Tibetan pigs

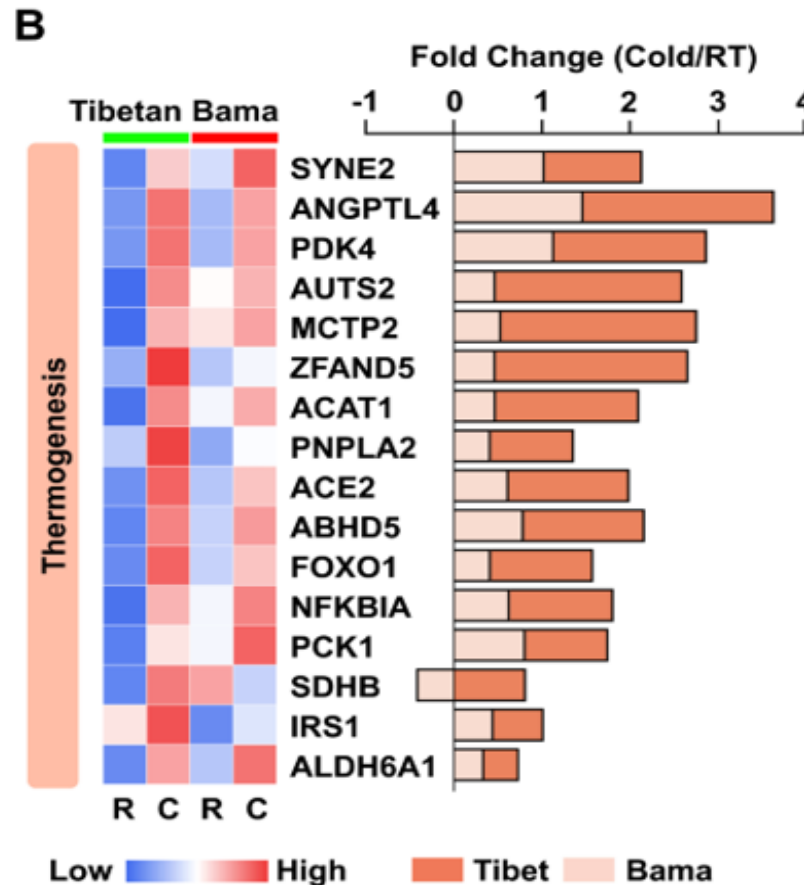


Cold induces a stronger transcriptional responses in the adipose tissues of Tibetan pigs

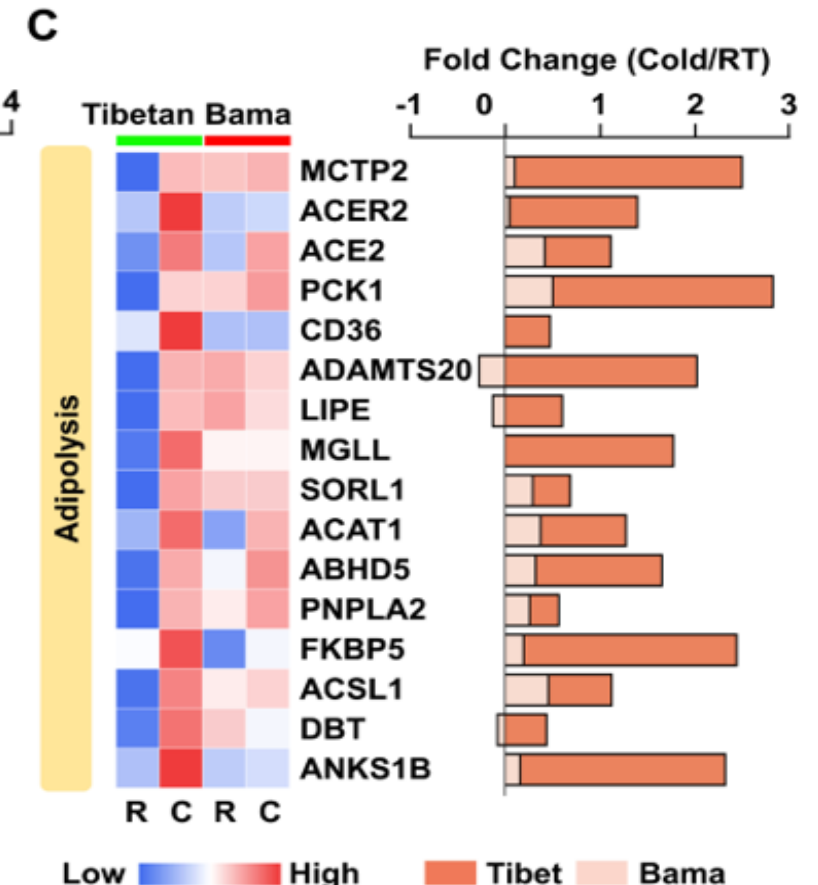
Adipogenesis



Thermogenesis

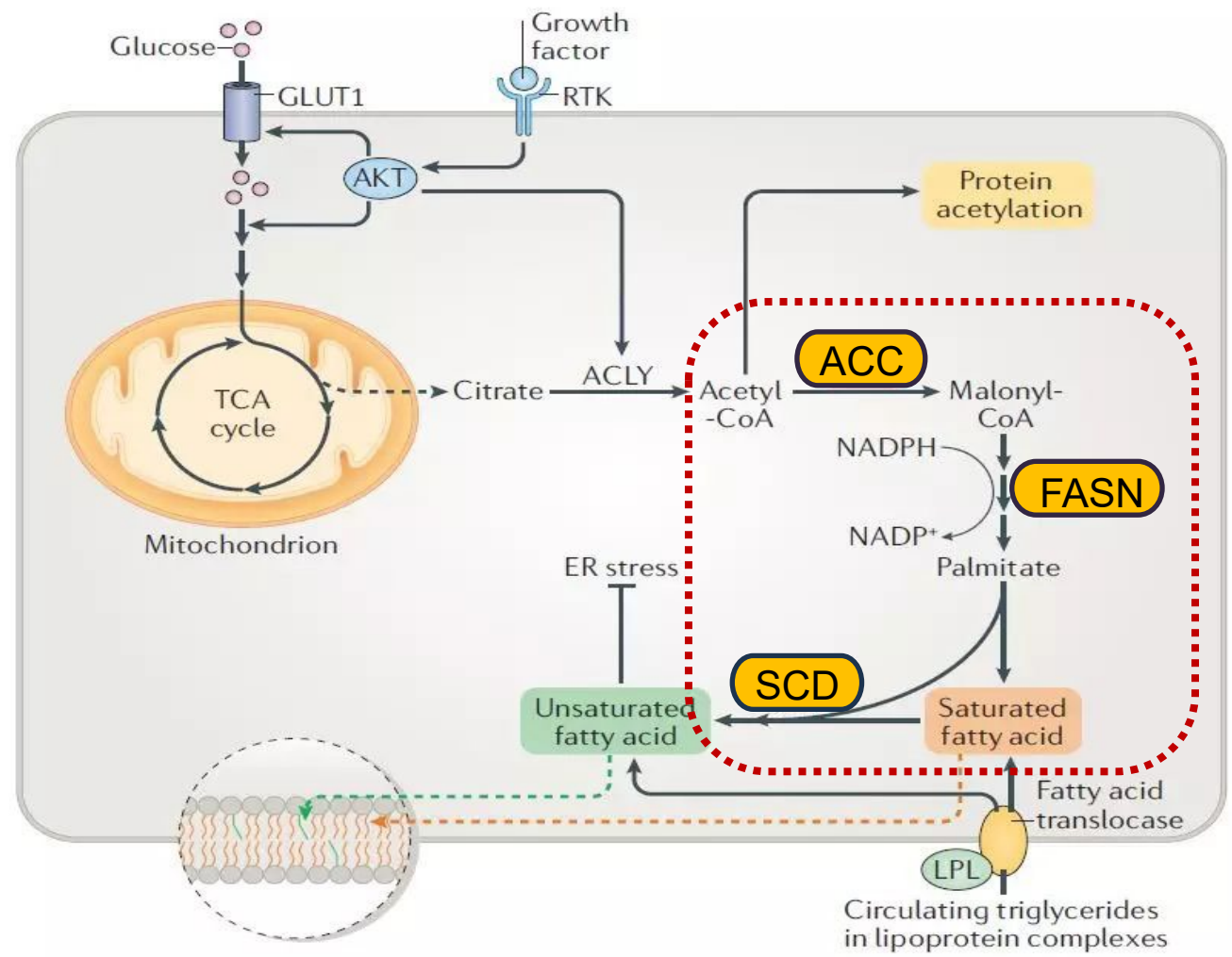
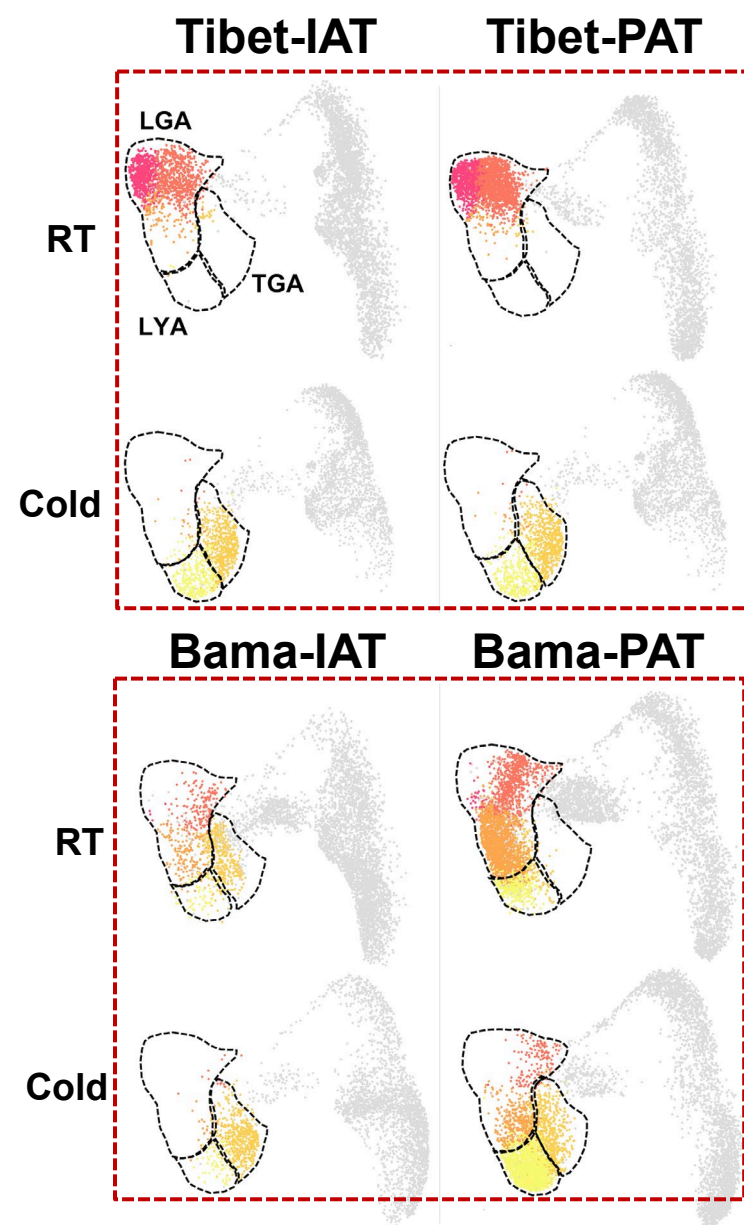


Lipolysis



**Whether beige adipocytes can be induced in Bama pigs
pharmacologically or genetically?**

Suppression of de novo lipogenesis (DNL) in both cold-treated pigs



Suppression of DNL genes induces beige formation in mice

Scd1 controls de novo beige fat biogenesis through succinate-dependent regulation of mitochondrial complex II

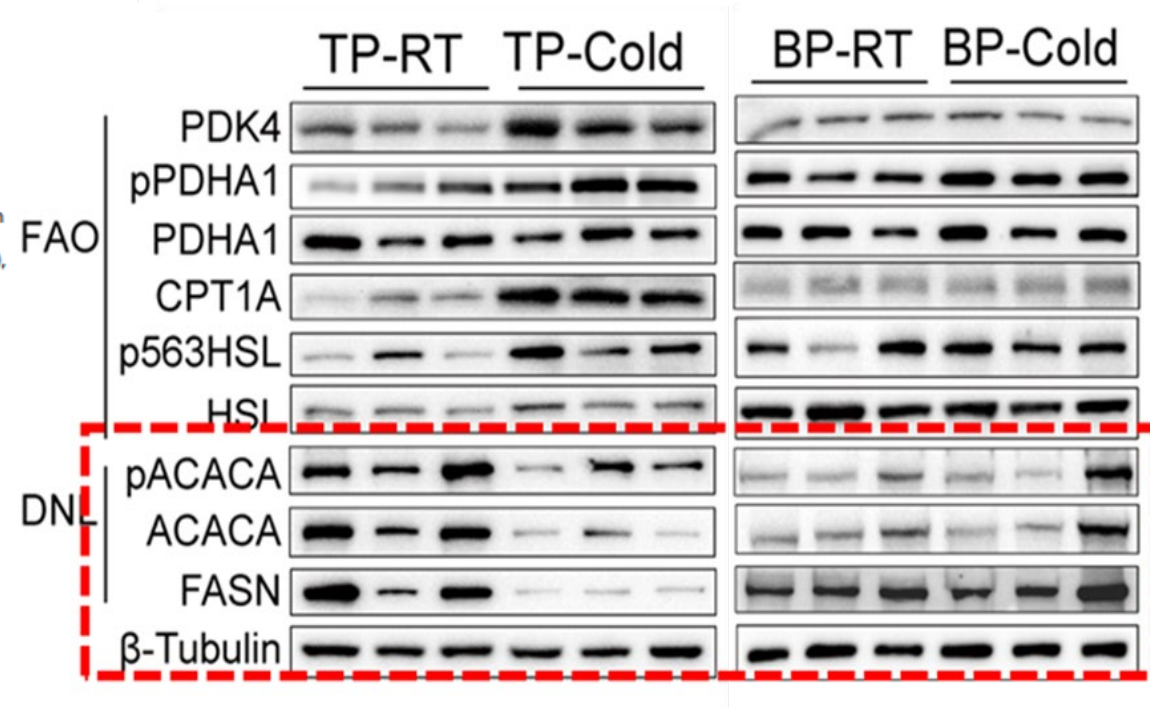
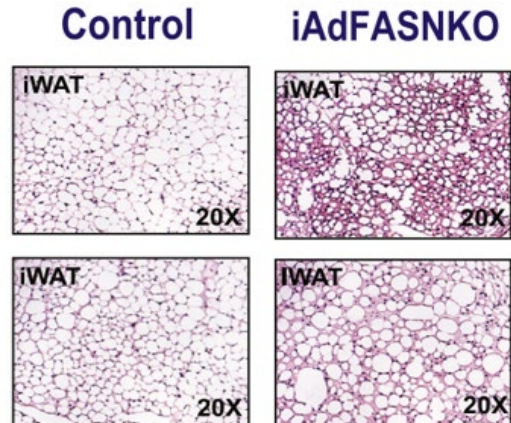
Keli Liu^{a,b}, Liangyu Lin^a, Qing Li^a, Yueqing Xue^a, Fanjun Zheng^a, Guan Wang^a, Chunxing Zheng^a, Liming Du^a, Mingyuan Hu^a, Yin Huang^a, Changshun Shao^c, Xiangyin Kong^a, Gerry Melino^d, Yufang Shi^{a,b,c,1}, and Ying Wang^{a,1}

^aCAS Key Laboratory of Tissue Microenvironment and Tumor, Shanghai Institute of Nutrition and Health, Shanghai Institutes for Biological Sciences, University of Chinese Academy of Sciences, Chinese Academy of Sciences, 200031 Shanghai, China; ^bSchool of Life Science and Technology, ShanghaiTech University, 200031 Shanghai, China; ^cThe First Affiliated Hospital of Soochow University, State Key Laboratory of Radiation Medicine and Protection, Institutes for Translational Medicine, Soochow University, 215123 Suzhou, China; ^dBiochemistry Laboratory, Istituto Dermopatico Immacolata (IDI-IRCCS), 00100 Rome, Italy; and ^eDepartment of Experimental Medicine, University of Rome Tor Vergata, 00133 Rome, Italy

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Adipocyte lipid synthesis coupled to neuronal control of thermogenic programming



Whether Inhibition of DNL pathway could induce Beige adipocyte in Bama pigs

Suppression of DNL pathway by ACC inhibitor, TOFA, induces beige formation in Bama pigs

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75th Annual Meeting of The European Federation of Animal Scien

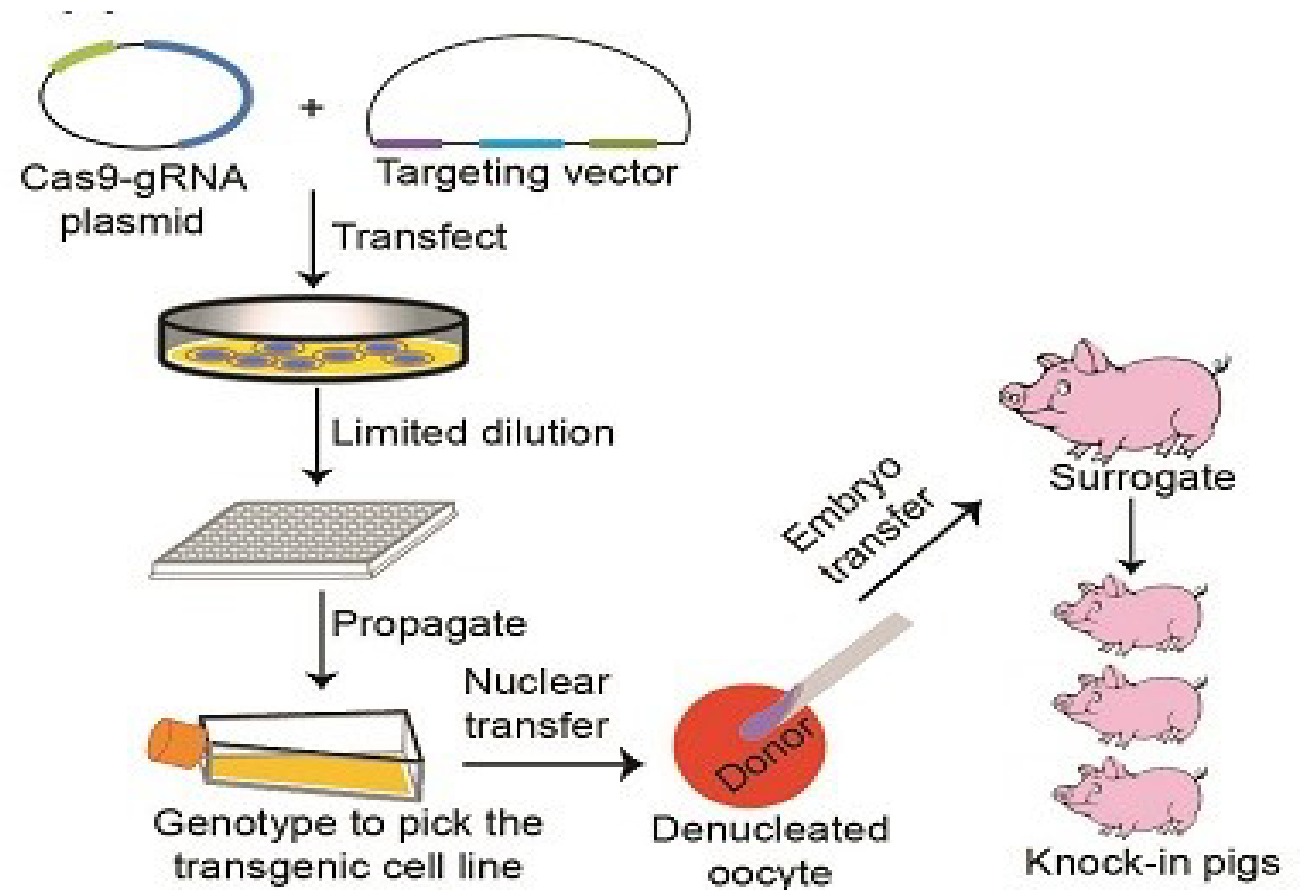
17:00 Acetyl-CoA Carboxylase 1 Inhibition Reduces Fat Deposition Through a Histone Acetylation Signaling Axis in Pigs

C. Tao, L. Zhang, J. Xu, Y. Wang

1040

4th Sep, Dr. Cong Tao will present this data (97#)

Gene editing strategy provides the tool for generation of GM pigs



Summary

- 1. Two Tibetan pig-specific cell subpopulations were identified;**
- 2. Upon cold stimulation, beige fat was recruited by both de novo beige adipogenesis and WAT browning in Tibetan pigs, while Bama pigs lack of de novo beige adipogenesis process;**
- 3. Beige adipocytes can be induced in Bama pigs pharmacologically.**

Acknowledgements

Institute of animal Science (CAAS)

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Dr. Jiali Liu

Jian Xu



Institute of Zoology (CAS)

Dr. Jianguo Zhao

Tianxia Liu

Yu Wang

