Pre- and postnatal development of adipose depots in meat animals with a specific focus on the pig

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ICoMST 2019

Outline

- Introduction
- Structure, location and functions of adipose tissues
- Fetal and postnatal development and growth of adipose tissues
- Factors affecting body adiposity and intramuscular fat deposition
- Conclusion

Adipose tissue : a tissue of great interest for meat producing animals

- **A significant compartment in the body in term of**
  - **mass**
  - **physiological functions**

- **An influence on production efficiency**

- Selection for lean growth to increase the lean/fat ratio
- Reduction in body fat

Adipose tissue : a tissue of great interest for meat producing animals

- **A role in the sensory, nutritional and technological qualities of meat and processed products**

Two parameters closely connected with the quality of meat

Intramuscular fat content (IMF)	- Sensory and technological qualities - Important for high quality products
Fatty acid composition	Nutritional and technological qualities

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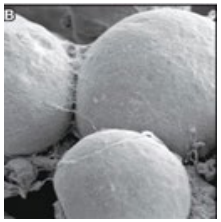
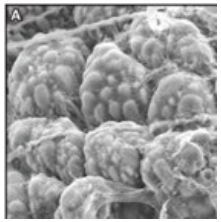
Two main types of adipose tissue with differences in morphology and functions



White adipose tissue (WAT)

- Predominates after birth
- Contains white adipocytes
- Important for the storage and release of energy



Brown adipose tissue (BAT)

- Abundant in newborns and hibernating animals
- Contains brown adipocytes
- A thermogenic function

Absent in pigs

(Lack of functional UCP1)

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Recent identification of a third type of cells in WAT: beige/brite adipocytes

- **Detected in mice** (Wu *et al*., 2012), **cattle** (Asano et al., 2013) **and sheep** (Pope *et al*., 2014)
- **Emerge in WAT depots in response to appropriate stimuli**
- **Store energy with the potential to express the mitochondrial membrane uncoupling protein 1 (UCP1)**
- **Beige adipocytes in pigs?**
  - still a controversy
  - cold-tolerant pigs (Tibetan) can maintain their body temperature through the “browning” of their WAT with an overexpression of UCP3 in the absence of UCP1 (Lin *et al.,* 2017)

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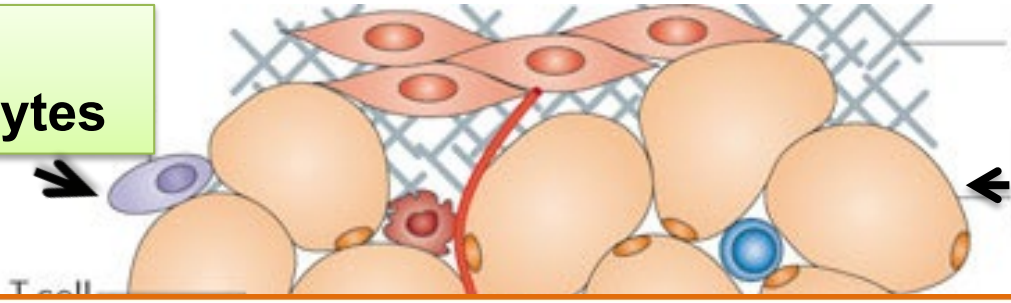
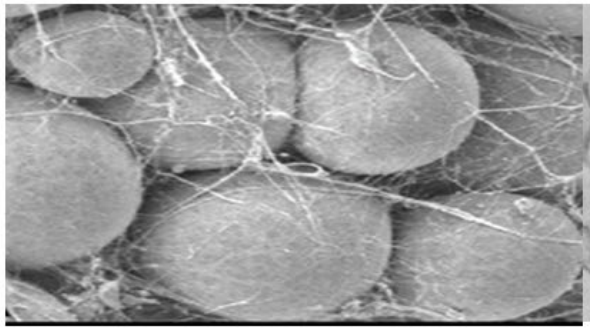
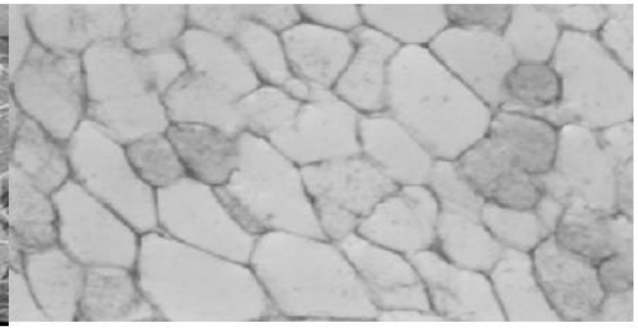
WAT contains many cell types

Stem cells
Pre-adipocytes



Adipocytes

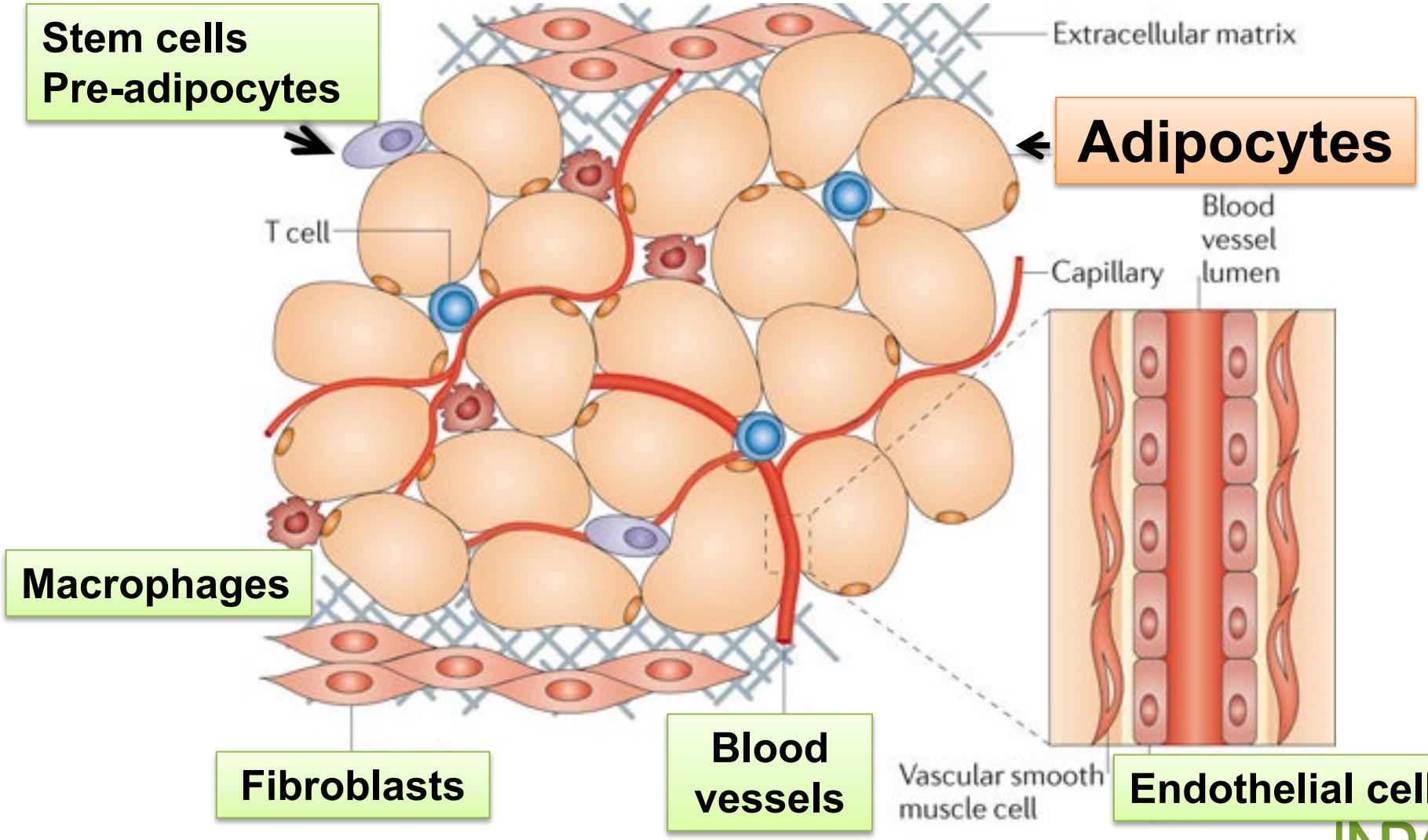




- **Predominating cells in WAT (40-50% of total cells)**
- **Spherical cells when isolated with a wide range of diameters (20-120 µm)**
- **Cells detected in several tissues**

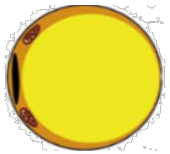
Adapted from Ouchi *et al.*, 2011

WAT contains many cell types



Adapted from Ouchi *et al.*, 2011

Features of brown, beige and white adipocytes

	Brown	Beige/Brite	White
	 < 40 µm 		
Shape of lipid droplets	**Multiple, small droplets**		**Single, large lipid droplet**
Mitochondria	**+++++**		**++**
UCP1	**High expression**	**Expression after cold exposure**	**Not detected**
Function	**Heat production with energy dissipation**		**Energy storage (triglycerides)**

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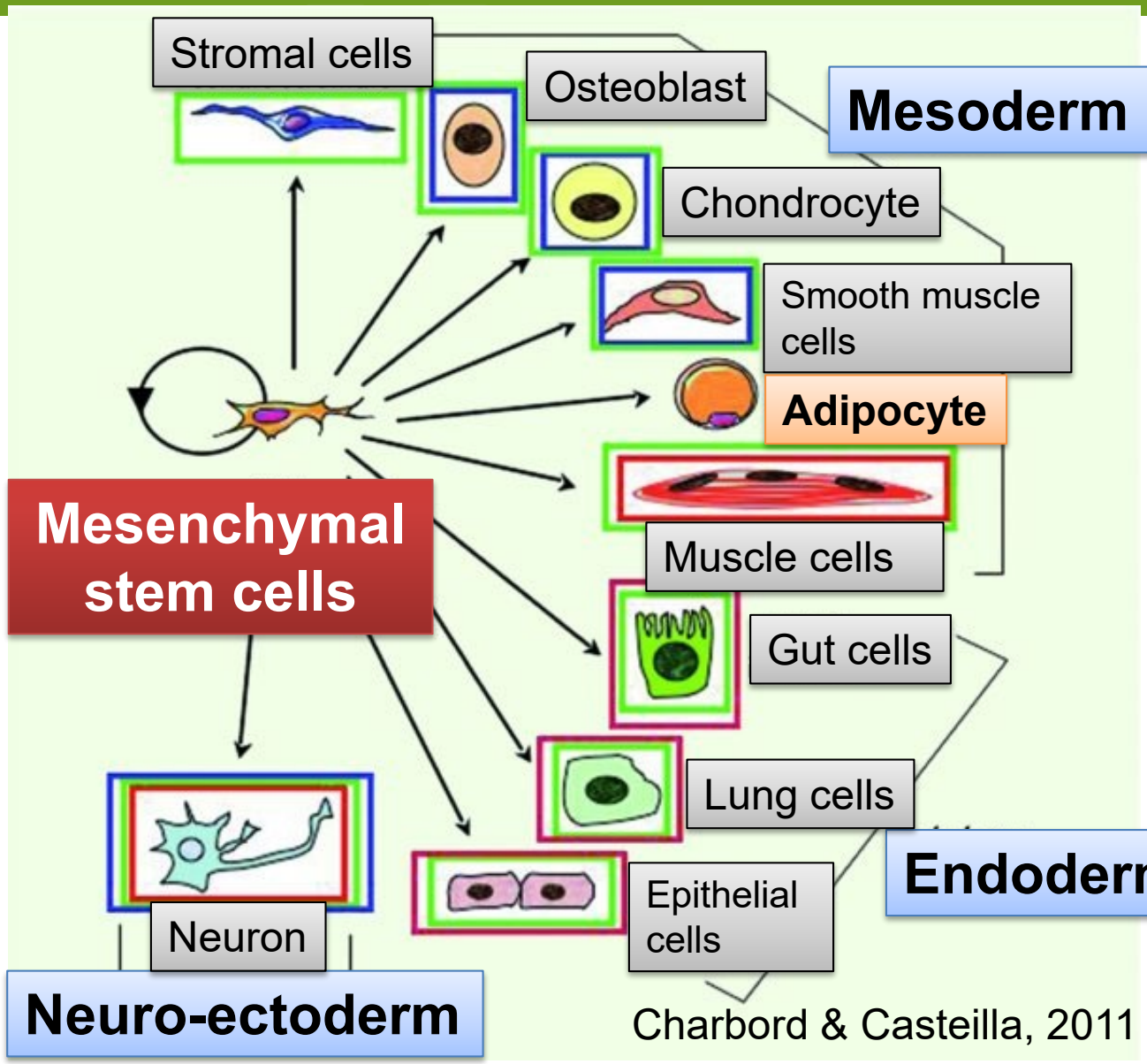
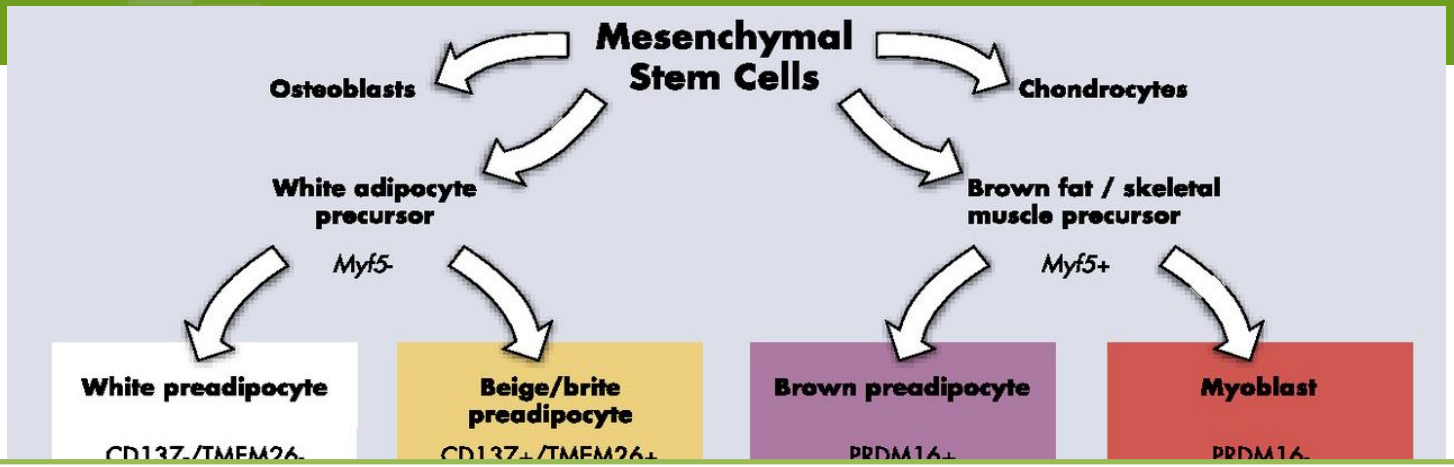
Origin of adipocytes?



Adipocyte

Mesoderm + Neural crest (?)

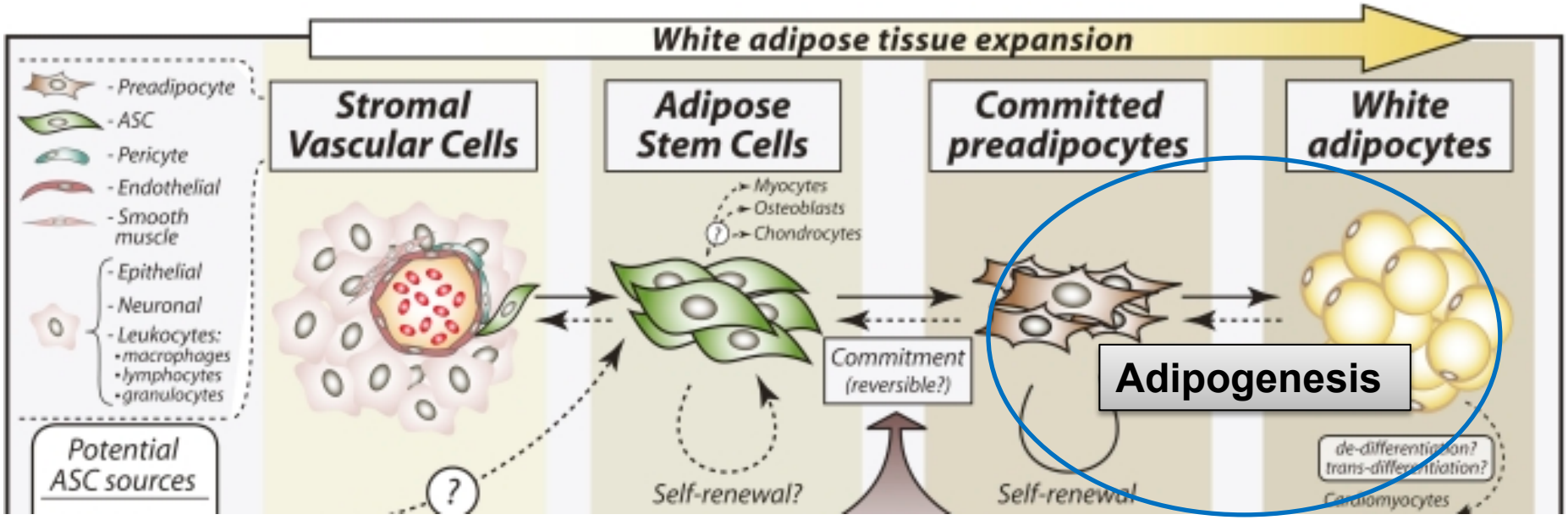
Origins of white, beige and brown adipocytes



- In contrast to other tissues, the embryonic origin of adipose cells remains the subject of debate
- Available data support the idea that progenitor cells are heterogeneous and may have different embryonic origin

Lee *et al*., 2013

From stem cells to white adipocytes



Proliferation/Multi lineage capacity
↓ DLK1, IGF2

Specific function
↑ specific adipocyte genes (LPL, FASN, FABP)

Regulators that affect the differentiation of white, beige and brown adipocytes

- A large field of investigation including in livestock
- Some recent studies are investigating the role of long non coding RNA on adipocyte differentiation (Wei *et al.,* 2019)
- Many studies investigate the transcriptome of WAT with the aim to identify molecules that may be useful to better control variation in fat content but the biological interpretation remain a challenge (Dalrymple & Guo, 2017; Baik *et al.,* 2017)

Physiological functions of adipose tissue

Protection

- An insulating layer (reduction of heat loss through the skin)
- A protective function (providing mechanical protection and support around the major organs)

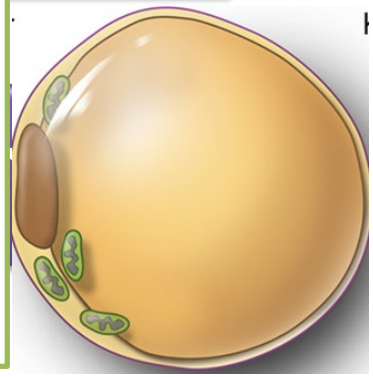
Physiological functions of adipose tissue

Protection

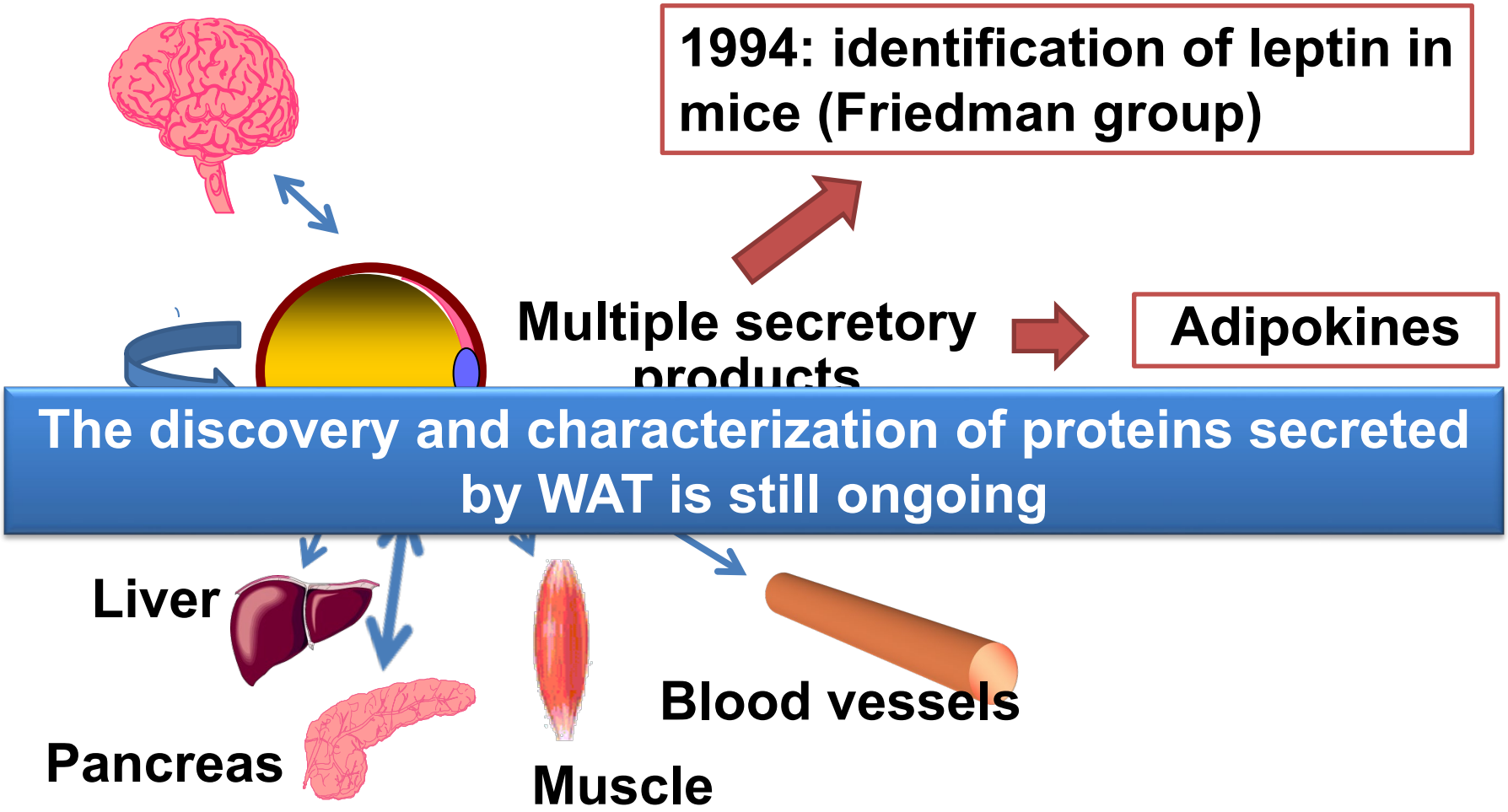
Energy storage

Storage and release of fatty acids and glycerol

Adipocyte: a central player in the control of energy balance and whole body lipid homeostasis

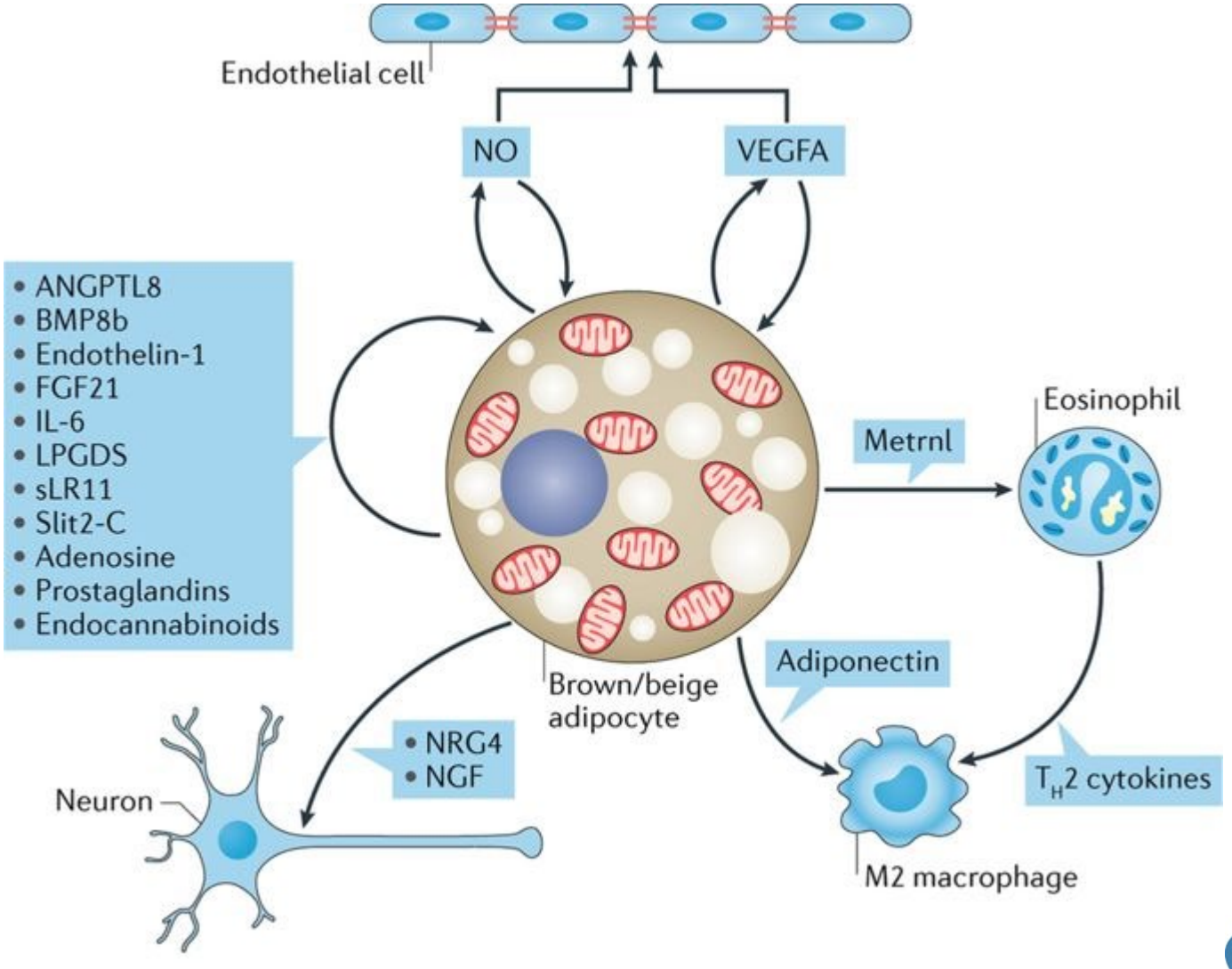


WAT: a secretory/endocrine organ



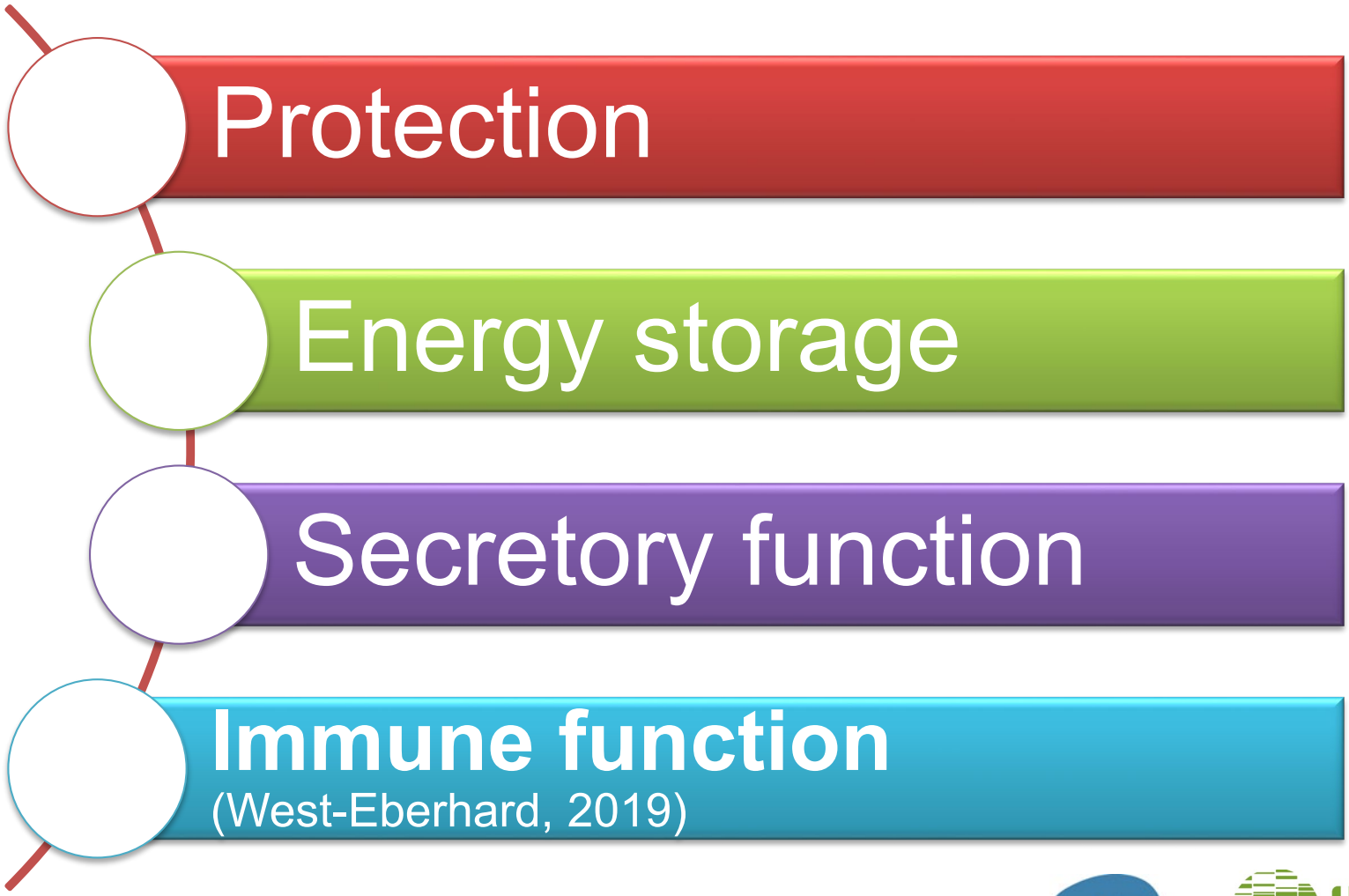
Lafontan, 2005; Haugen & Drevon, 2007; Rodríguez *et al.*, 2015, Giralt et al., 2016

The secretory function of BAT



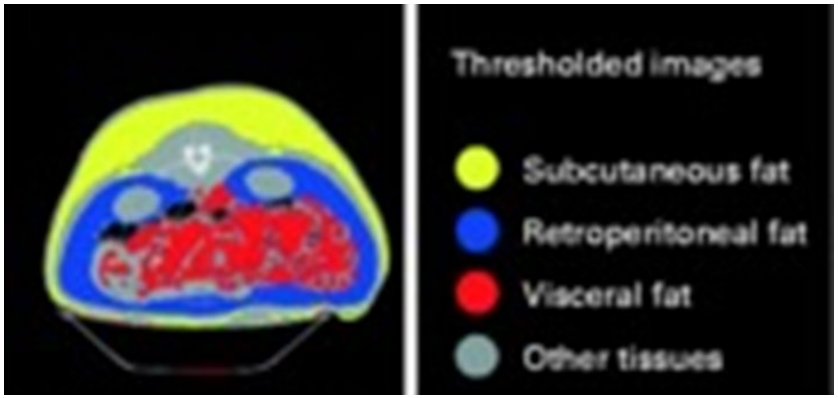
Villaroya *et al.*, 2017 **Nature Reviews | Endocrinology**

Physiological functions of adipose tissue



WAT: : a number of individual depots in the body

Adiposity distribution (CT scan)
(lumbar vertebra, L2, Val-Laillet *et al.*, 2010)



- **Under the skin**
- **In the abdominal cavity (surrounding viscera such as mesenteric and perirenal fat depots, around epididymis, etc.)**
- **Within the musculature**
  Inter- and intra-muscular depots
- **Within the bone marrow**

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WAT: features of IMF depots

IMF

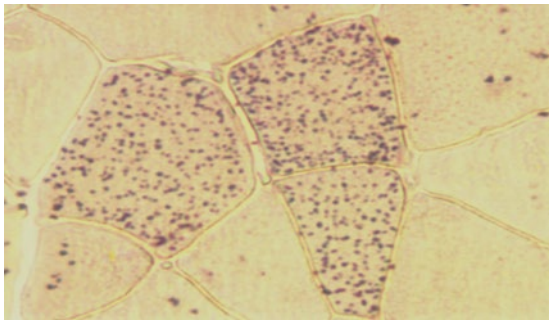
Phospholipids
Structural lipids

Relatively constant levels
(i.e., ranging from 0.5-1%
of fresh muscle in pigs)

Triglycerides
Storage lipids

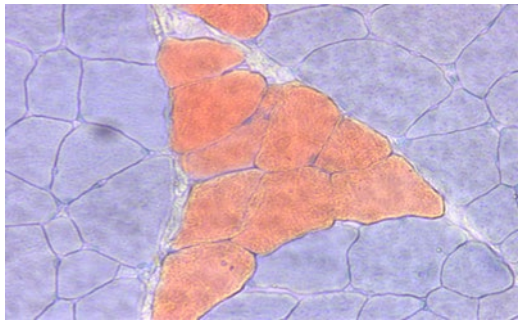
Highly variable levels

5–20%



Lipid droplets
in the cytoplasm
within myofibers

80%



Small groups of cells
located between muscle
fiber and fiber bundles

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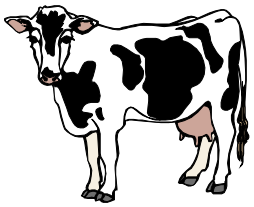
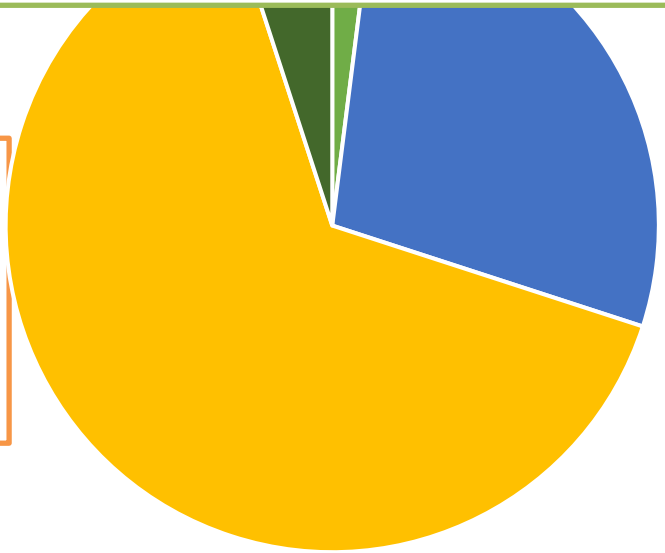
The relative proportions of WAT depots

The relative size of these depots differs between species



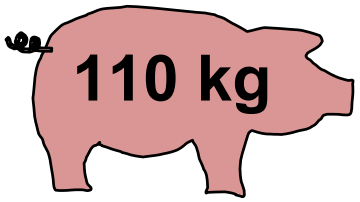
700 kg

SCAT: 12%
Intermuscular AT: 43%



Subcutaneous AT (65-75%)

Intermuscular AT (25-33%)



Dumont & Février, 1957; Girard *et al.*, 1998; Monziols *et al.*, 2005

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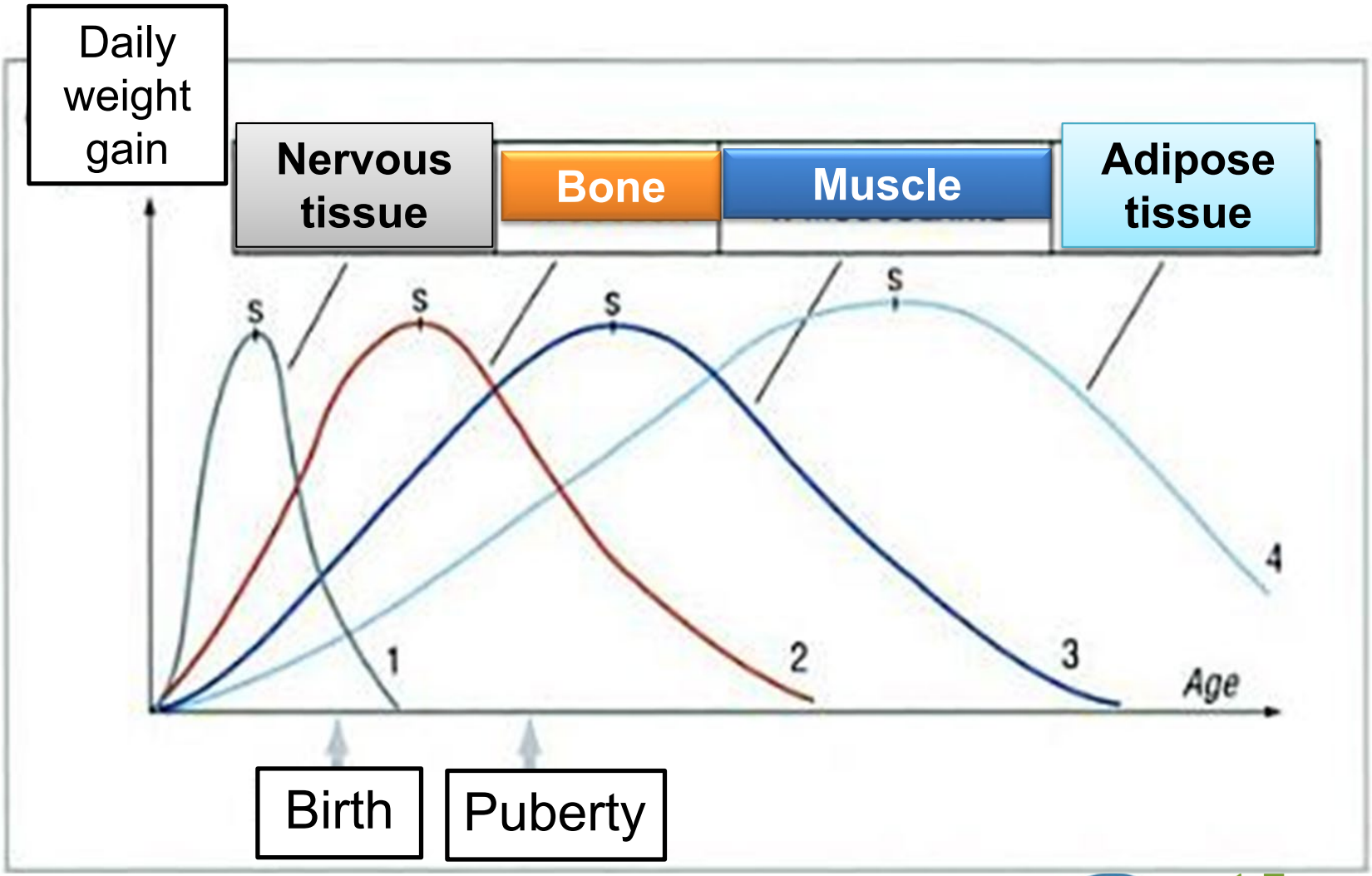
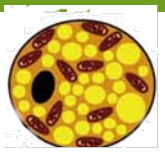
Tissue accretion according to age



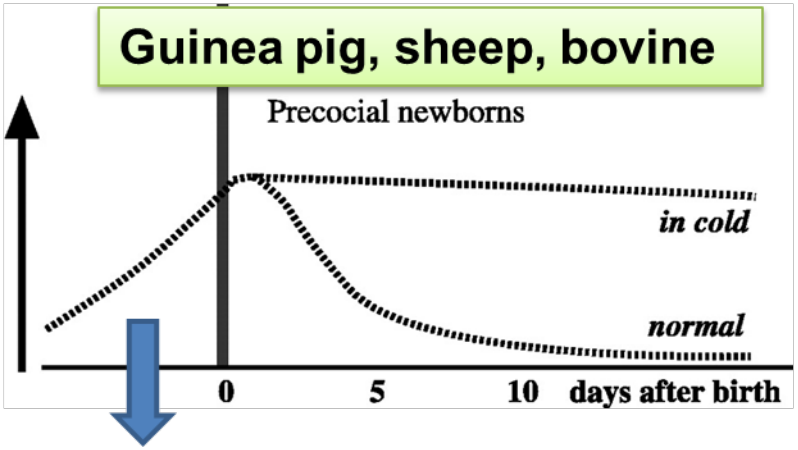
Age-related changes in BAT



Found in mammals with exceptions: not detected in pigs

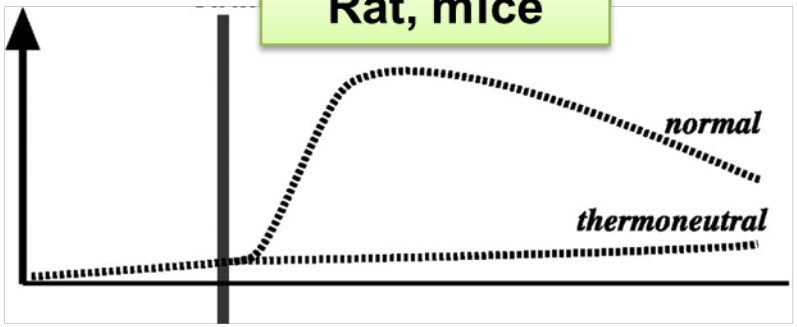
Birth

Guinea pig, sheep, bovine



Birth

Rat, mice



180 and 260 dpc fetuses

↳ perirenal adipose tissue is a mix of white and brown adipocytes

- **present in adults: hibernating animals, rodents, humans +cow…**
- **BAT → WAT in large mammals ?**

Cannon & Nedergaard, 2004; Taga *et al.*, 2012

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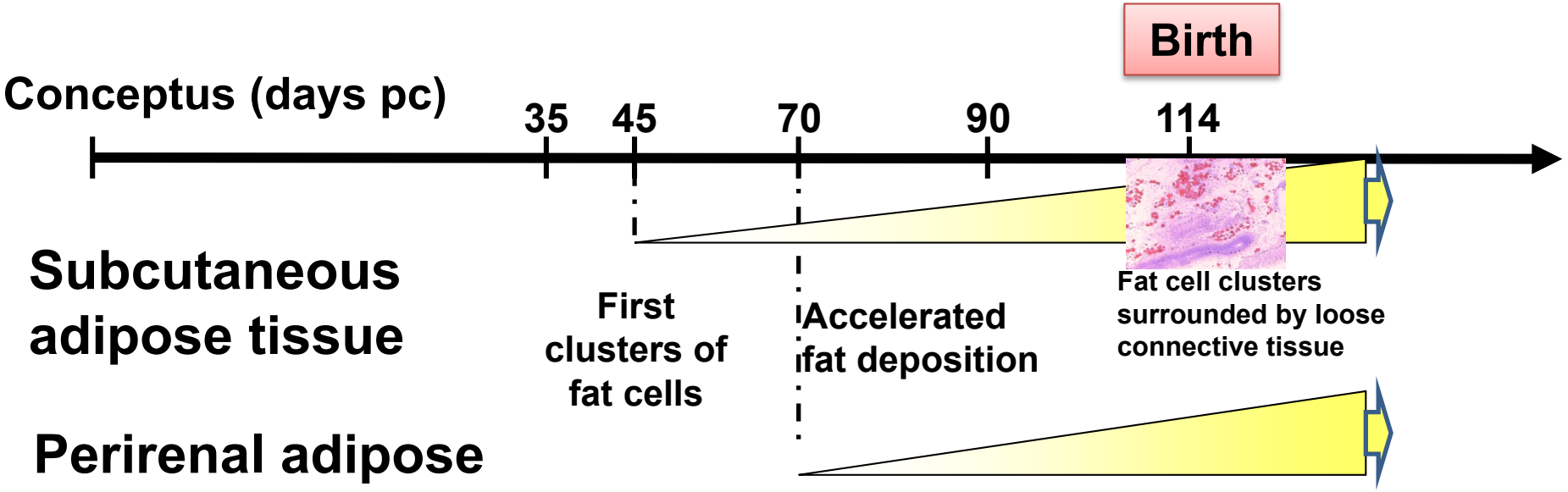
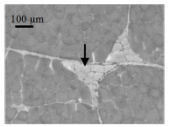
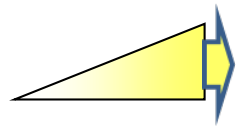
Prenatal and neonatal development of WAT





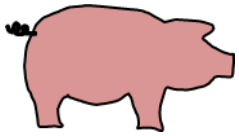


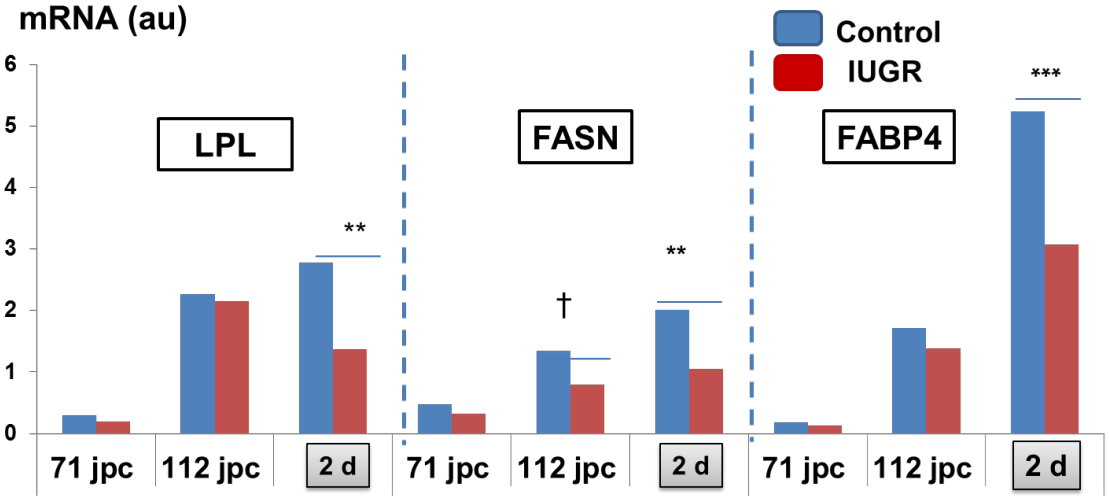
Adipose tissue development differs according to depot and according to species (PAT: the first detected in cattle)

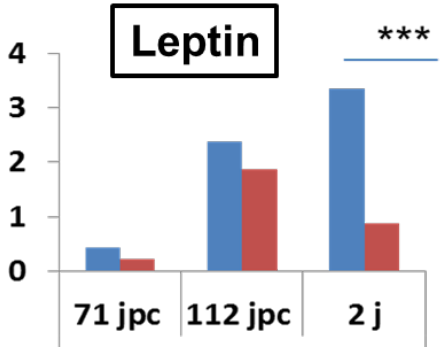
↑ adipose mass throughout life

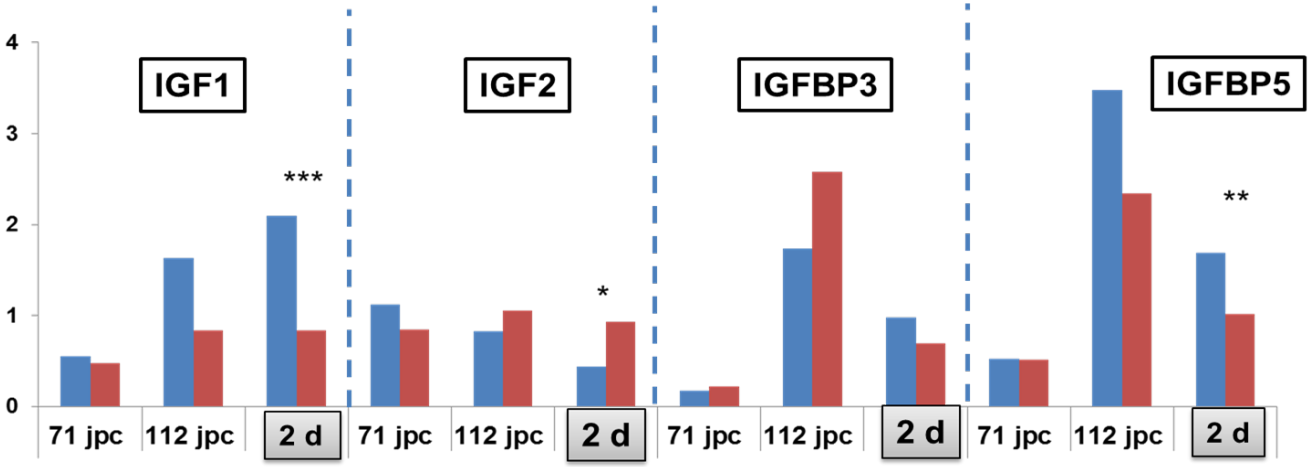
Mourot , 2001; Hauser *et al.*, 1997

Many changes occurs in the expression of genes during the prenatal and neonatal period



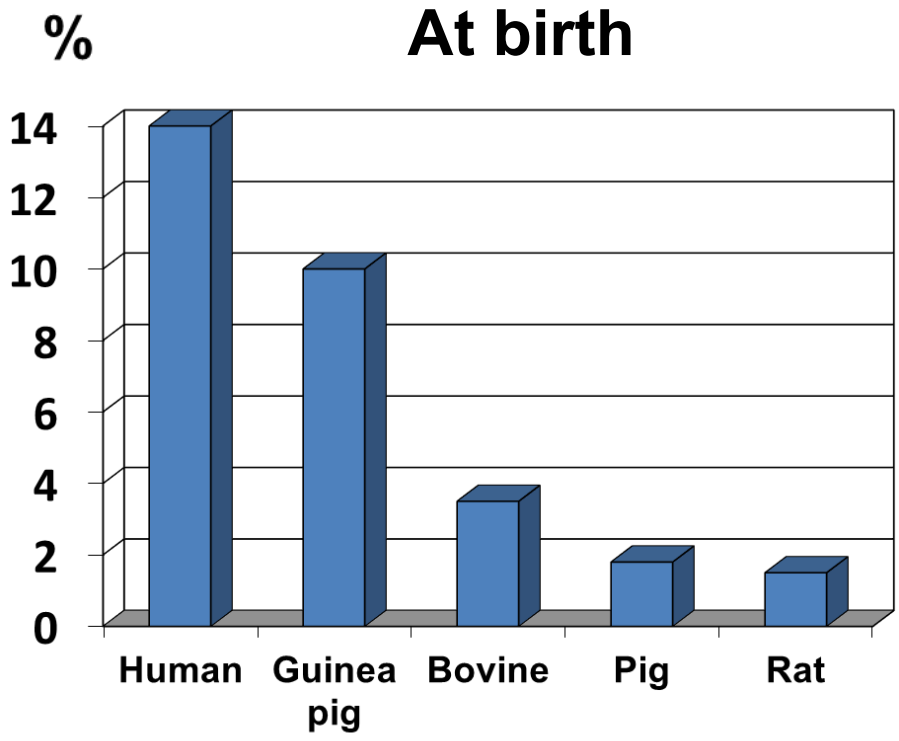


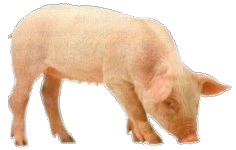


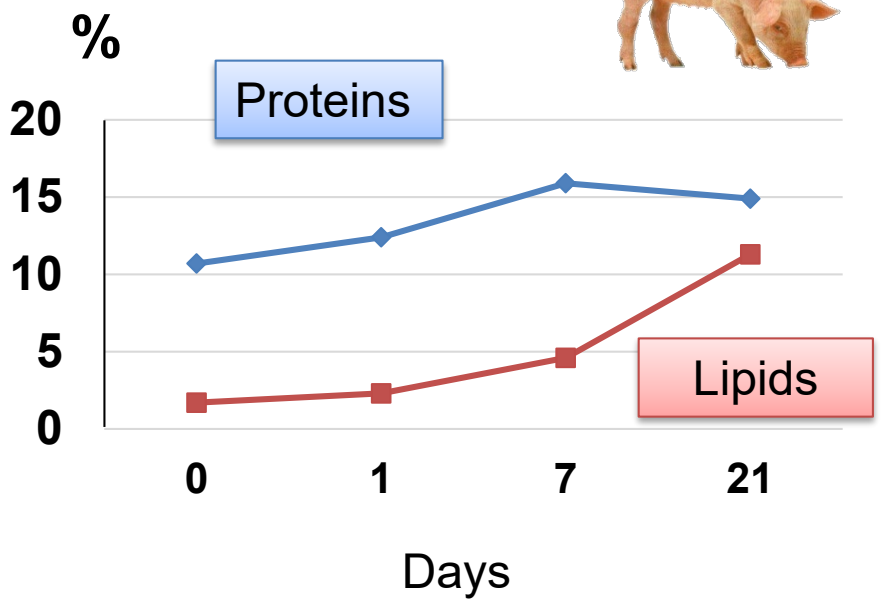


Gondret *et al.*, 2013

Body fat mass (%) in the neonatal period

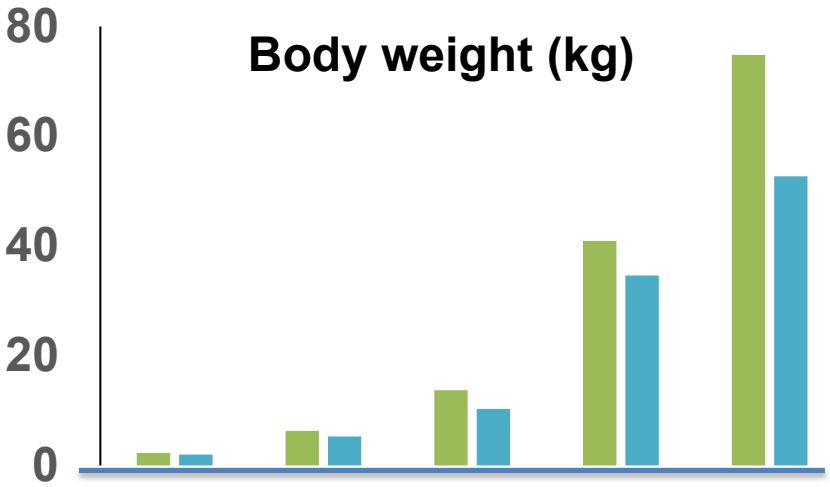


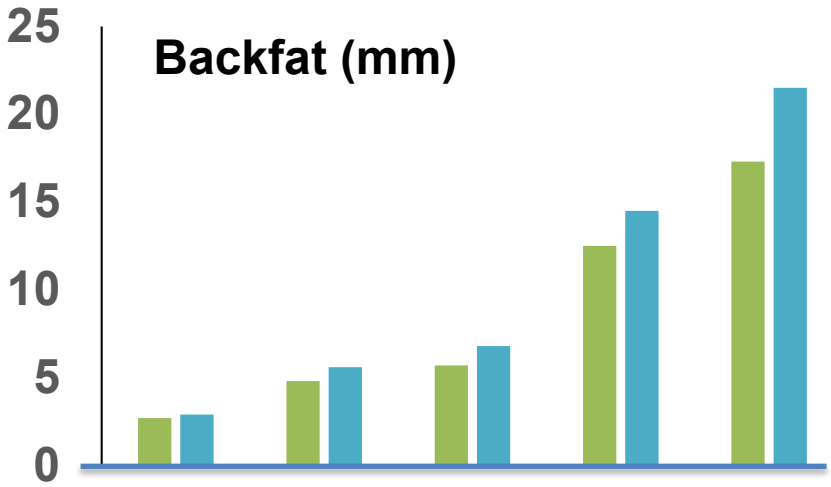


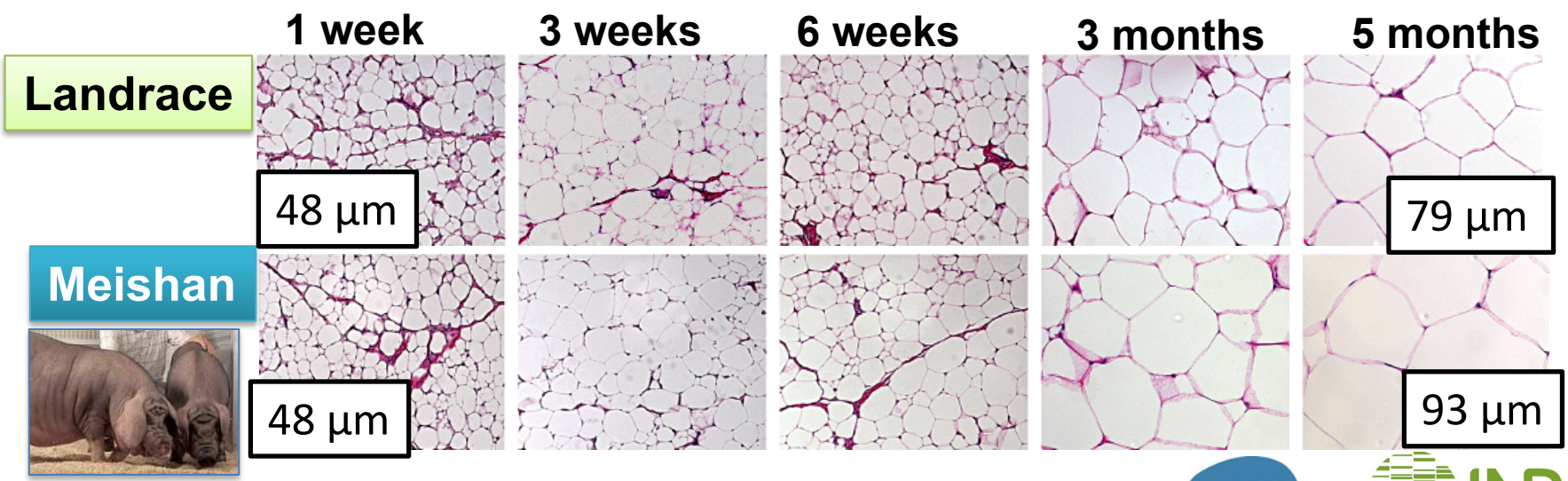


Large differences between species

Cellular development of sc adipose tissue



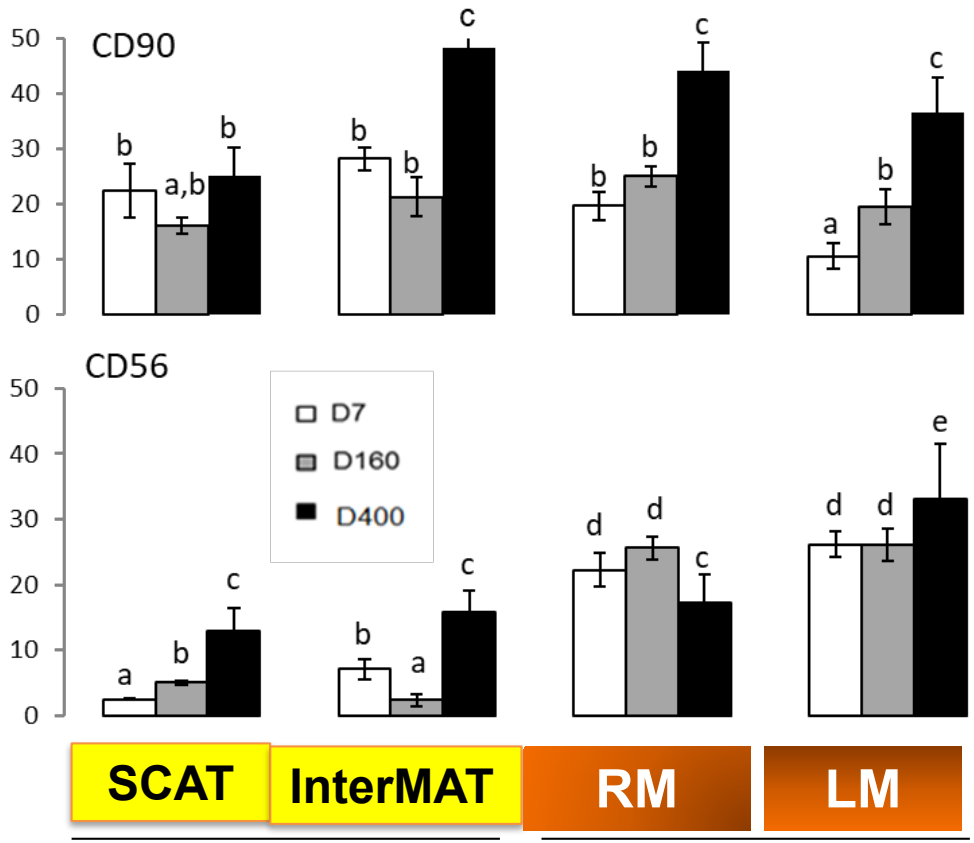




Nakajima *et al.*, 2011

Adult stem cells in porcine WAT and skeletal muscle

Positive cells with adipogenic properties (%)

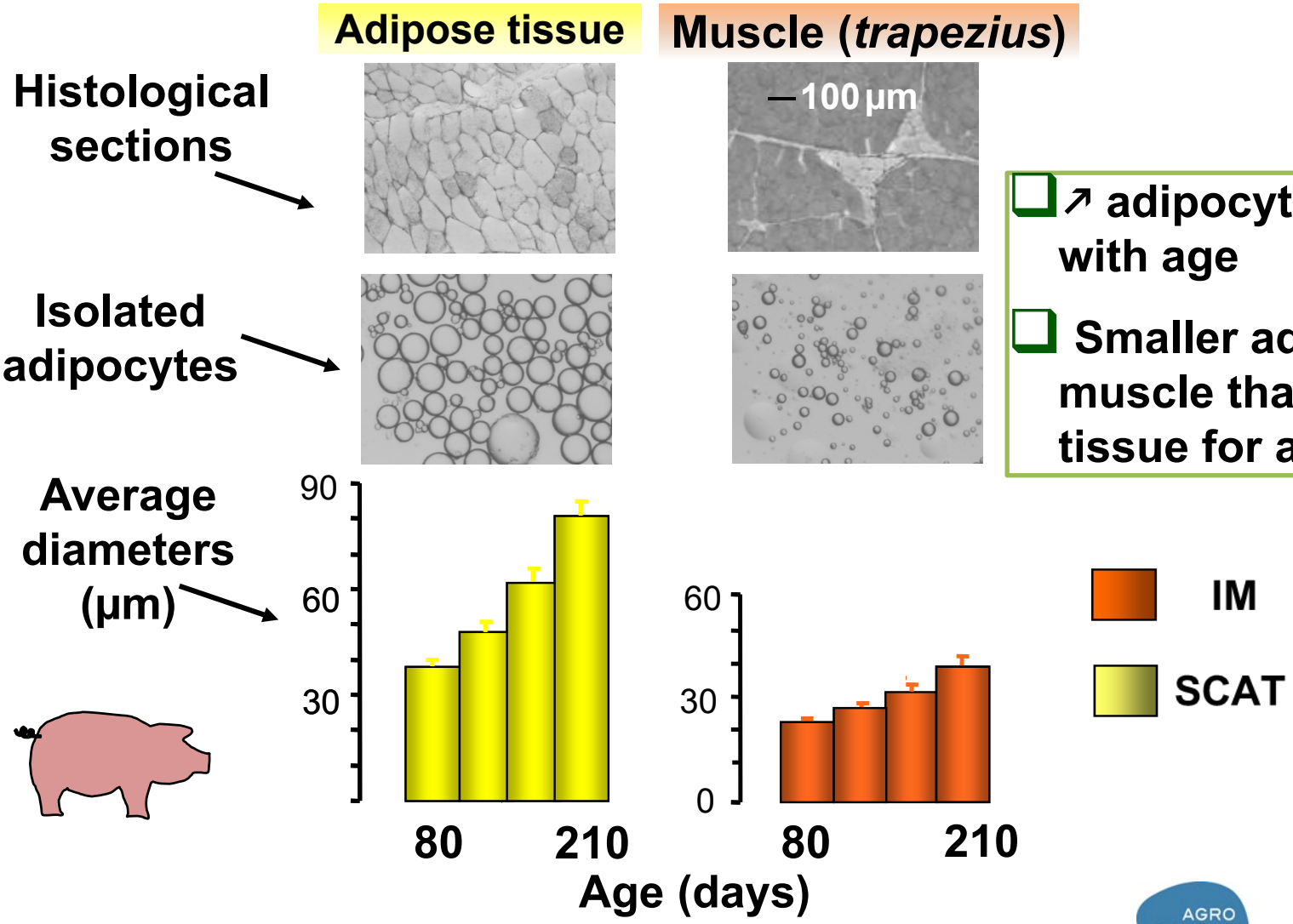


Age-related changes in stem cell populations with the ability to differentiate into adipocytes

A potential for increasing the number of adipocytes during the postnatal period

Perruchot *et al.*, 2013

Site-specific development of adipocytes

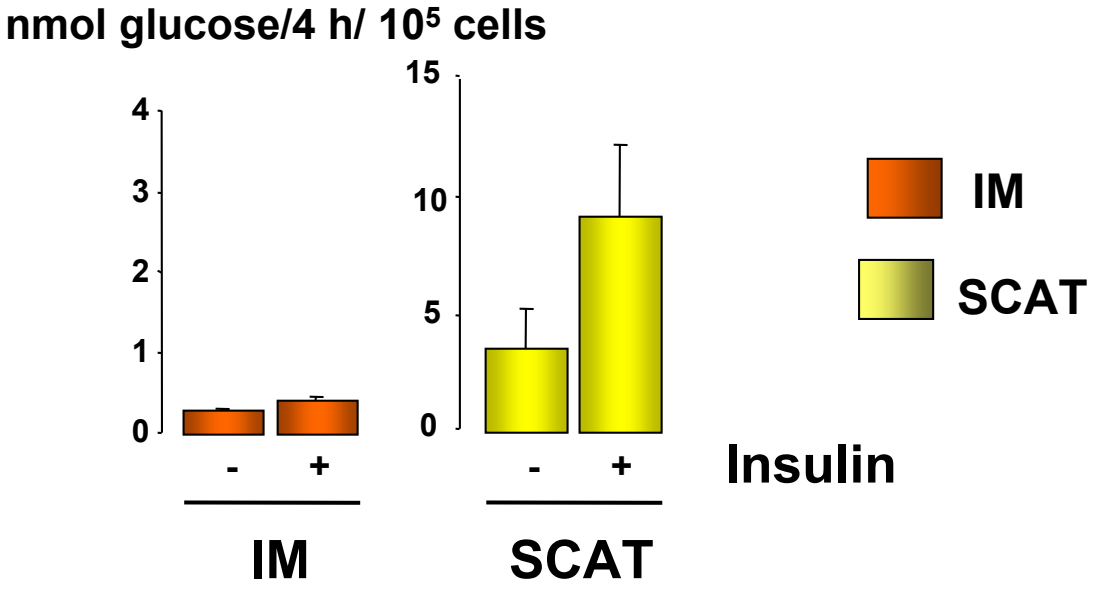


- ↗ adipocyte diameters with age
- Smaller adipocytes in muscle than in adipose tissue for a given age

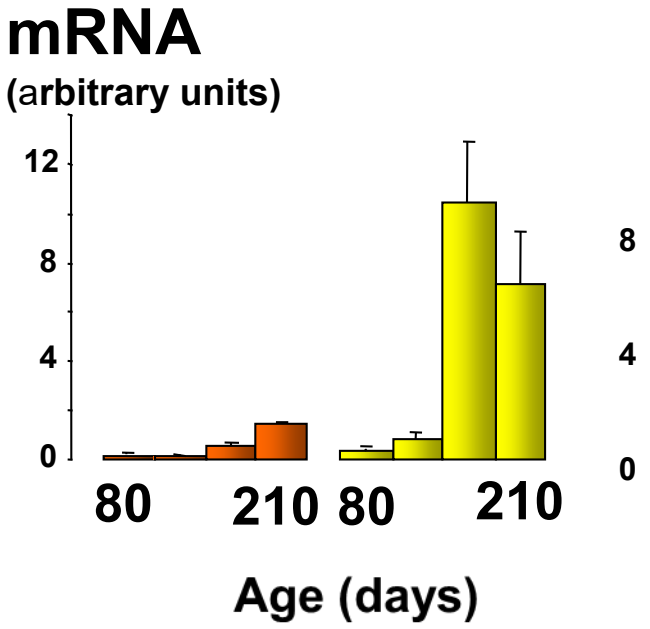
Gardan *et al.*, 2006

Differences in the physiology of adipocytes according to adipose depots

Lipogenesis
(adipocytes from 80-d-old pigs)



Leptin

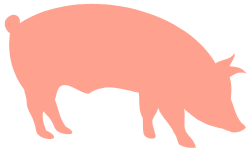


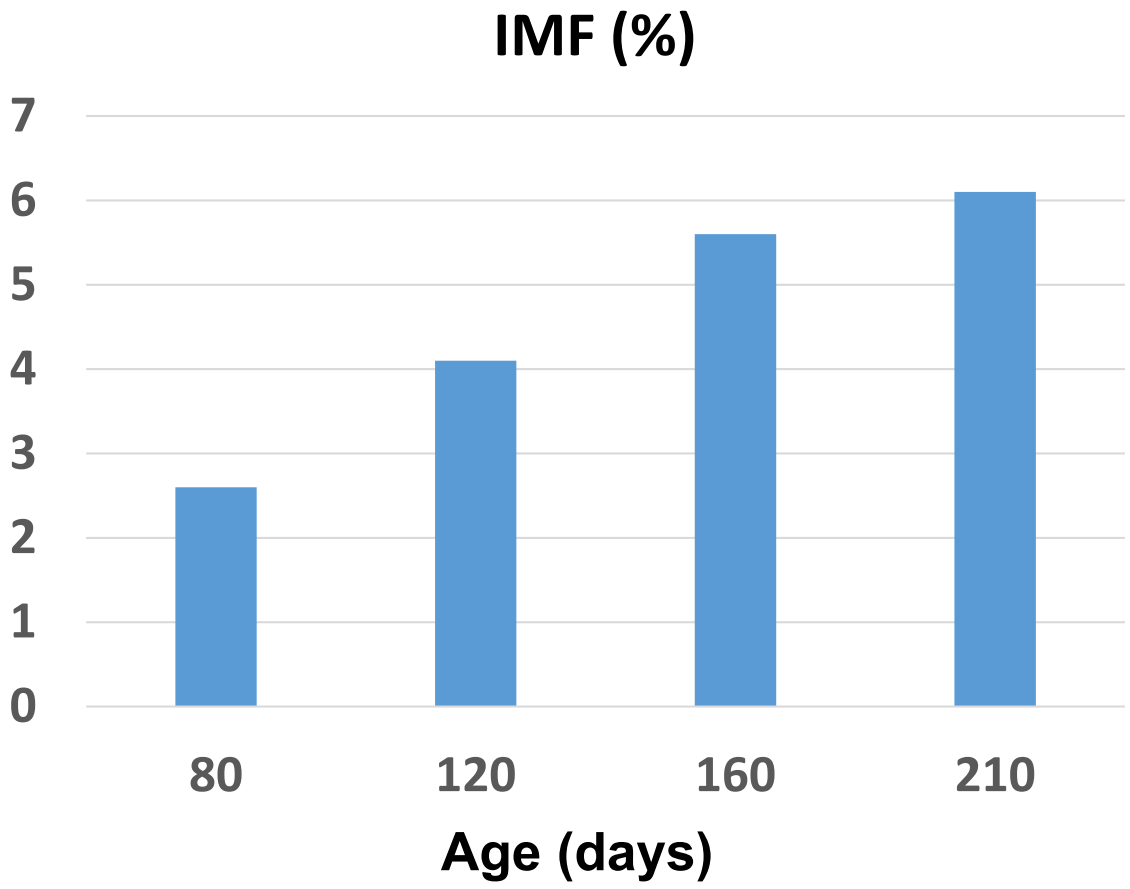
- **Basal rate: IM << SC**
- **insulin-stimulated rate: IM << SC**

SCAT >> IM

Gardan *et al.*, 2006

IMF content increases with age in the trapezius muscle





Gardan *et al.*, 2006

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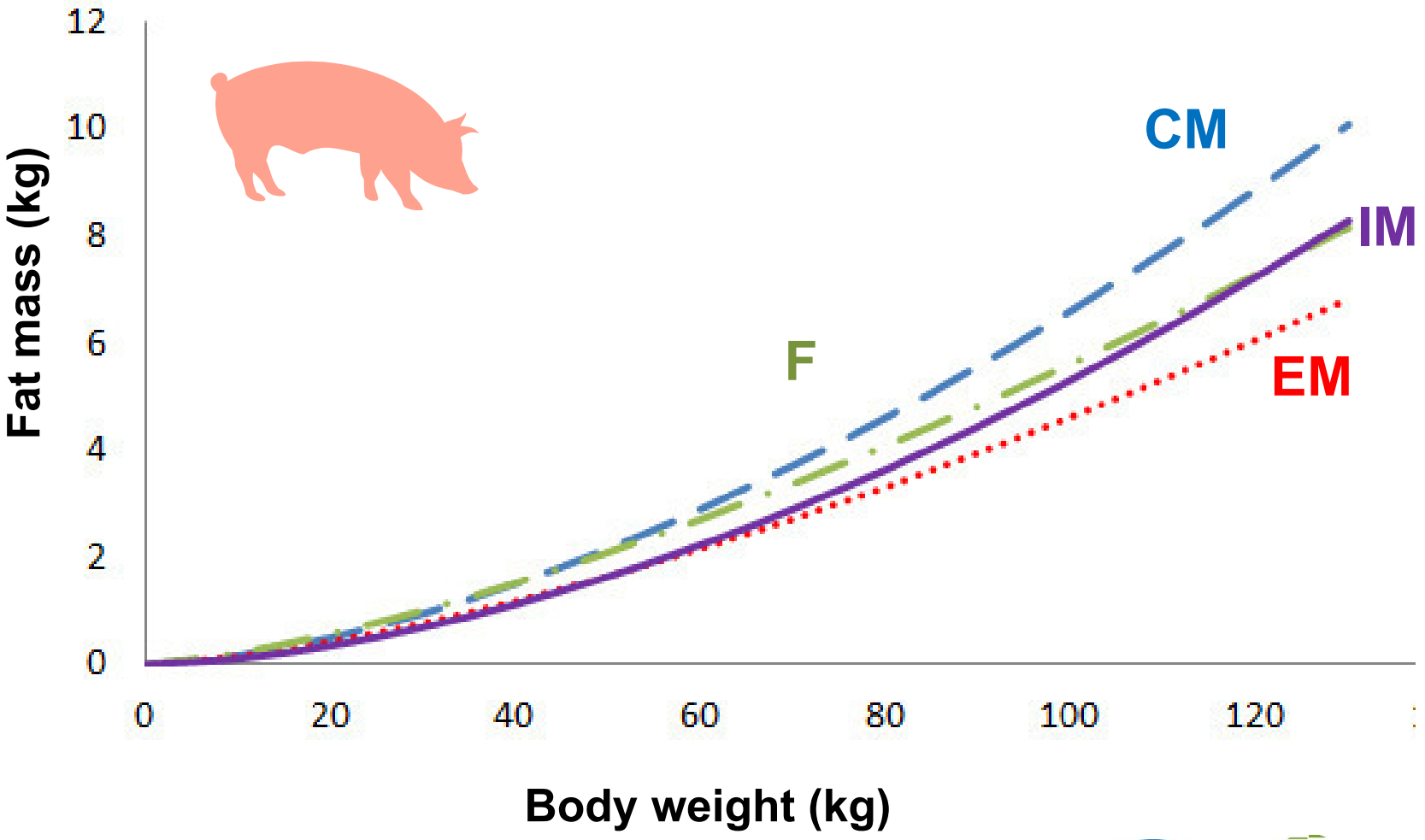
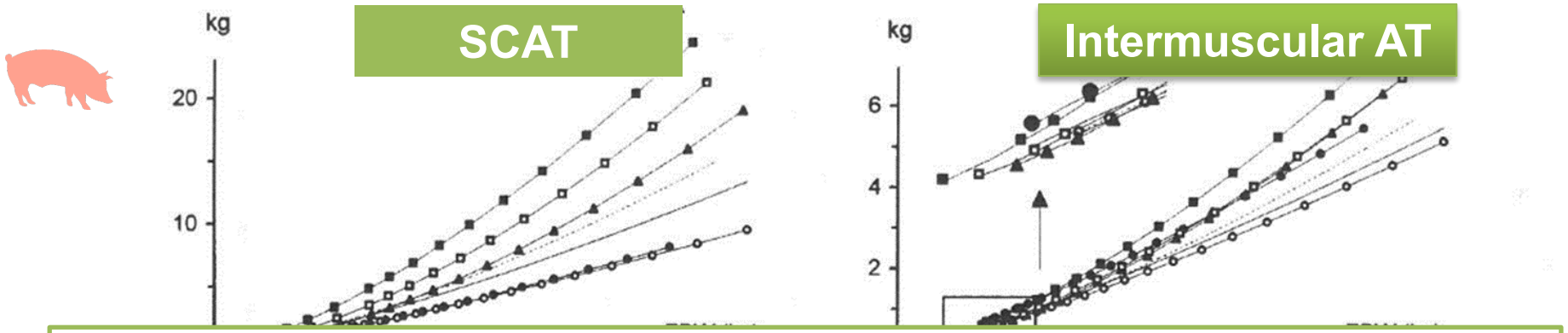
Influence of age and sex on body fat mass



Carabús *et al.*, 2017

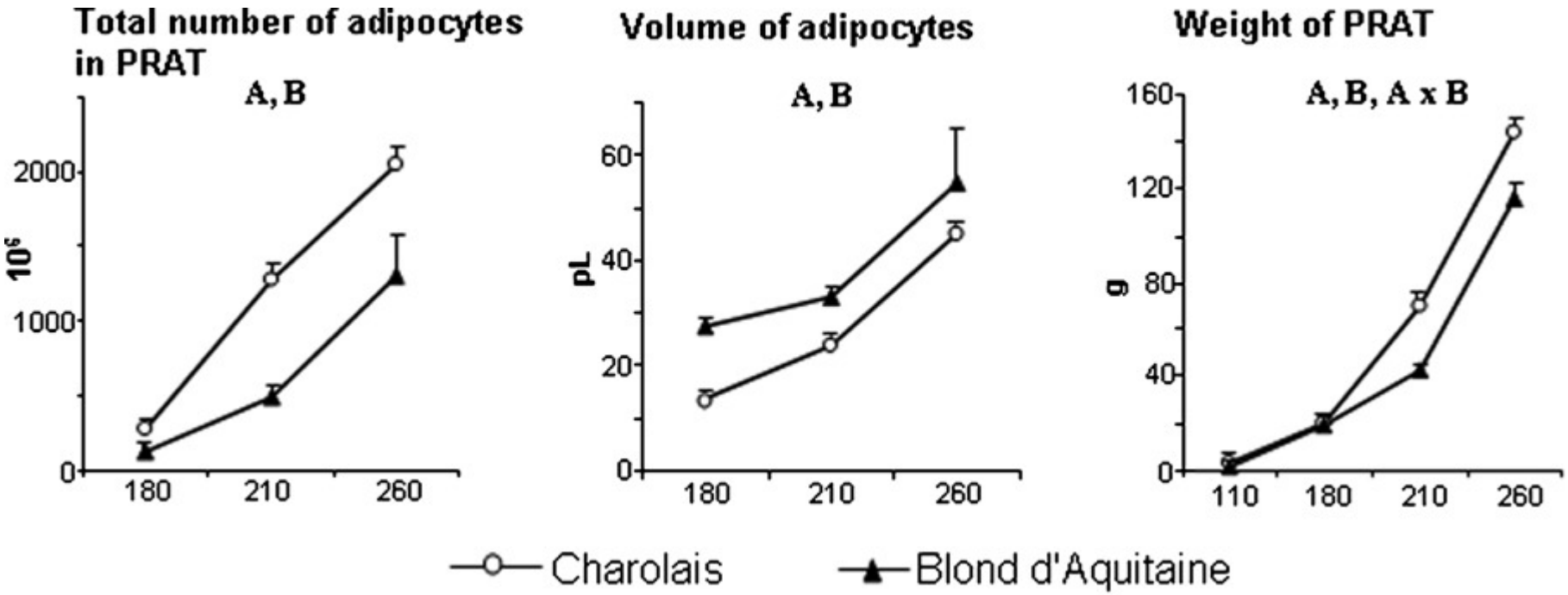
Mass of WAT depots in different pig breeds



- The difference between breeds increases with body weight
- Differences between breeds are less important in intermuscular adipose tissue than in other depots

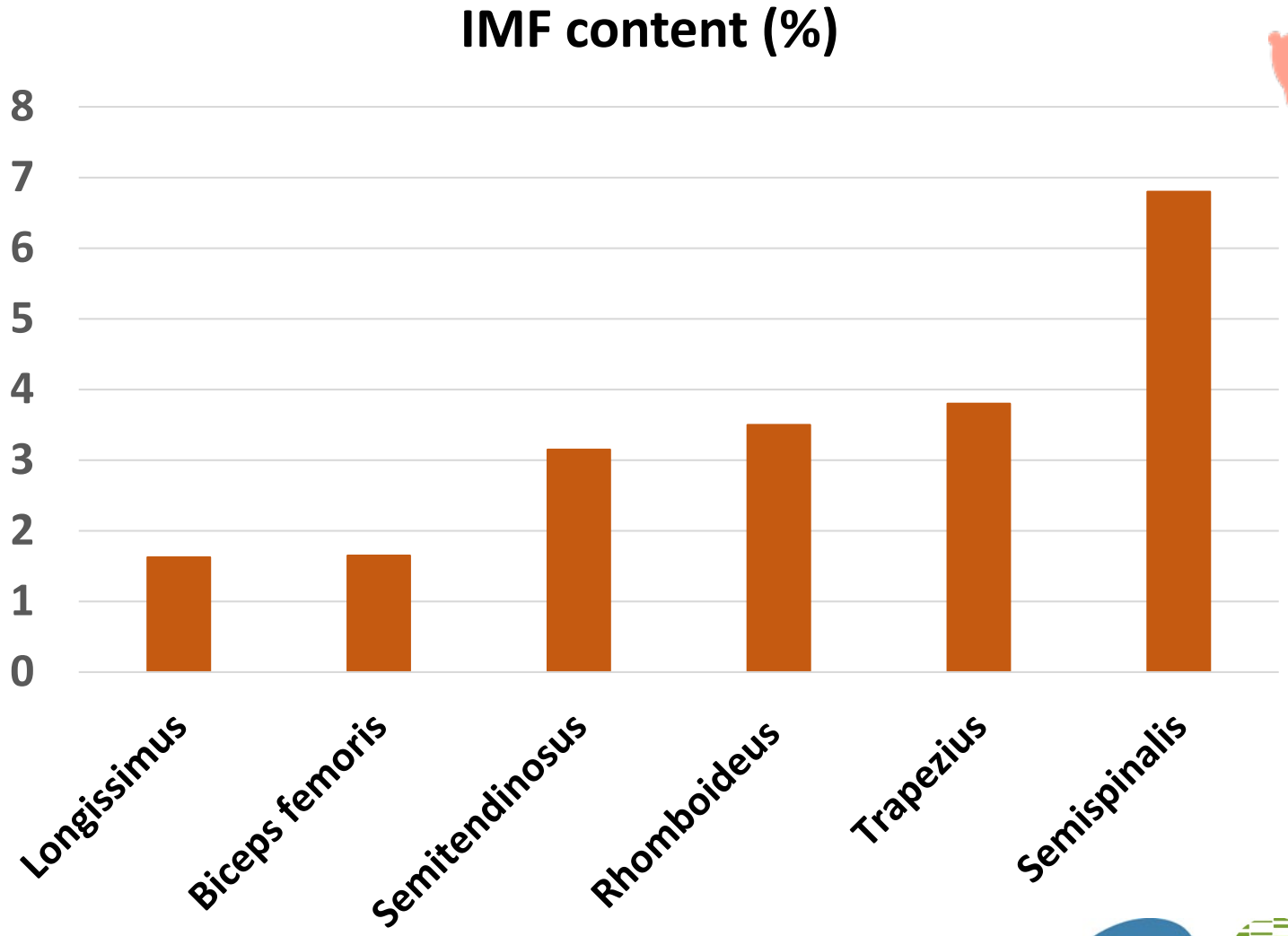
Kouba *et al.*, 1999

Perirenal WAT at 110, 180, 210, and 260 days post-conception in Charolais and Blond d'Aquitaine



Taga *et al.*, 2011

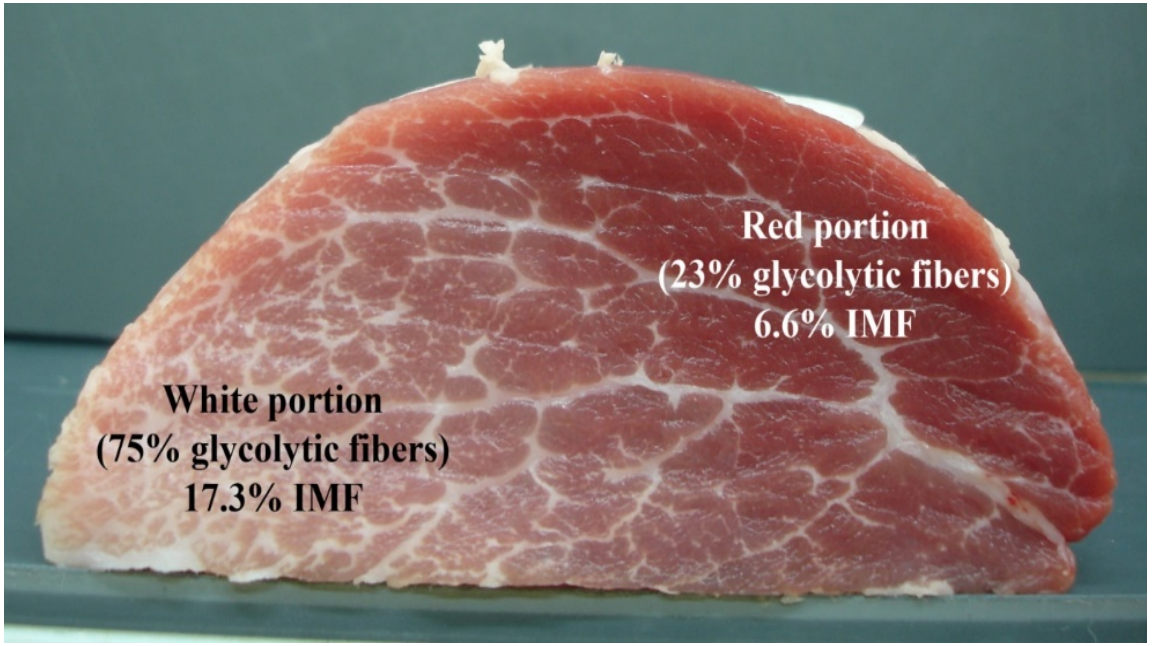
IMF content varies between muscles



Maignel *et al*., 2013; Tyra *et al*., 2013; Font-i-Furnols *et al*., 2018

IMF content depends on anatomical location within some muscles

Semitendinosus muscle cross section from a Basque pig (145 kg live weight)



The IMF content is about three times greater in the white glycolytic than in the red oxidative portion of muscle

Listrat *et al.*, 2015

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IMF content depends on breeds

Muscle cross-sections of LM

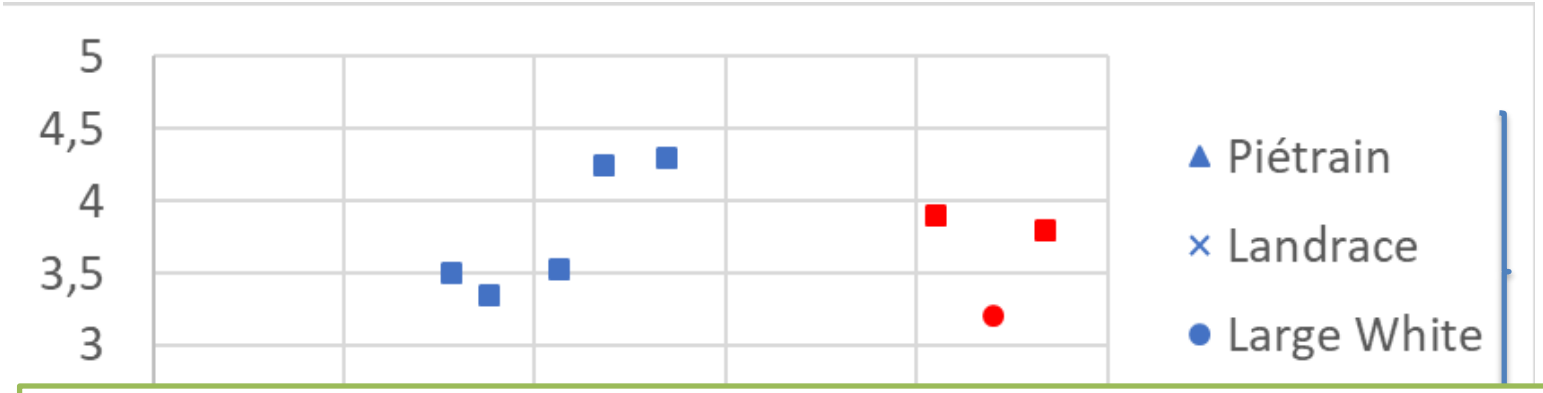
Belgian Blue bull
24 mo of age
IMF content: 0.5%

Japanese Black steer
26 mo of age
IMF content: 33% IMF

Albrecht *et al.*, 2017

IMF content and backfat thickness in different pig breeds

IMF in longissimus (%)



Selected breeds

- ❑ The European conventional breeds (Large White, Landrace or Pietrain) have a low general adiposity
- ❑ Duroc pigs have limited BFT and IMF content varies according to studies
- ❑ Meishan pigs have moderate IMF content and high BFT
- ❑ French local breeds have a high overall adiposity (BFT and IMF content)

Schwob *et al.*, 2019

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Influence of nutrition on fat mass/fatty acid composition

Nutrition and fat mass

- Many studies in this area of research
- Studies dealing with the impact of early nutrition on later adipose tissue development

Relationship between the nature of the ingested fat and meat fatty acid composition

- Monogastric animals: it is possible to change the FA composition of meat through the feed (Pork and chicken may be enriched with long-chain n-3 by inclusion of fish oil in the diet)
- Enrichment of beef and lamb is more challenging due to the extensive modification of dietary lipids by the rumen microbiome.

(Wood *et al*., 1999; Hocquette *et al.,* 2010; Kouba & Mourot, 2011; Lebret *et al*., 2015; Scollan *et al.,* 2017)

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In summary

- **Several types of adipose tissue**
- **A number of individual depots in the body with**
  - **variable sizes**
  - **specific physiological properties**
- **AT development occurs later than skeletal muscle development: it is initiated prenatally except for intramuscular adipose tissue**
- **Body fat mass: low at birth** (<2% in pigs) **but a large increase after birth**

In summary

- The postnatal fat expansion
  - is associated with changes in cell populations of adult stem cells
  - involves the hypertrophy of adipocytes (accumulation of TG in the adipocyte lipid droplets)
  - involves the recruitment of adult stem cells to generate new adipocytes
- WAT development differs according to depots, species, sex, breeds
- IMF content varies according to anatomical muscle origin, age, breeds
- Developmental differences in the physiology of adipocytes according to adipose depots (SCAT vs IMF)

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Challenges / Future research directions

- **Challenges for meat quality improvement**
  - **Sensory quality: a need to increase IMF content but a need of invisible fat**
  - **Nutritional quality: a search of healthy fat (PUFA)**
  - **Technological qualities: the requested fat depends on the product**
- **A need to increase our knowledge on**
  - **adult stem cells: an emerging field of research for livestock species**
  - **the mechanisms involved in the control of adipogenesis in different depots**
- **A search of strategies to better control IMF content to meet the diverse needs of producers and consumers**

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Thank you for your attention

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