

La leptine, du métabolisme au cerveau : Nouvelles pistes pour le Rett

Jean-Luc Gaiarsa

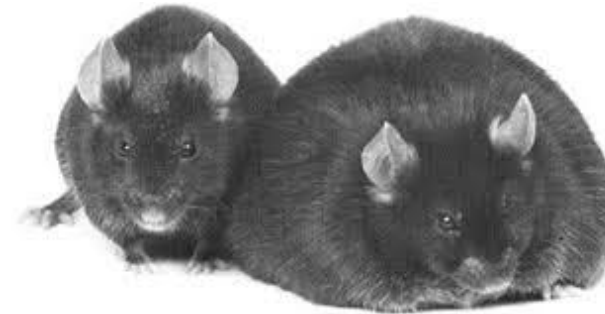
11-12 octobre 2025, 37^{èmes} JNSR

La leptine : Hormone de satiété

1950

OBESSE, A NEW MUTATION IN THE HOUSE MOUSE*

ANN M. INGALLS, MARGARET M. DICKIE AND G. D. SNELL
Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine



1994

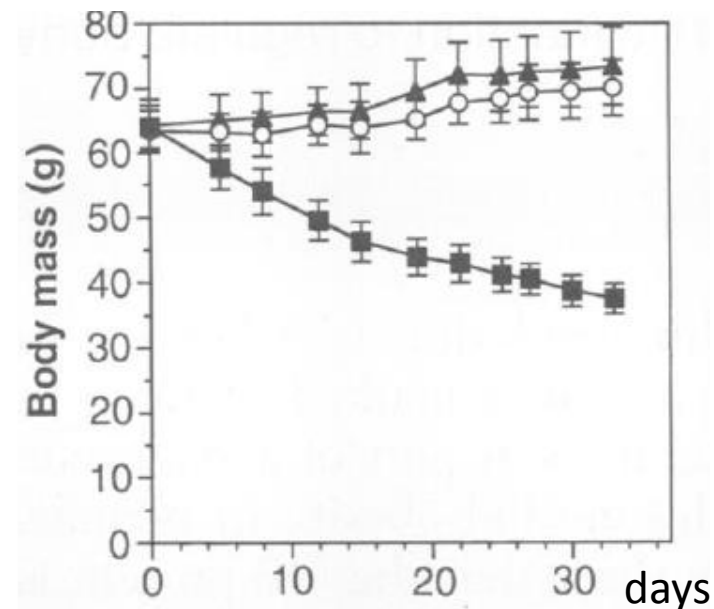


Positional cloning of the mouse *obese* gene and its human homologue

Yiying Zhang^{*‡}, Ricardo Proenca^{*‡}, Margherita Maffei[†], Marisa Barone^{*‡},
Lori Leopold^{*‡} & Jeffrey M. Friedman^{*‡†}

*Harvard Medical Institute, †The Rockefeller University, 1230 York Avenue, New York, New York, 10021, USA

Leptine du grec leptos: mince



1995

Weight-Reducing Effects of the Plasma Protein Encoded by the *obese* Gene

Jeffrey L. Halaas, Ketan S. Gajiwala, Margherita Maffei,
Steven L. Cohen, Brian T. Chait, Daniel Rabinowitz,
Roger L. Lallone, Stephen K. Burley, Jeffrey M. Friedman*

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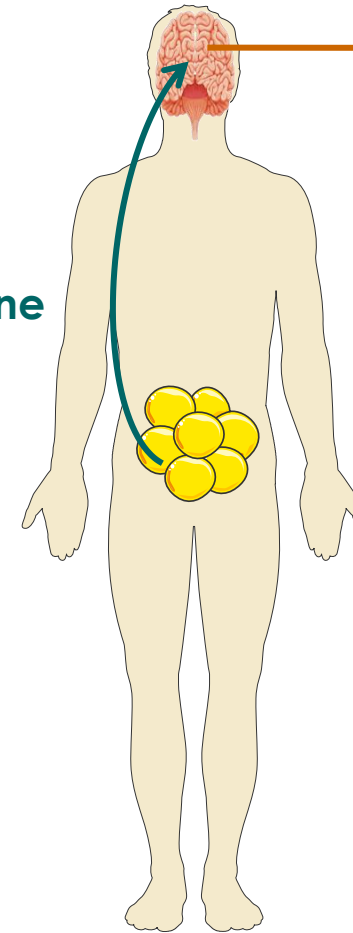
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Leptine

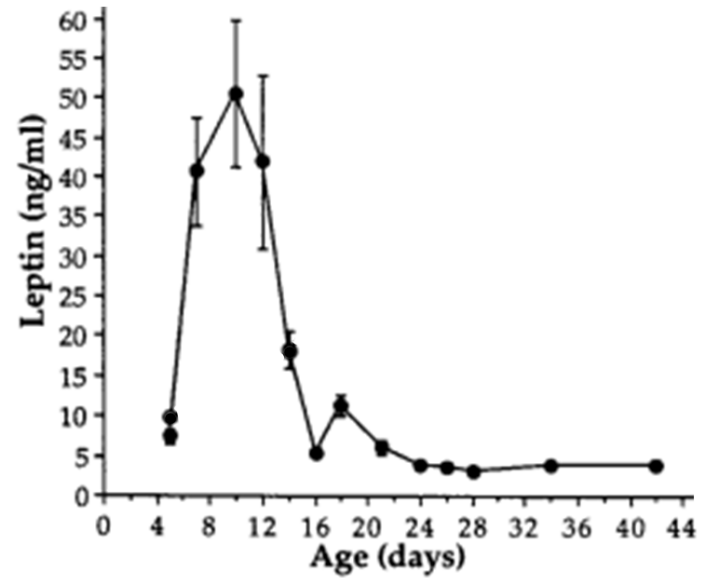


Hypothalamus

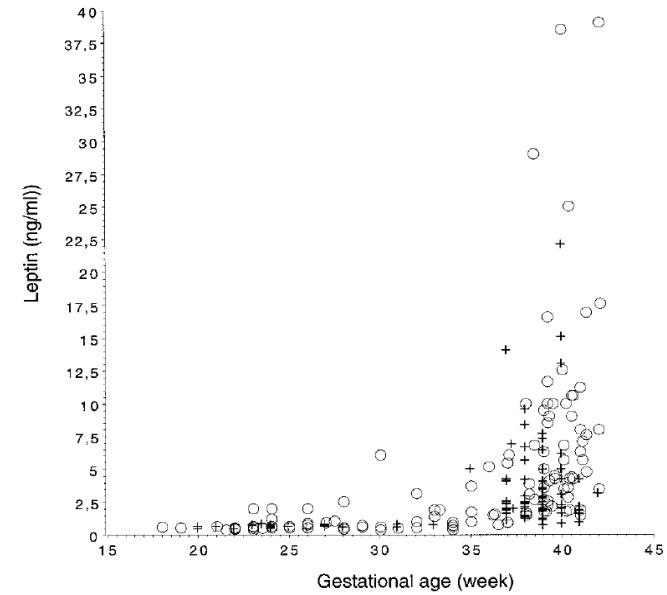
(-) Prise alimentaire

(+) Dépense énergétique

La leptine : Hormone de satiété. Oui mais pas uniquement



Devaskar et al., 1997

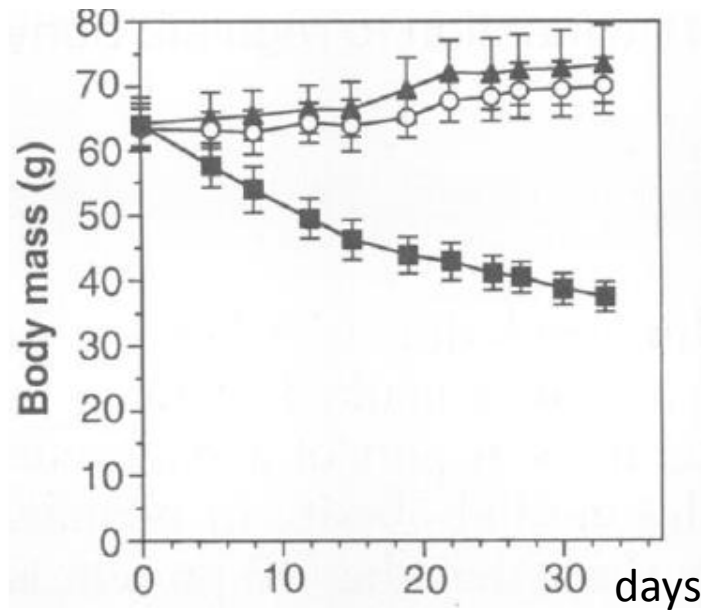


Jacquet et al., 1998

La leptine : Hormone de satiété. Oui mais pas uniquement



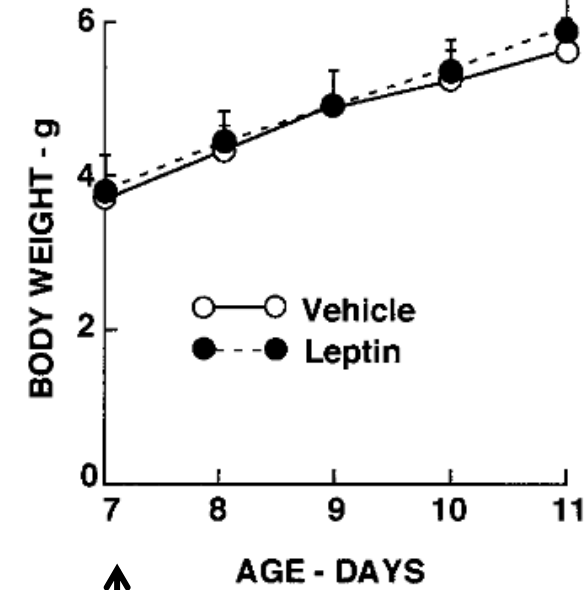
Souris adulte



↑
Leptine

Halaas et al., 1995

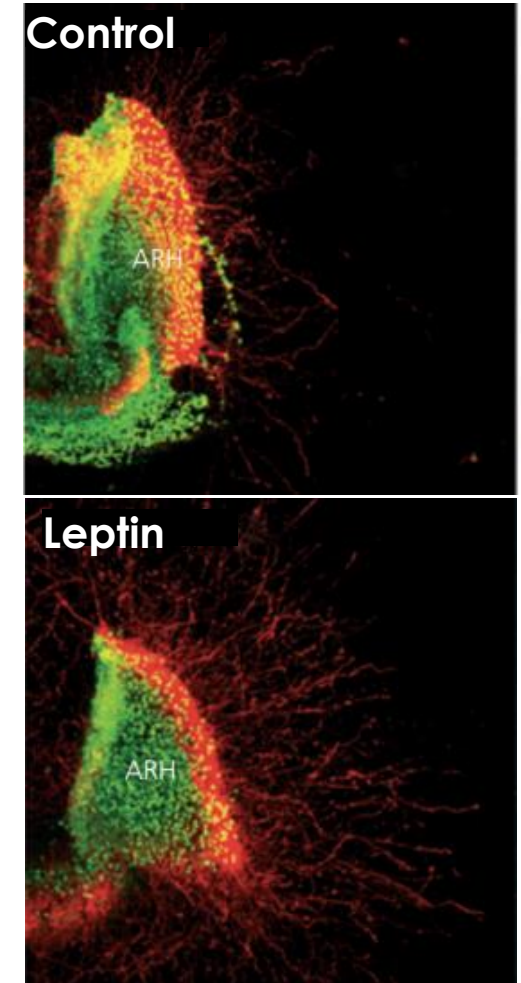
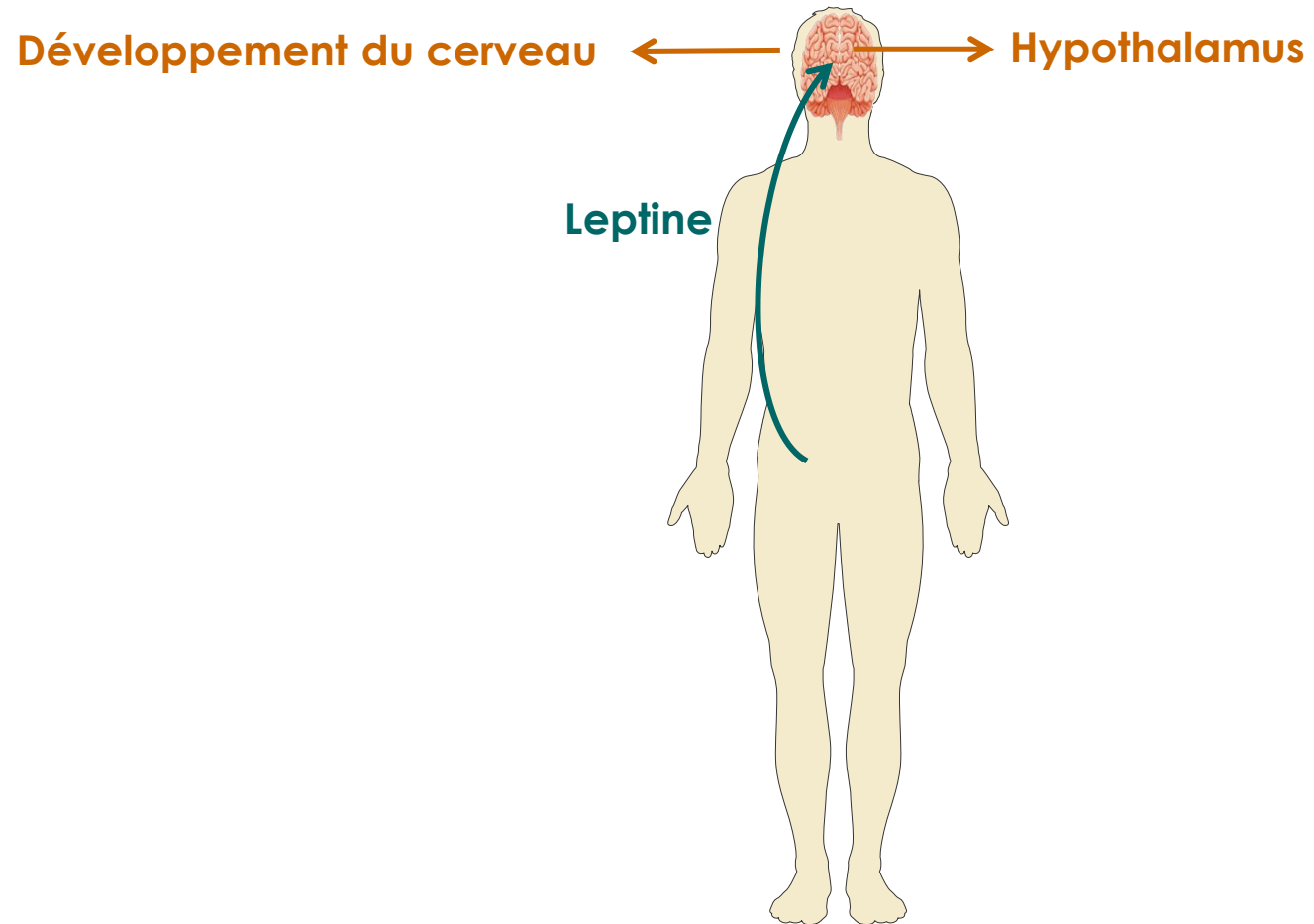
Souris jeune



↑
Leptine

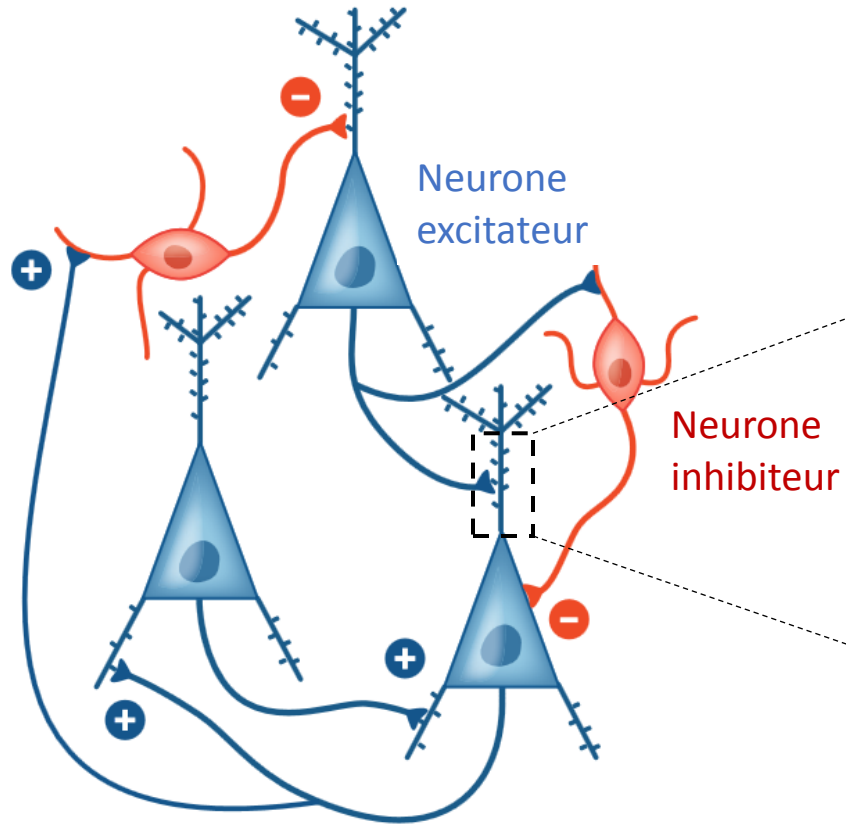
Mistry et al., 1999

La leptine : Un facteur neurotrophique

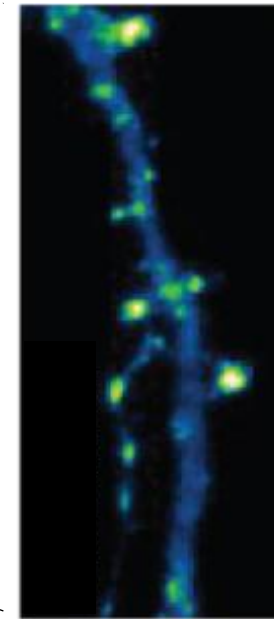


La leptine : Un facteur neurotrophique

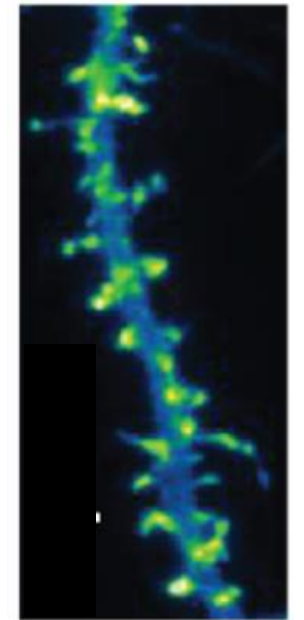
G. Wayman



Contrôle



leptine



Dhar et al, 2014

La leptine : Un facteur neurotrophique

G. Wayman



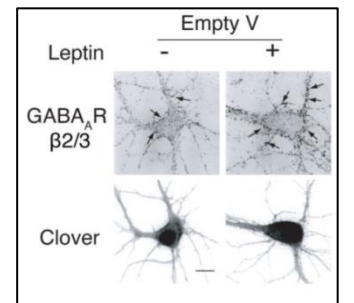
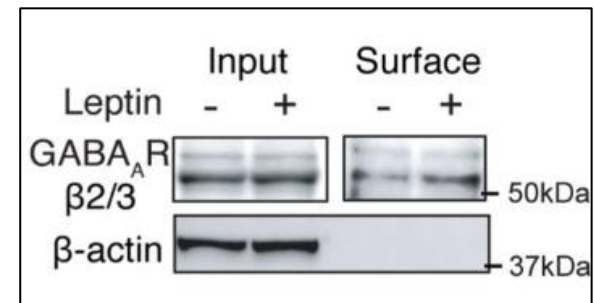
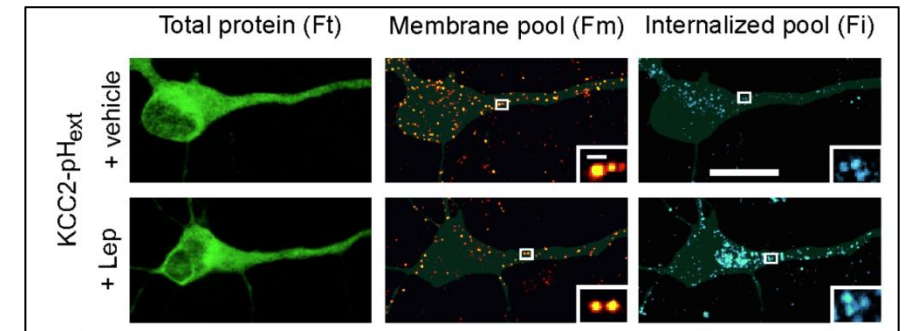
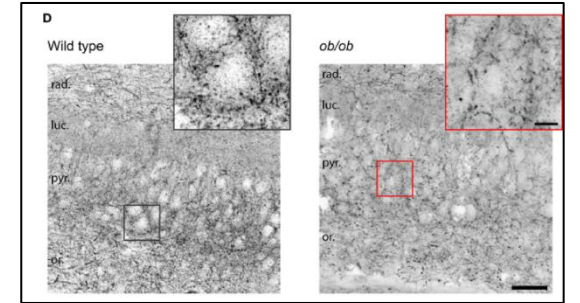
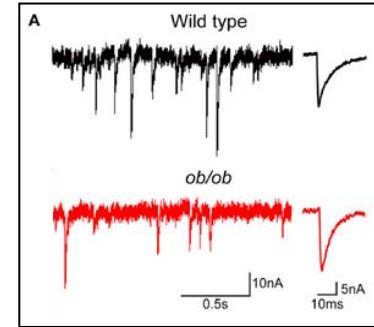
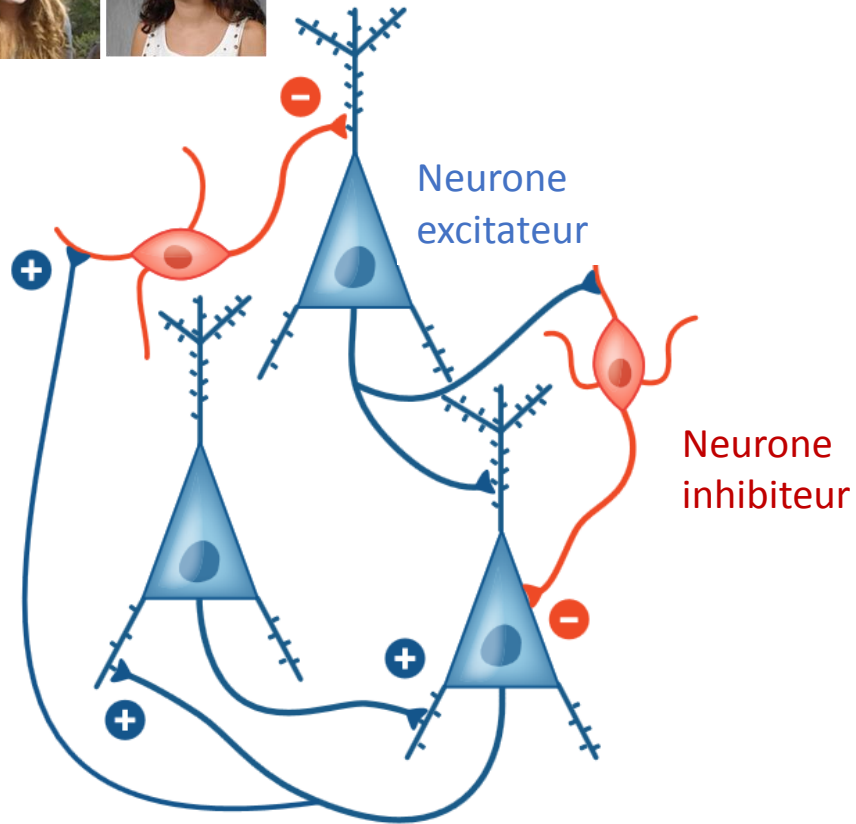
D. Guimond



C. Dumon



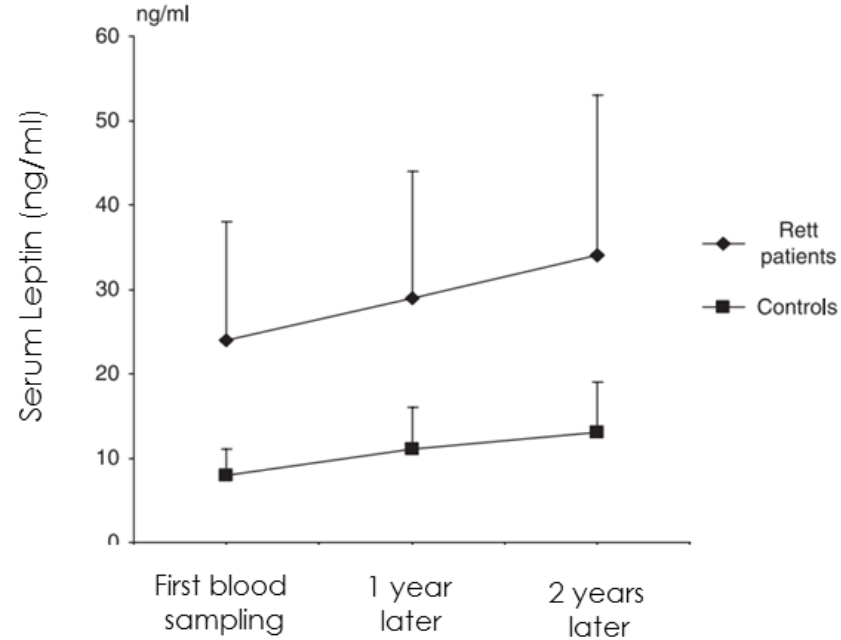
S. Sahin



Les taux de leptine sont anormalement élevés dans le RTT



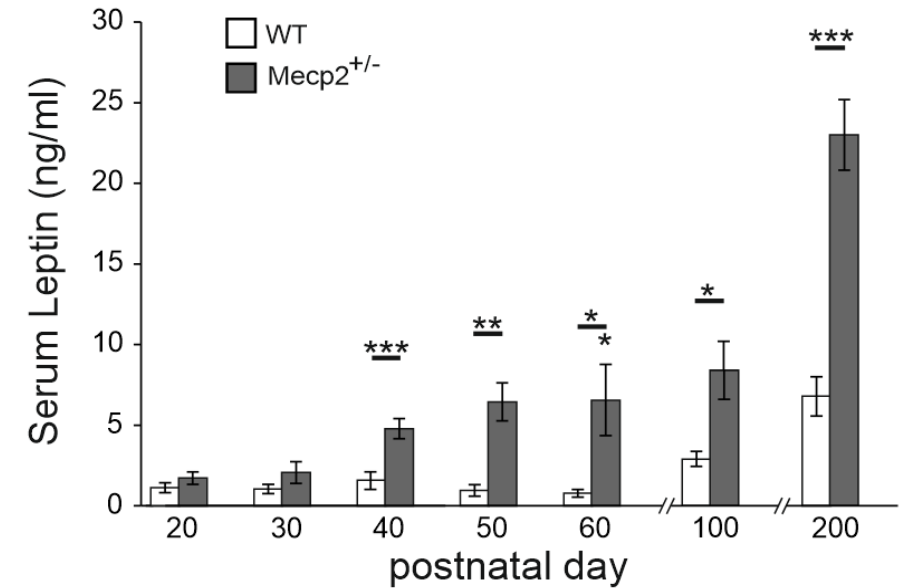
Âge moyen 9 ± 3 ans



Acampa et al., 2008; Blardi et al., 2007; 2009.



Mecp2^{tm1-1} bird



Park et al., 2014; Torres-Andrade et al., 2014; Fukuda et al., 2019.

La leptine: Une hormone aux multiples fonctions



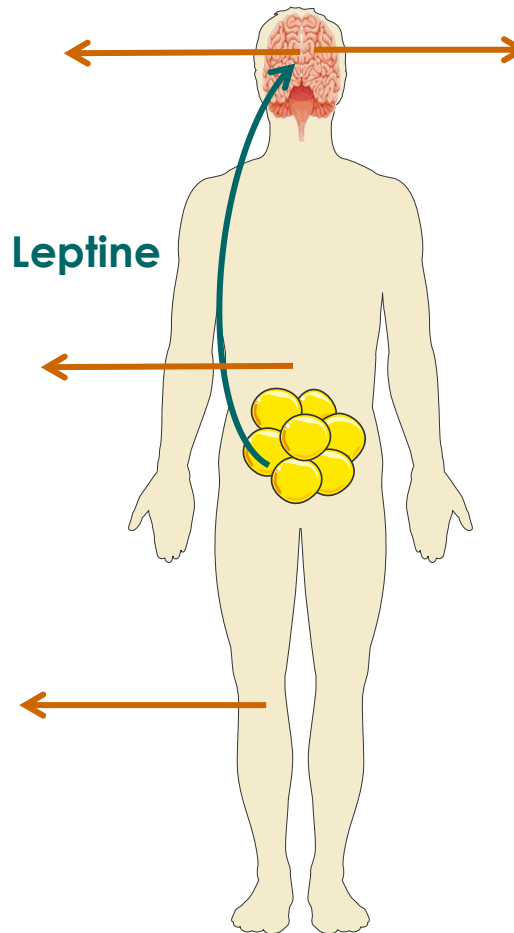
Développement du cerveau



Développement des organes

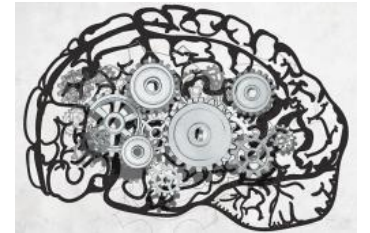


Minéralisation osseuse
Masse musculaire



Fonctionnement du cerveau

- Satiété
- Puberté
- Motricité
- Mémoire
- Emotions
- Respiration
- Rythme cardiaque
- Pression artérielle



Contribution de la leptine au syndrome de Rett : Protocole



Mecp2^{tm1-1} bird
(Guy et al., 2001)



• Symptômes

- Motricité réduite
- Difficultés respiratoires
- Anxiété
- Troubles cognitifs
- Epilepsie
- Système gastro-intestinale (mobilité, microbiote)
- Métabolisme
- Système osseux
- Atrophie musculaire
- Perte de poids (mâle)
- Mort prématurée (mâle)

• Au niveau neuronal :

- Atteintes morphologiques
- Altération balance excitation/inhibition
- Diminution plasticité synaptique

40 50

⏟

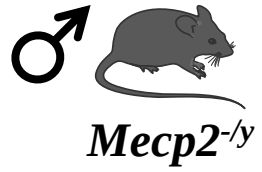
Injectons sous-cutanées quotidiennes:

- anti-leptin (5µg/g)
- Solvant (placebo)

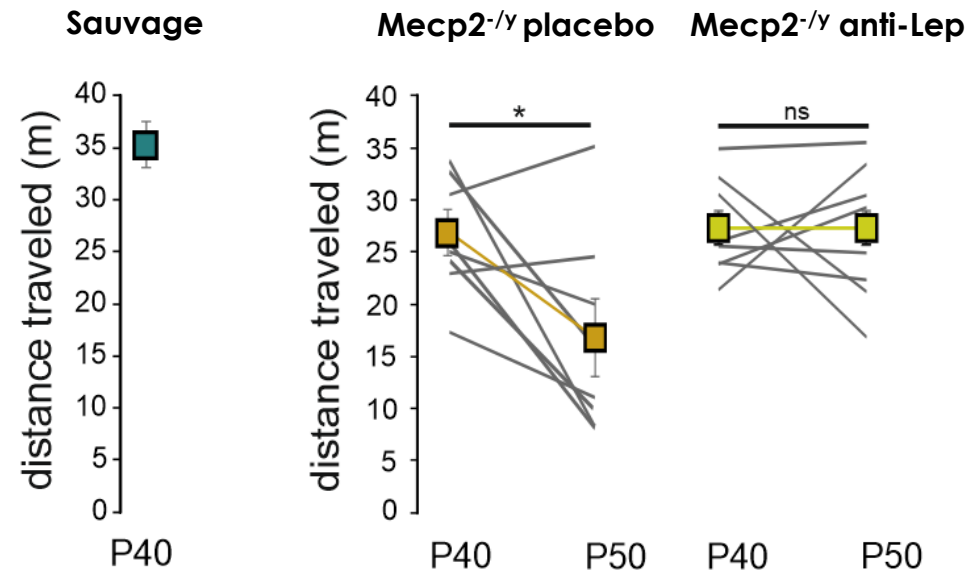
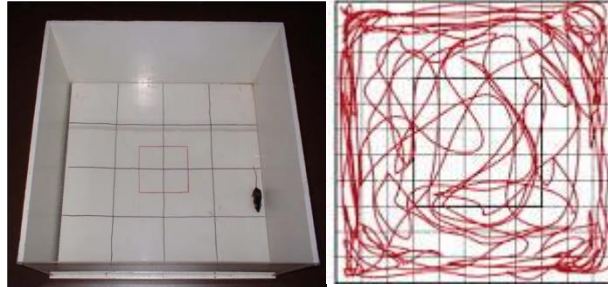
Leptine



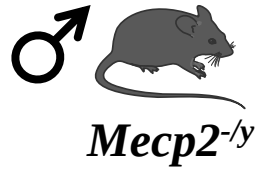
Contribution de la leptine au syndrome de Rett



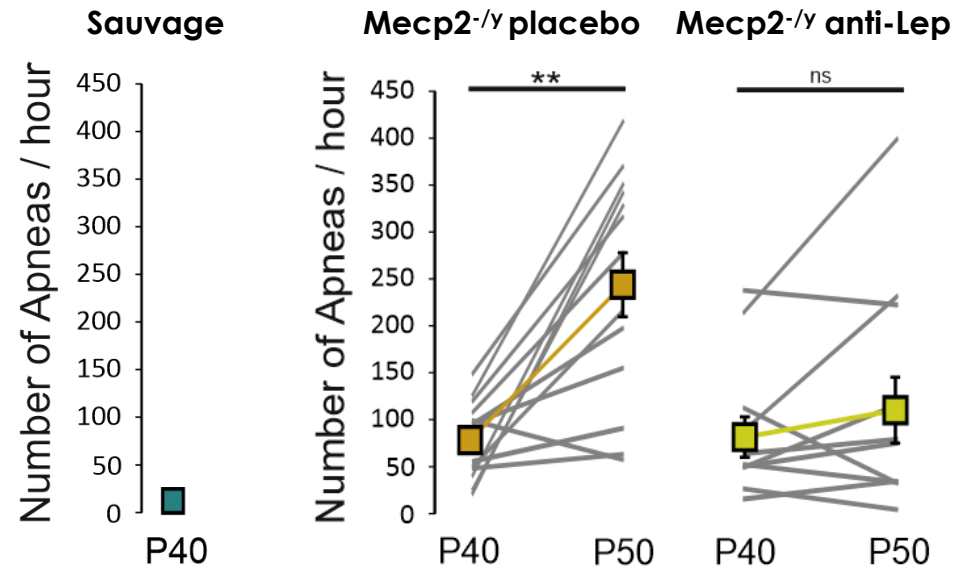
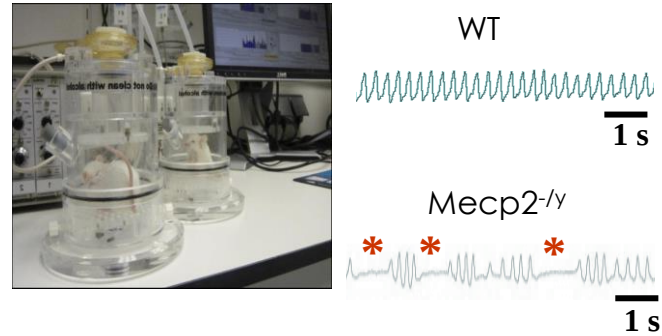
Activité locomotrice



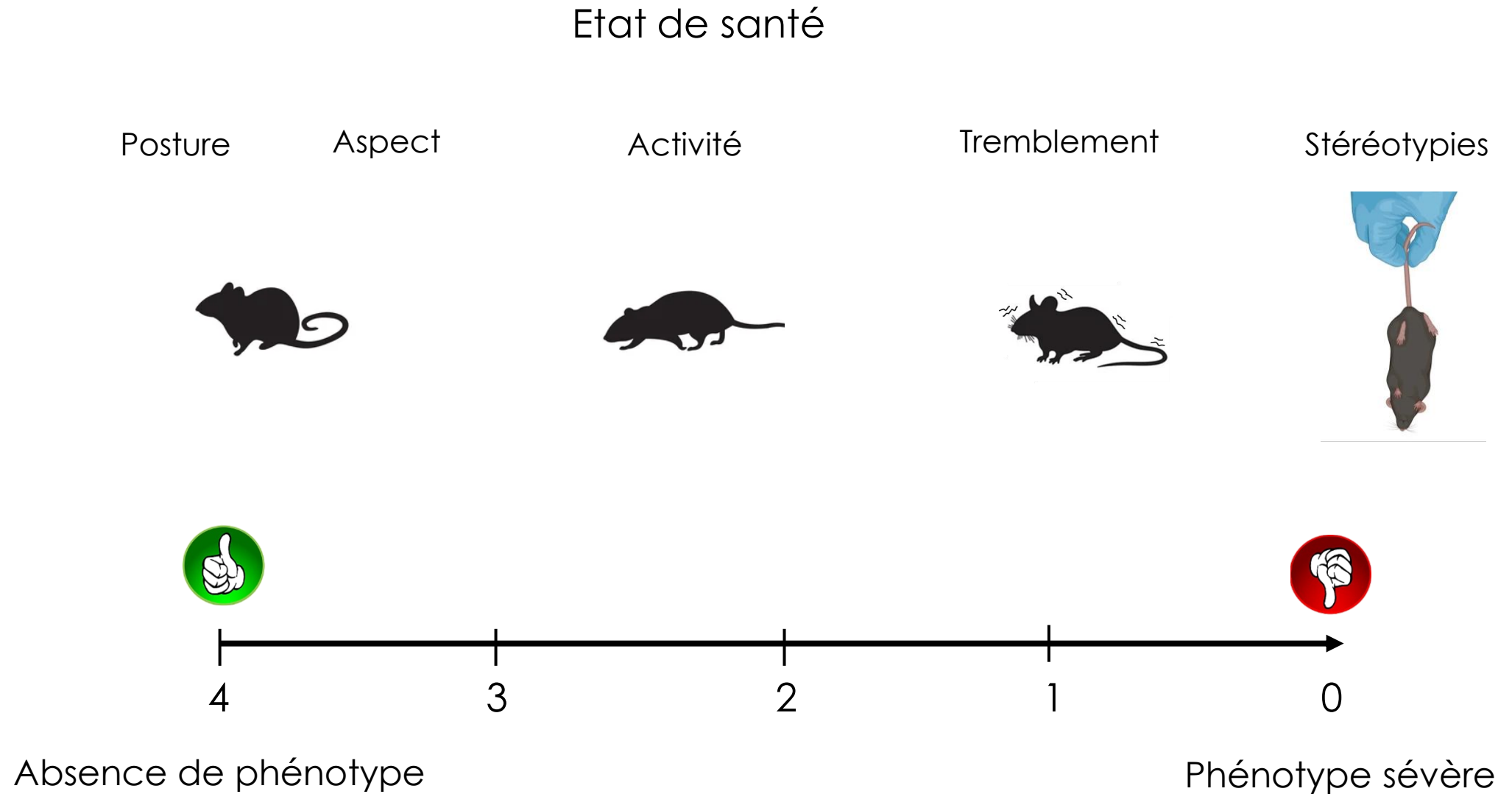
Contribution de la leptine au syndrome de Rett



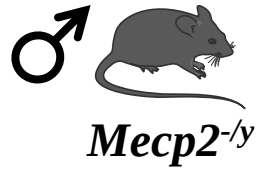
Activité respiratoire



Contribution de la leptine au syndrome de Rett



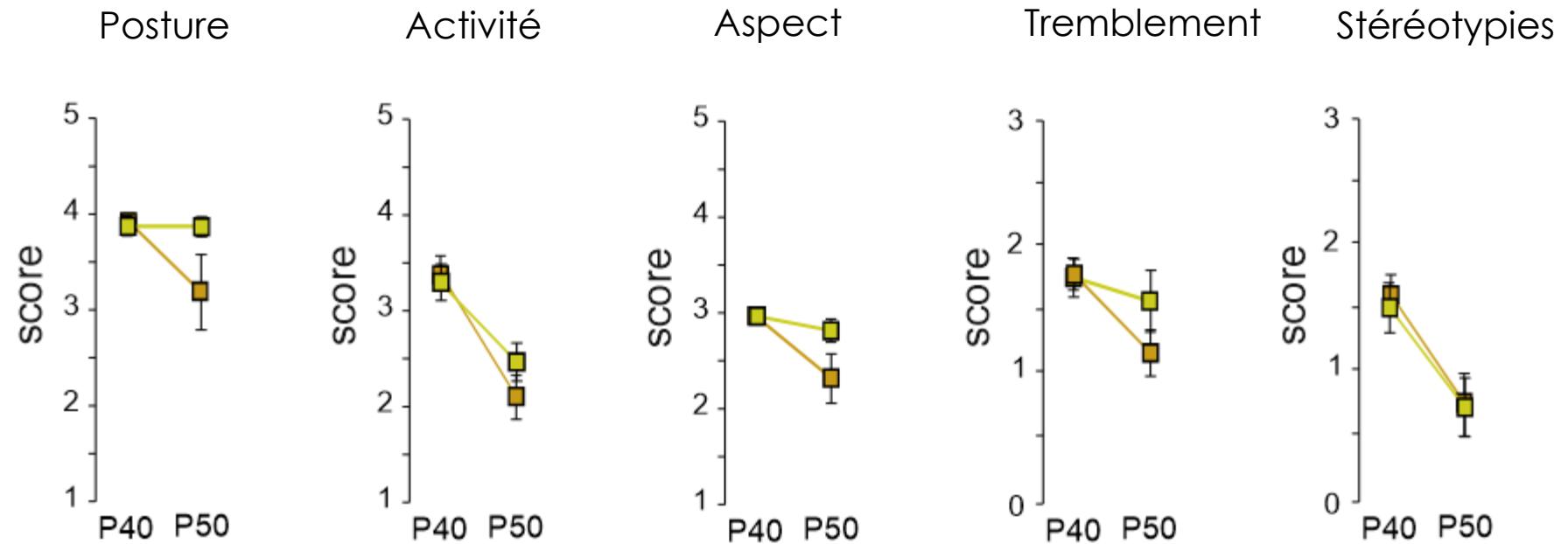
Contribution de la leptine au syndrome de Rett



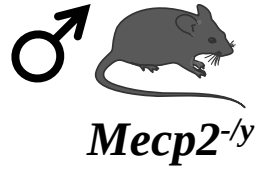
Etat de santé

■ *Mecp2^{-/-}* placebo

■ *Mecp2^{-/-}* anti-Lep



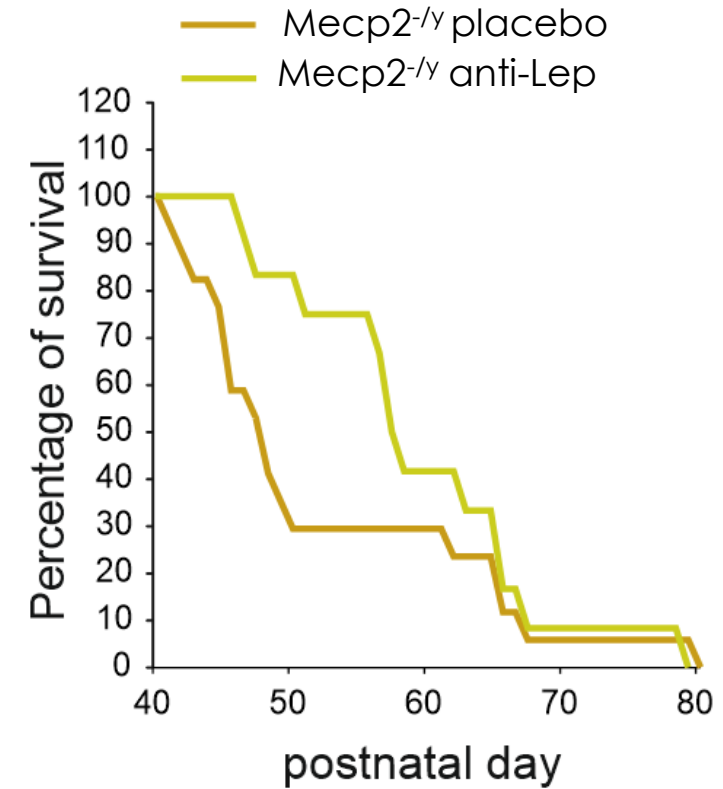
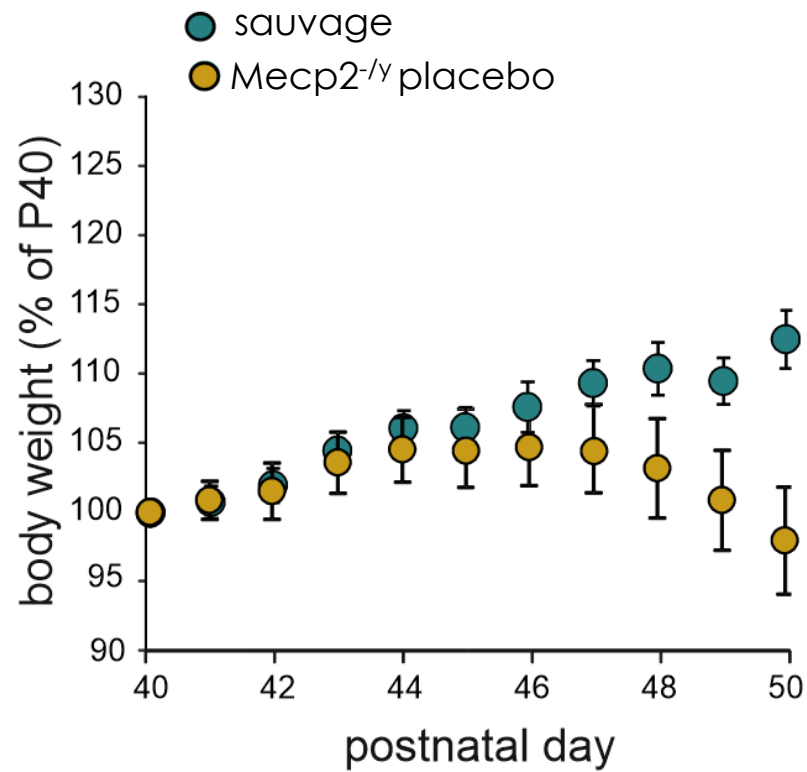
Contribution de la leptine au syndrome de Rett



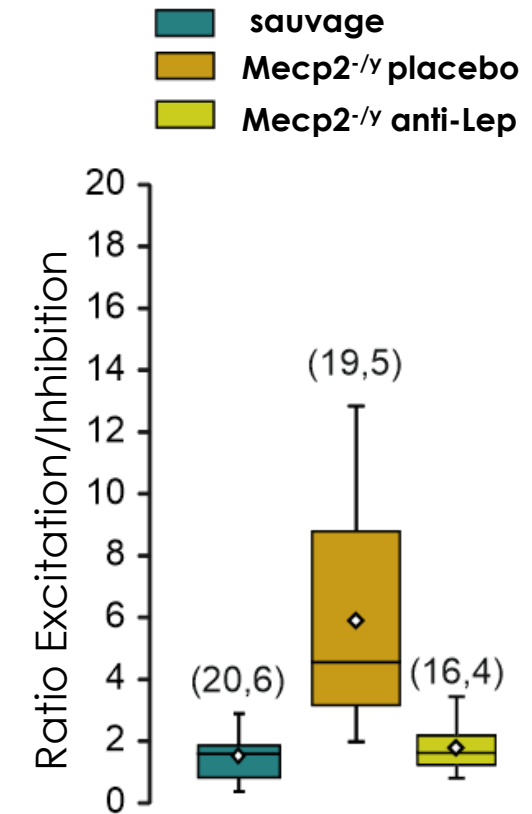
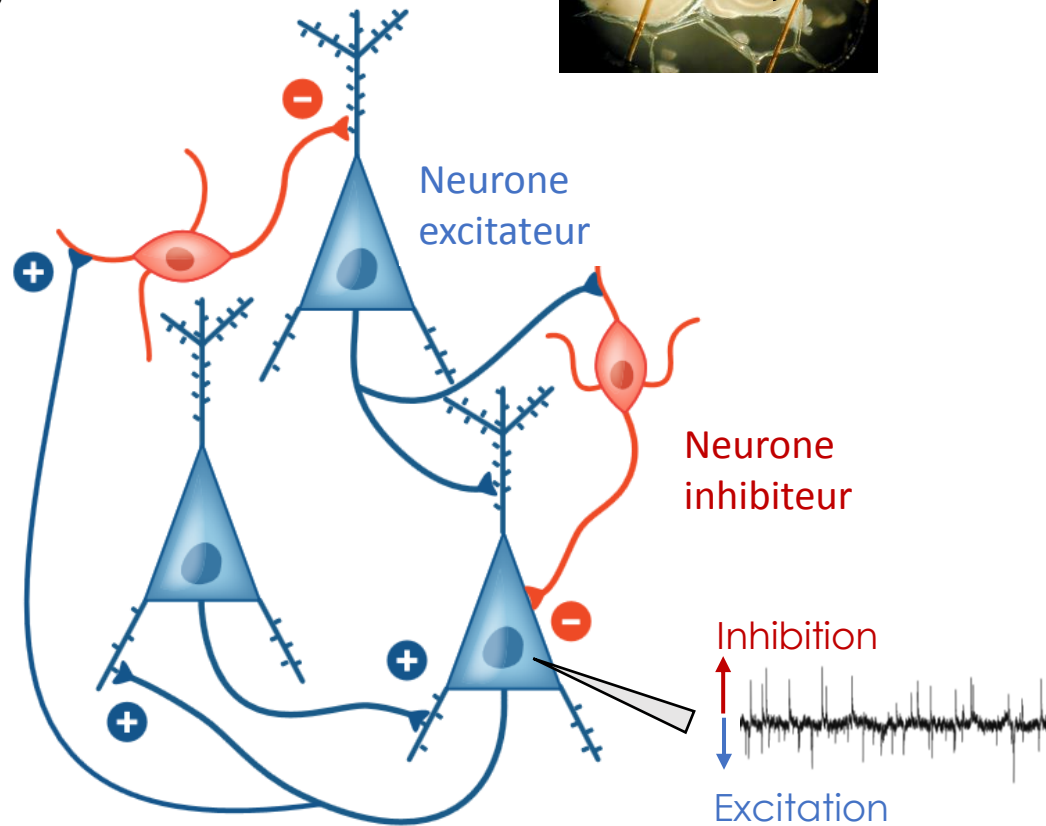
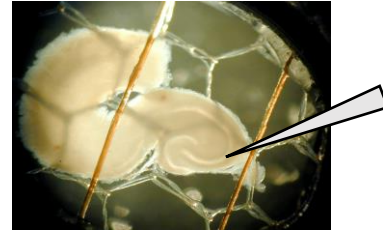
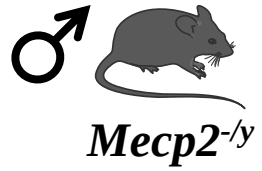
Prise de poids



Espérance de vie



Contribution de la leptine au syndrome de Rett



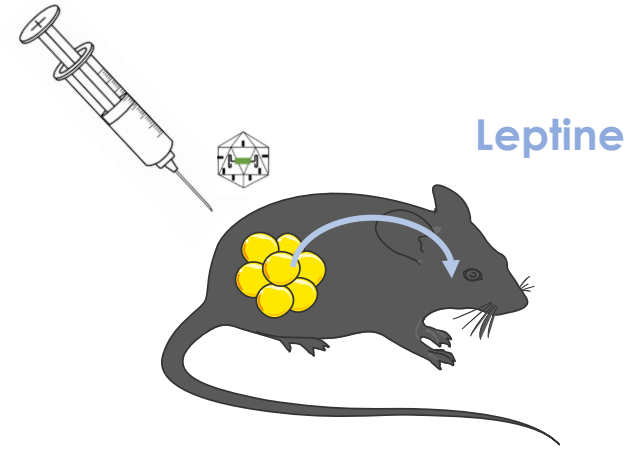
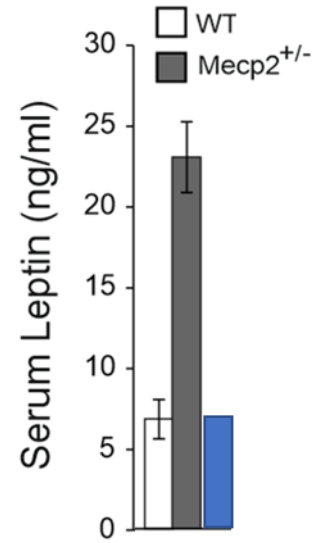
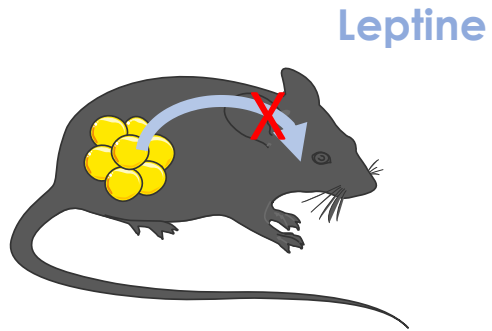
Conclusions

Le blocage de la leptine prévient l'aggravation de certains symptômes chez les souris Rett.

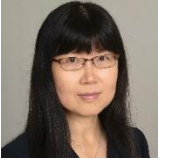
La leptine n'est pas un simple témoin de la maladie.

Elle participe activement à la progression des symptômes ?

Développer une stratégie thérapie génique visant la production de leptine



Développer une stratégie thérapie génique visant la production de leptine

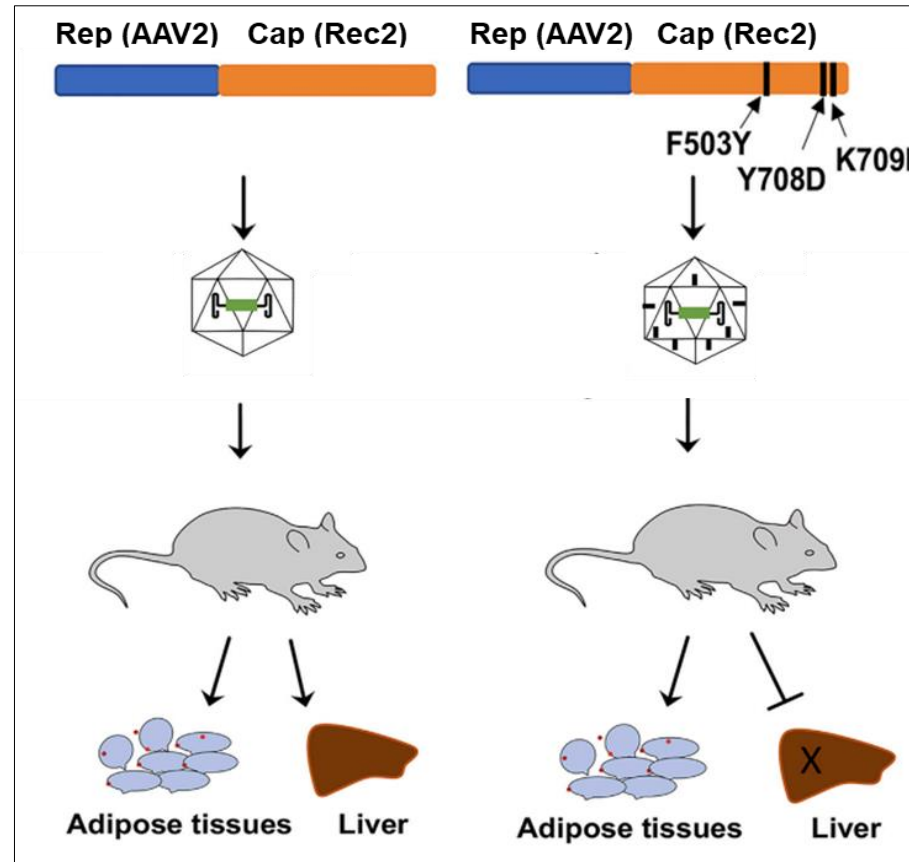


Cao lei, Ohio State University

Article

Development of an adipose-tropic AAV capsid ablating liver tropism

Wei Huang,^{1,2} Rhiannon Bates,^{1,2} Bhavya Appana,^{1,2} Tawfiq Mohammed,^{1,2} and Lei Cao^{1,2,3,*}

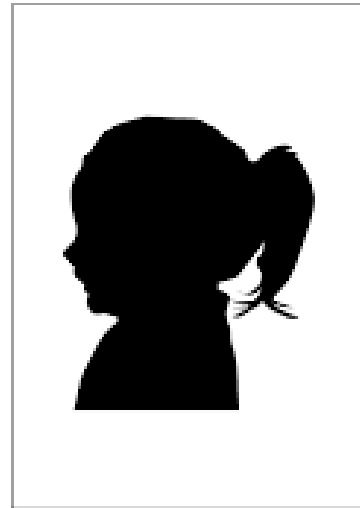
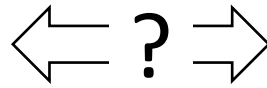


La leptine : un biomarqueur diagnostique et pronostique du Rett ?



Pr. M. Milh, la Timone

Taux sanguin de leptine



- Sévérité
- Progression
- Mutation

Equipe F. Muscatelli à INMED

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Y. Belaidouni

M. Brosset-Heckel

D. Diabira

C. Gestreau

A. Limonssier-Benkemoun

V. Matarazzo

M. Meger

C. Menuet

I. Medina

F. Omnes

P. Porcher

F. Schaller

R. Tyzio

U. Zayan

Plateformes INMED

Q. Cesar (Animal facility)

M. Kurz (Histology)

F. Bader (Mice genotyping)

Collaborations

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G.A. Wayman, WSU, Pullman, WA.

C. Santos, Phenotype Expertise, Marseille.

L. Cao, OSU, Columbus, OH.

