

Peut-on négliger le sexe dans la recherche biomédicale ?

Dr Colette DENIS

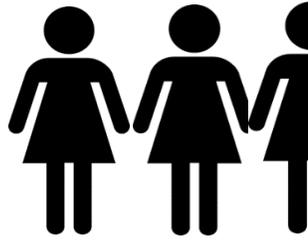
FEMMES & SCIENCES
a s s o c i a t i o n

arpège réseau
genre

- Sexe: caractéristiques biologiques qui différencient les hommes des femmes, comme les organes reproducteurs, les chromosomes, les hormones, etc.
- Genre: rôles qui sont déterminés socialement, les comportements, les activités et les attributs qu'une société considère comme appropriés pour les hommes et les femmes.
- Santé humaine: sexe et genre en interaction permanente
- Recherche sur animaux ou des cellules: sexe

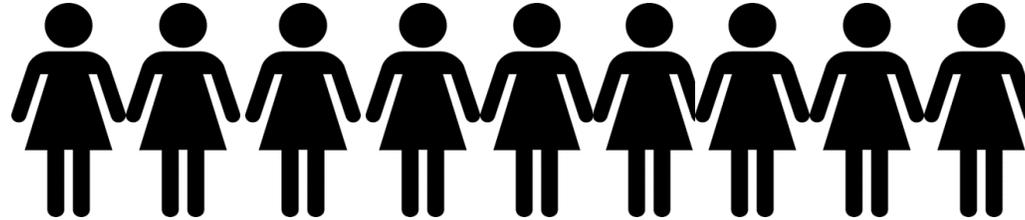
Maladies de femmes vs maladies d'hommes ?

Polyarthrite rhumatoïde

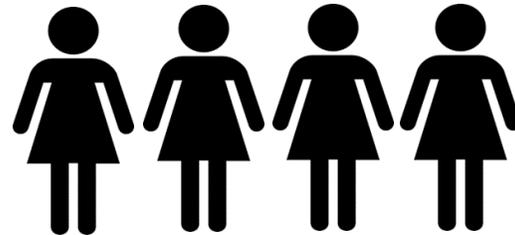


Lupus

Cholangite biliaire primitive

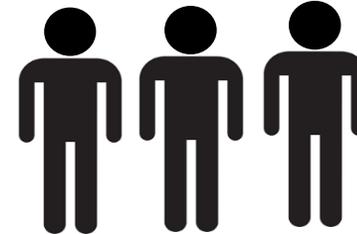


Covid long

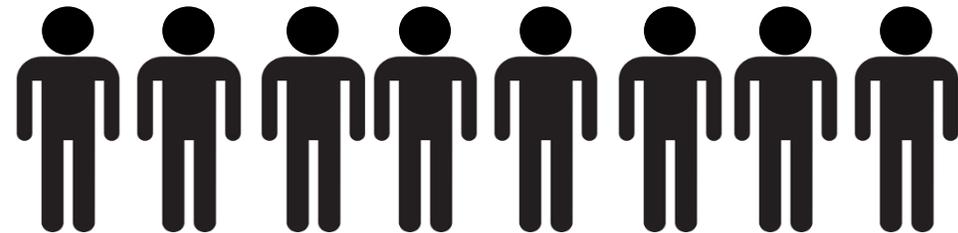


Maladies de femmes vs maladies d'hommes ?

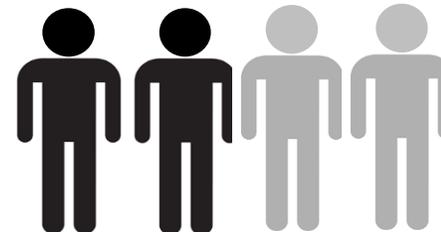
Ulcère duodéal



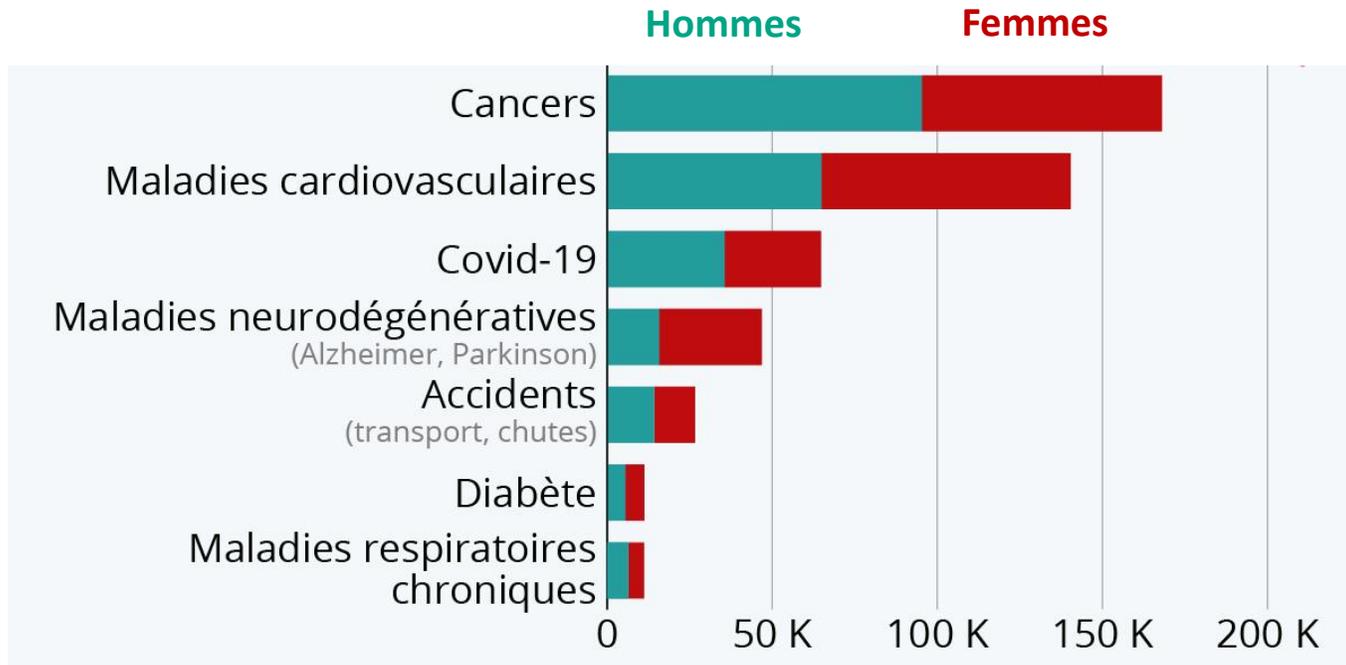
La goutte

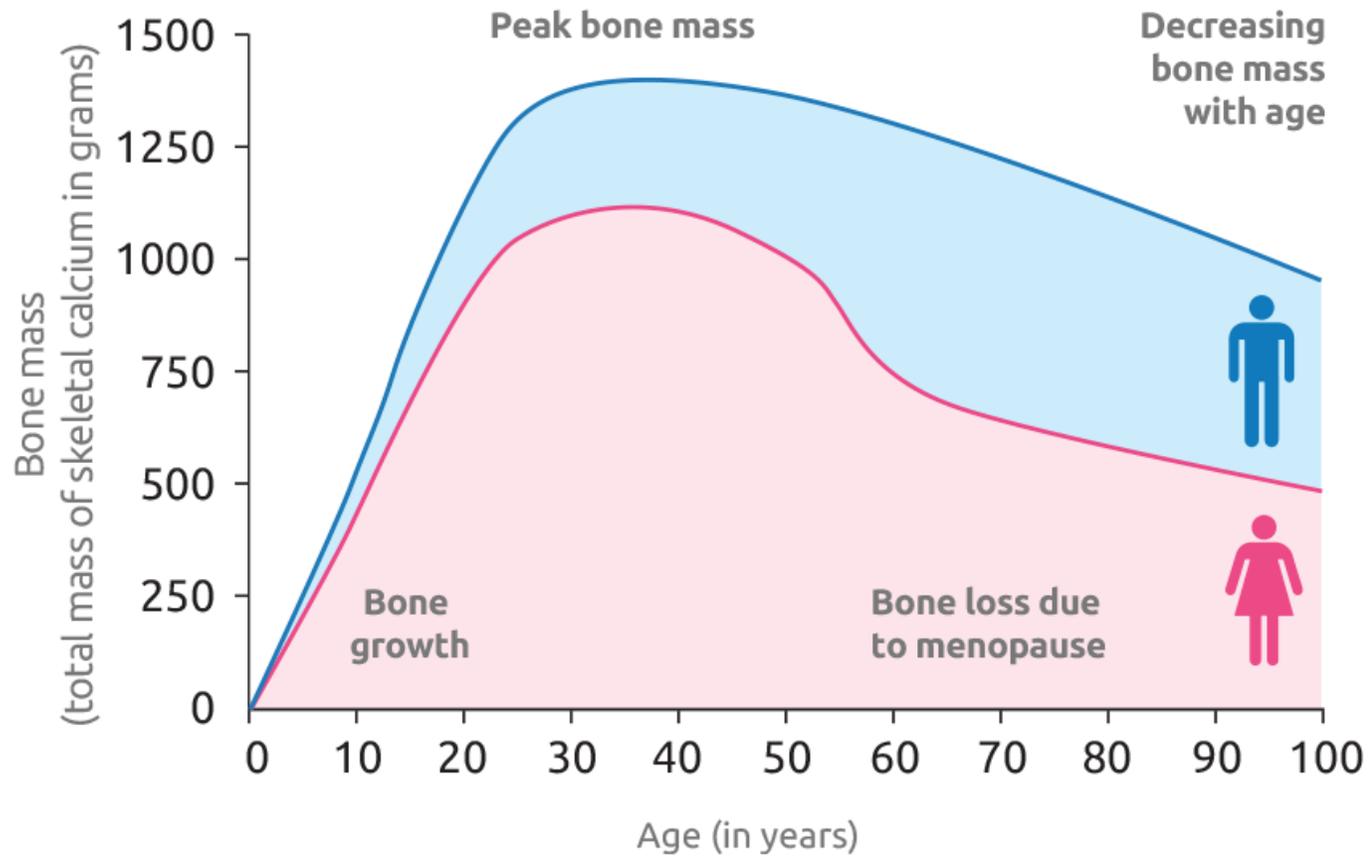


Troubles du spectre autistique



Causes de mortalité en France (2020)

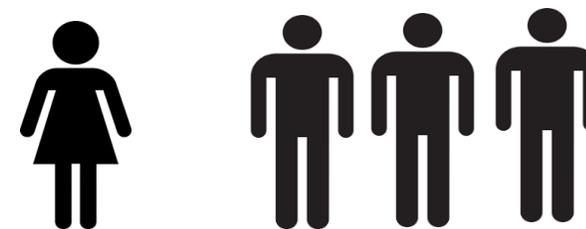
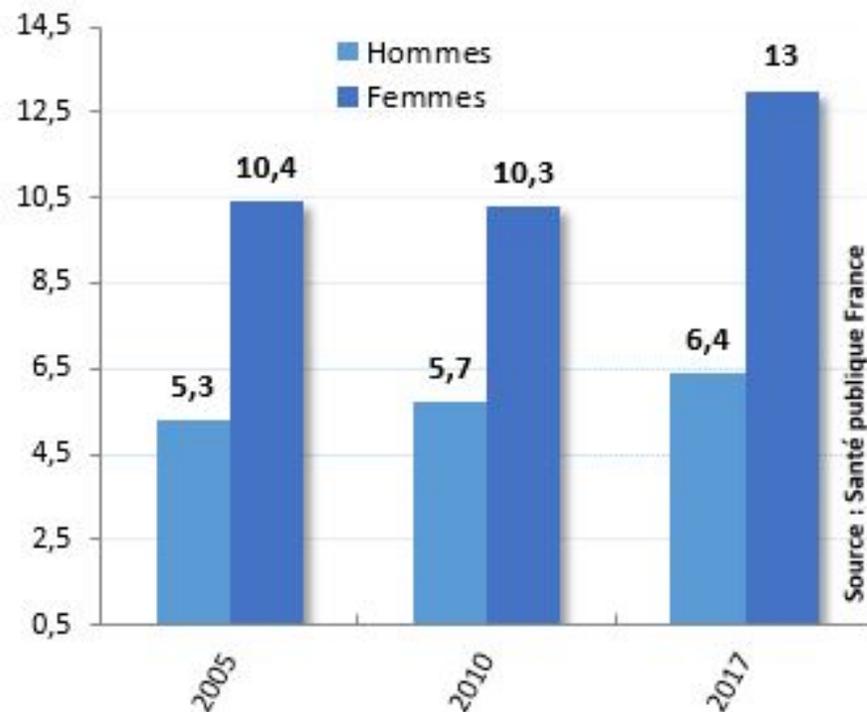




Mortalité après fracture sévère
Hommes > Femmes

Personnes ayant connu au moins un épisode dépressif dans l'année, données 2017 en %

© Centre d'observation de la société



Mort par suicide

A

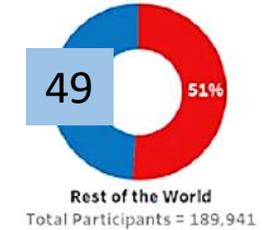
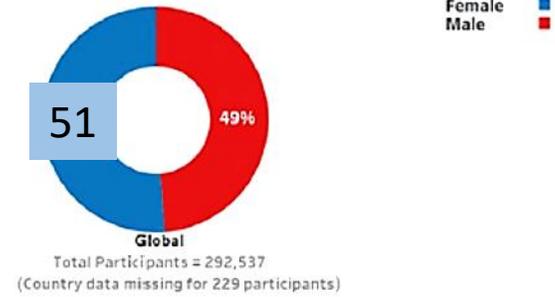
Progress and opportunities for women in clinical trials: A look at recent data and initiatives from the U.S. FDA

Kaveeta P. Vasisht,^{1,*} Bridget M. Nugent,^{1,*} and Janet Woodcock²

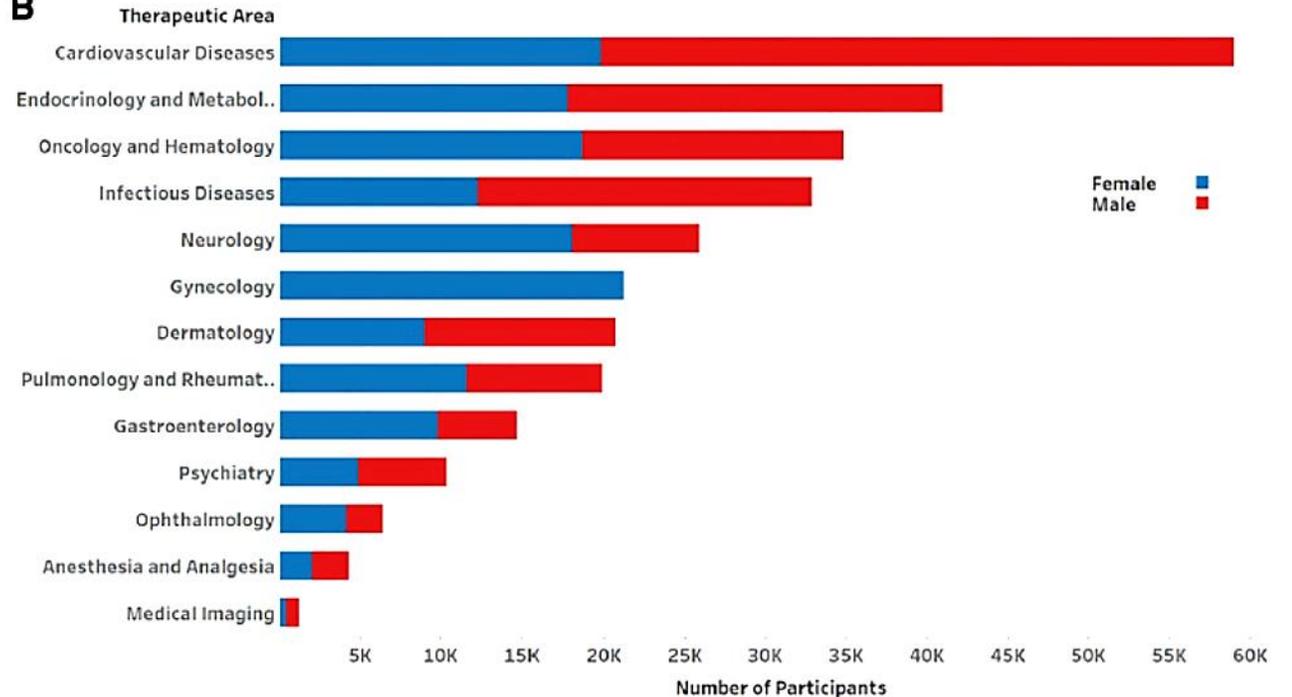
Med 2, 456–504, May 14, 2021

Essais cliniques 2015-2019 Pour 231 candidats médicaments

Sex Distribution



B



	% de femmes dans les essais thérapeutiques (USA)
1970	9
2006	40
2015-2019	56

Et en recherche biomédicale ?

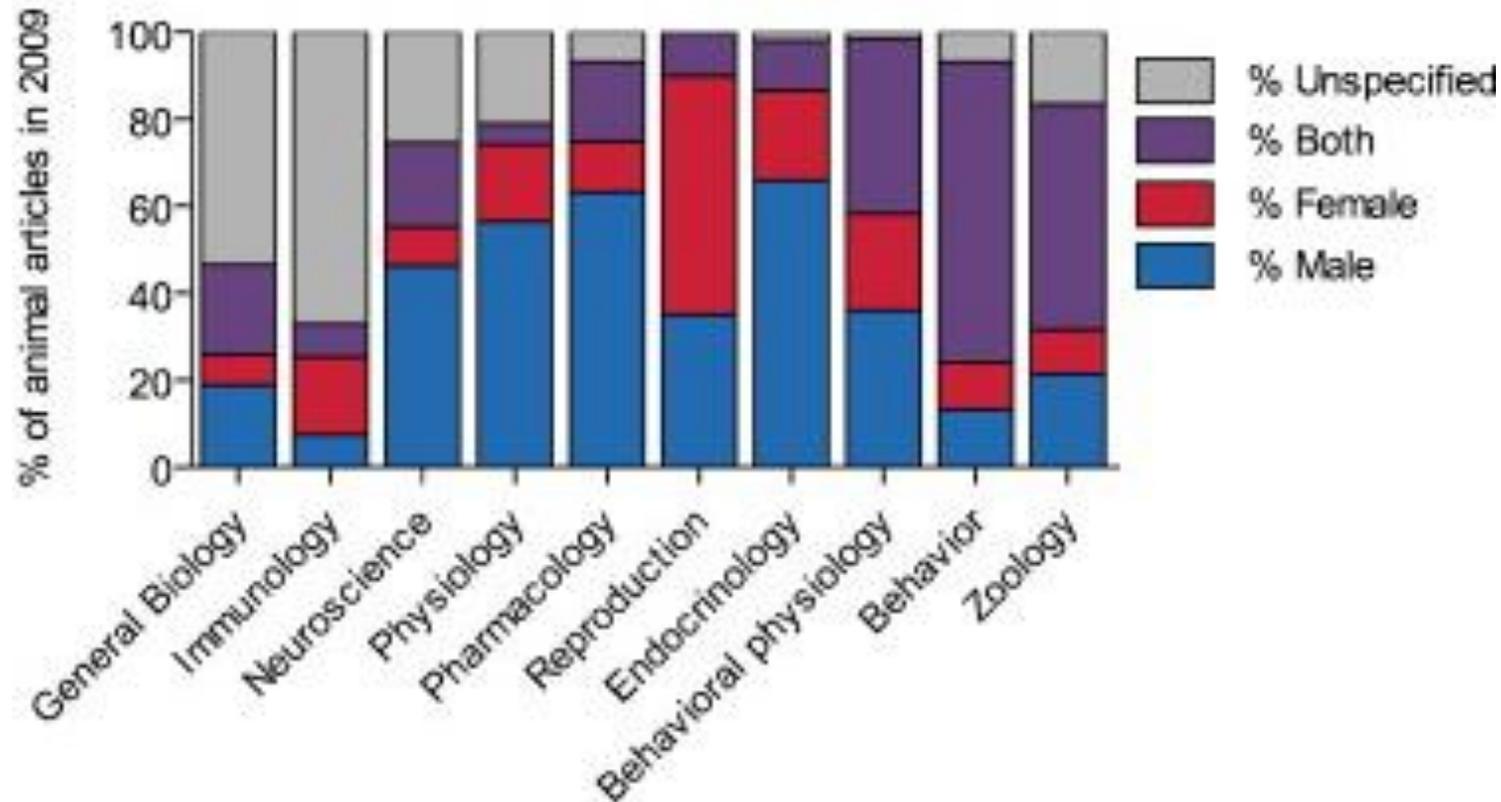


Sex bias in neuroscience and biomedical research

Annaliese K. Beery^a, Irving Zucker^{b,c,*}

Neuroscience and Biobehavioral Reviews 35 (2011) 565–572

Analyse de plus de 2000 articles dans des journaux représentatifs de la discipline

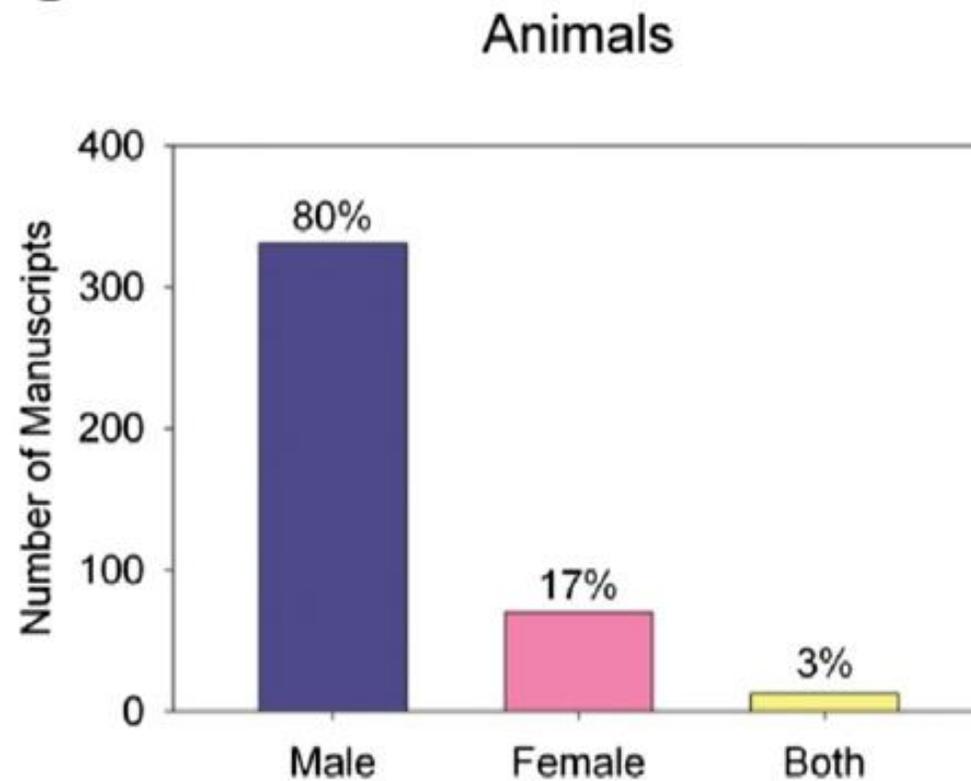


Sex bias exists in basic science and translational surgical research

Dustin Y. Yoon, MD, MS,^a Neel A. Mansukhani, MD,^a Vanessa C. Stubbs, MD,^a
Irene B. Helenowski, PhD,^b Teresa K. Woodruff, PhD,^{c,d} and Melina R. Kibbe, MD,^{a,d} Chicago, IL

(*Surgery* 2014;156:508-16.)

Plus de 600 articles

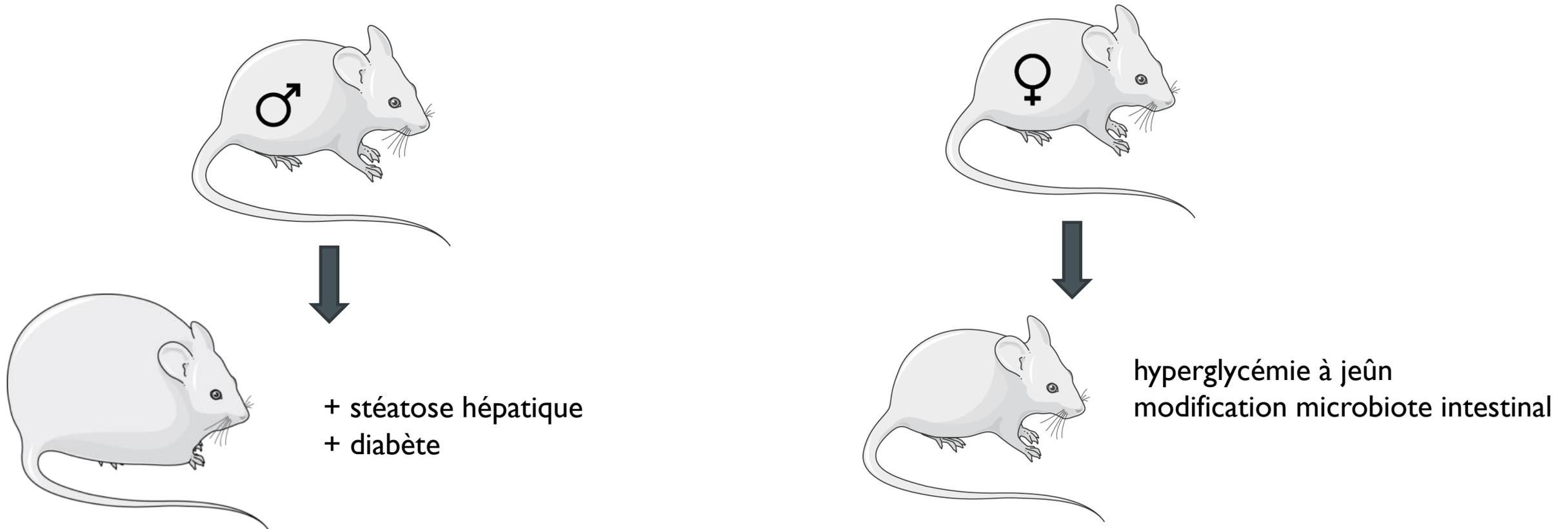


En dehors de la reproduction, la physiologie des femelles diffère-t-elle de celle des mâles ?

Metabolic Effects of a Chronic Dietary Exposure to a Low-Dose Pesticide Cocktail in Mice: Sexual Dimorphism and Role of the Constitutive Androstane Receptor

Céline Lukowicz,¹ Sandrine Ellero-Simatos,¹ Marion Régnier,¹ Arnaud Polizzi,¹ Frédéric Lasserre,¹ Alexandra Montagner,¹ Yannick Lippi,¹ Emilien L. Jamin,^{1,3} Jean-François Martin,¹ Claire Naylies,¹ Cécile Canlet,^{1,3} Laurent Debrauwer,^{1,3} Justine Bertrand-Michel,² Talal Al Saati,⁴ Vassilia Théodorou,¹ Nicolas Loiseau,¹ Laïla Mselli-Lakhal,¹ Hervé Guillou,¹ and Laurence Gamet-Payrastré¹

Environ Health Perspect. 2018



	Mâles	Femelles
Traitement streptozotocine ou alloxane, modèles génétiques: rats Zucker diabetic fatty (ZDF) et Otsuka Long Evans Tokushima Fatty (OLETF); souris Akita, New Zealand obese (NZO).	Diabétiques	Peu ou pas atteintes
Régimes High Fat Diet	Obèses	Peu atteintes

A Guide for the Design of Pre-clinical Studies on Sex Differences in Metabolism

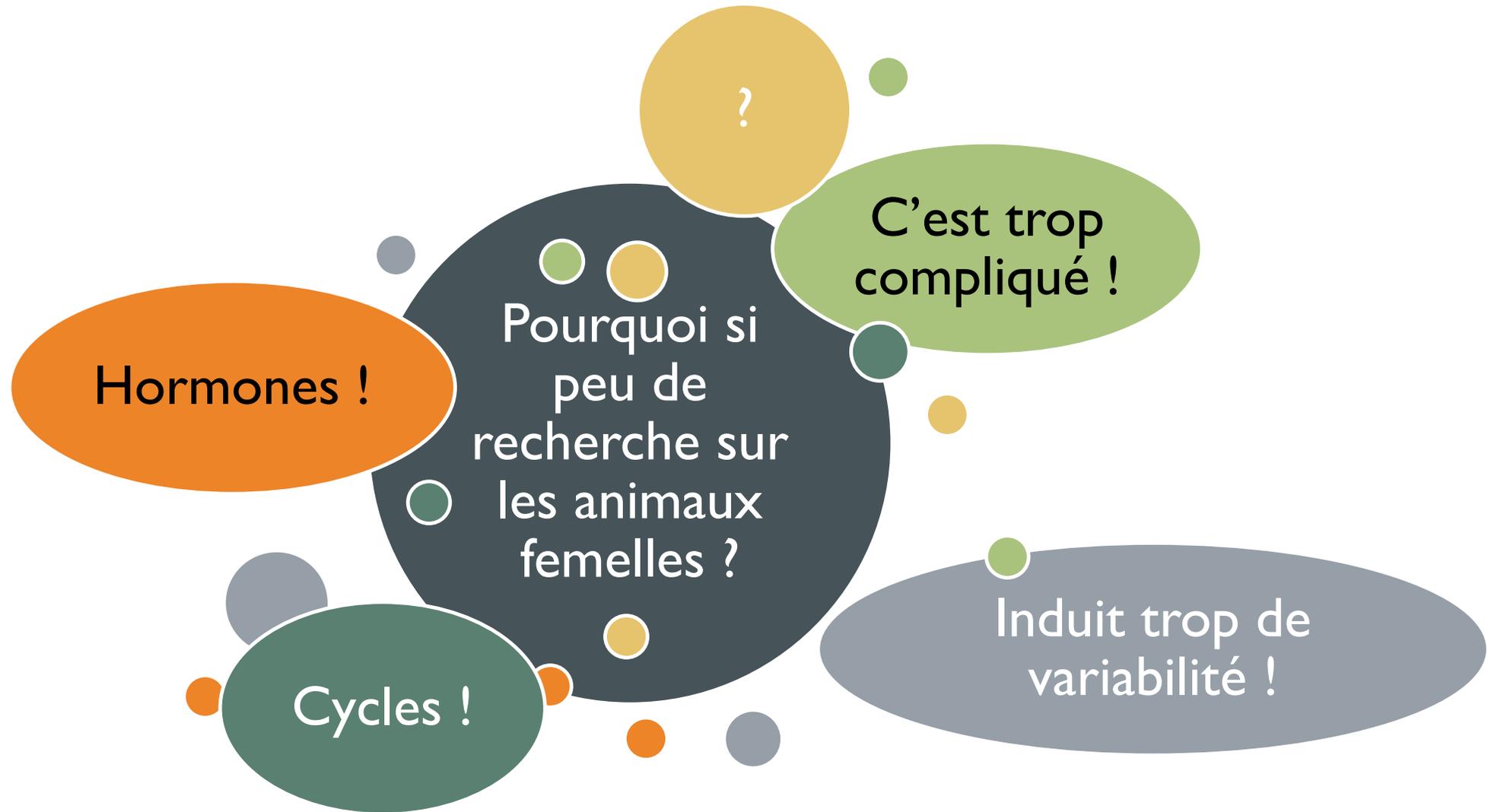
Franck Mauvais-Jarvis,^{1,*} Arthur P. Arnold,² and Karen Reue³

¹Diabetes Discovery & Gender Medicine Laboratory, Section of Endocrinology & Metabolism, Department of Medicine, Tulane University Health Sciences Center, New Orleans, LA 70112, USA

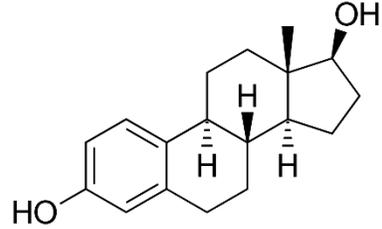
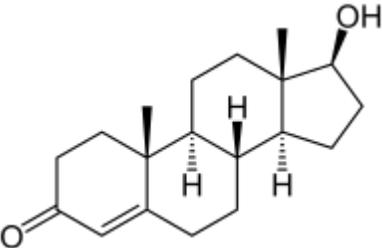
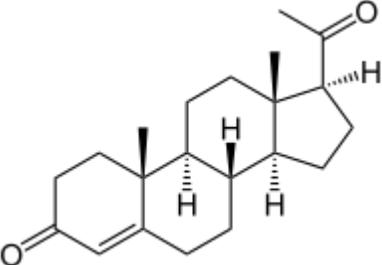
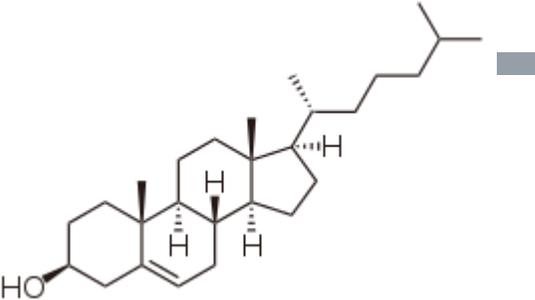
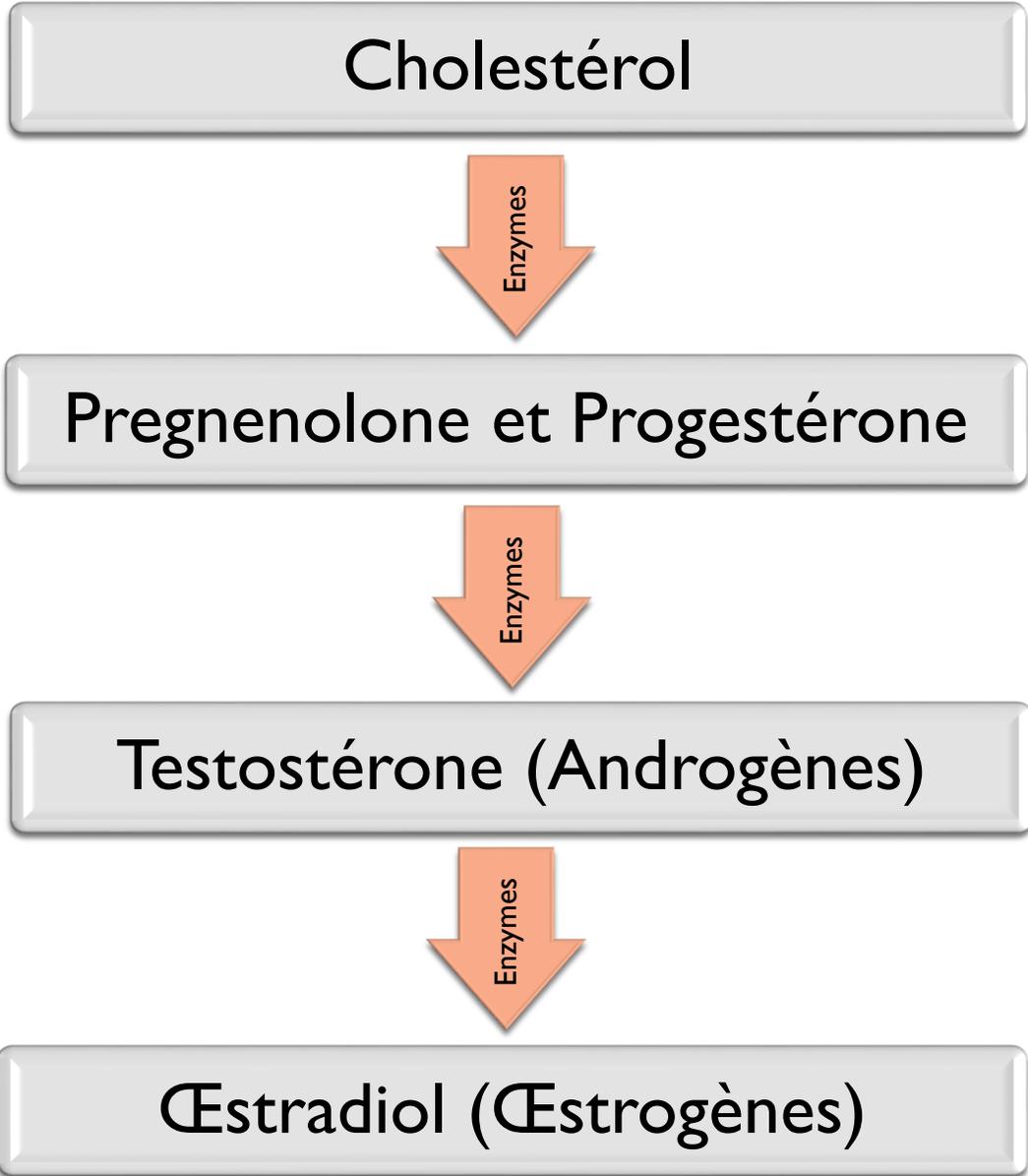
²Department of Integrative Biology & Physiology

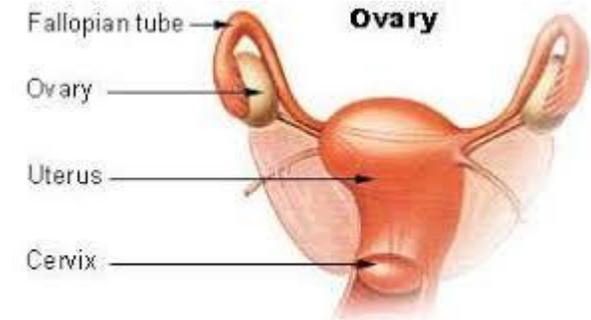
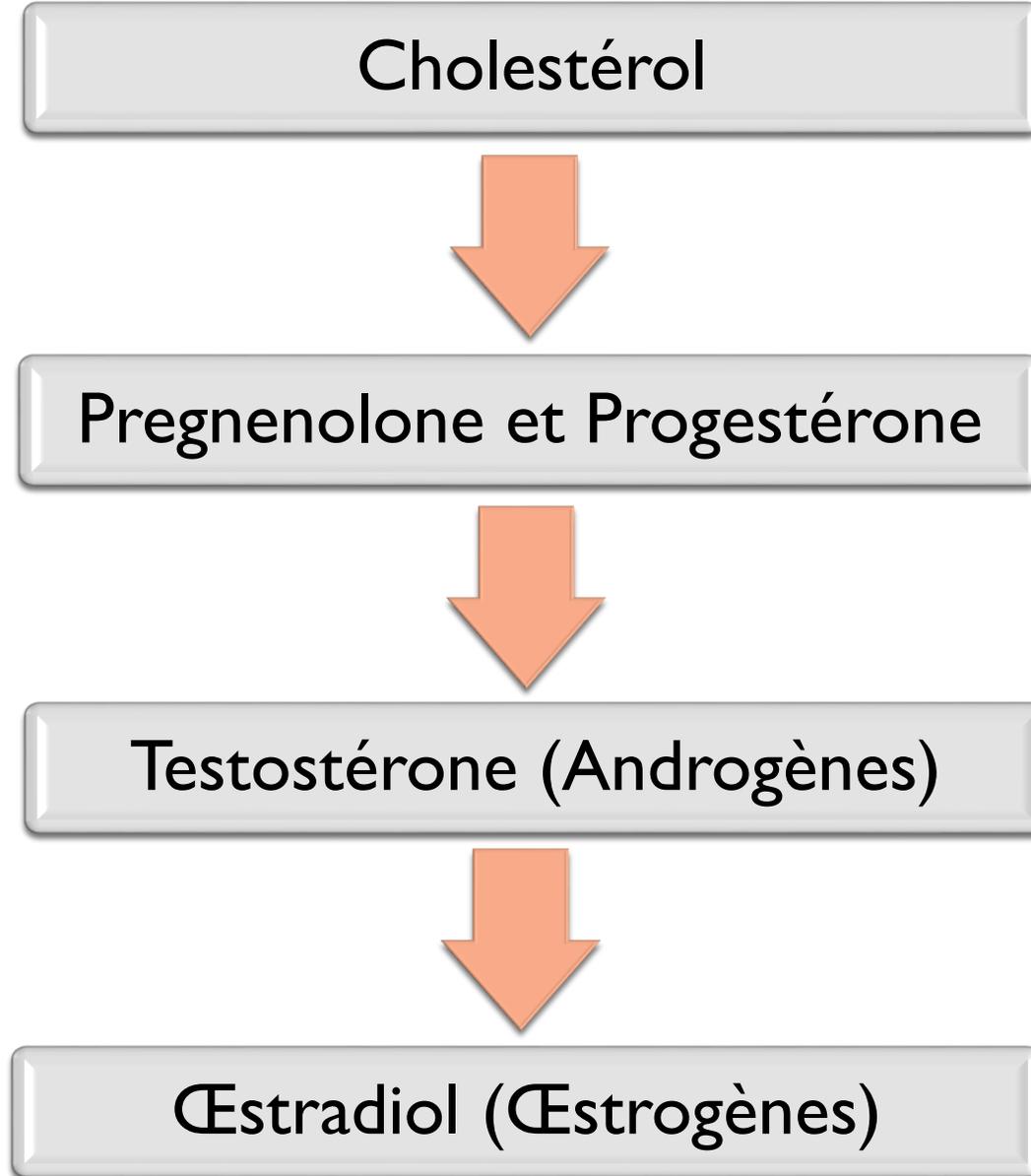
³Department of Human Genetics, David Geffen School of Medicine University of California, Los Angeles, CA 90095, USA

Cell Metabolism 25, June 6, 2017 © 2017 Elsevier Inc.



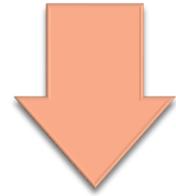
Hormones STEROÏDES: voies de synthèse



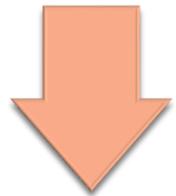


Testicules

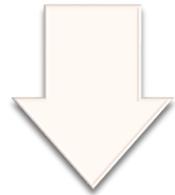
Cholestérol



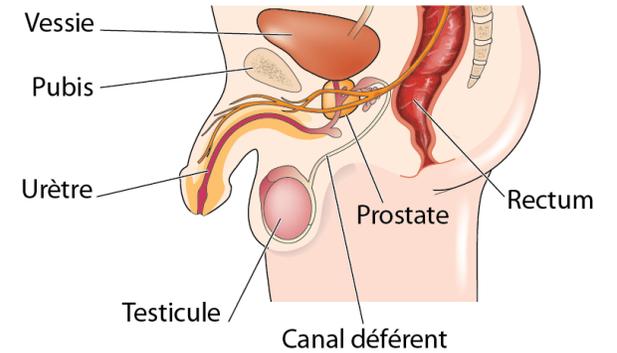
Pregnenolone et Progestérone



Testostérone (Androgènes)



Œstradiol (Œstrogènes)

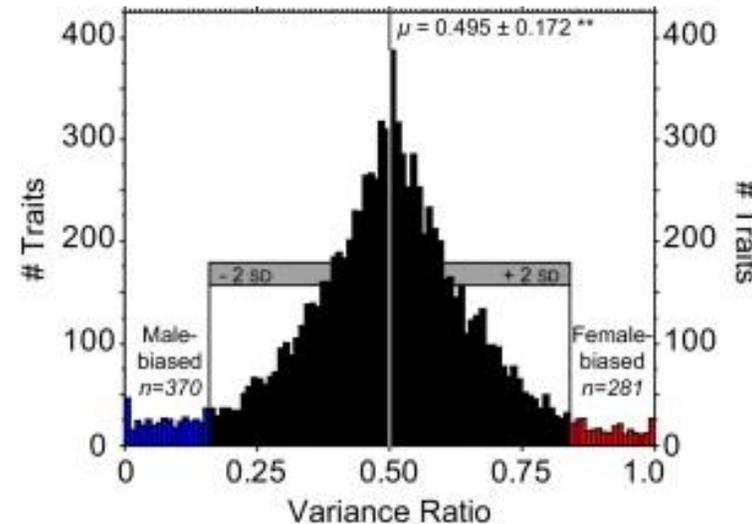
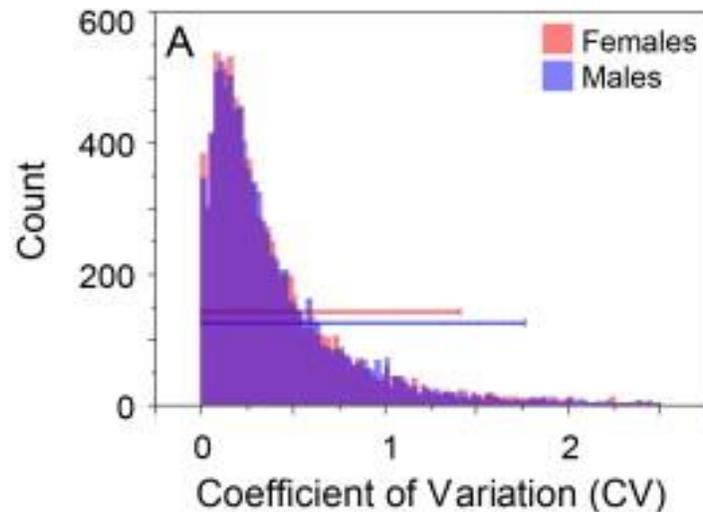


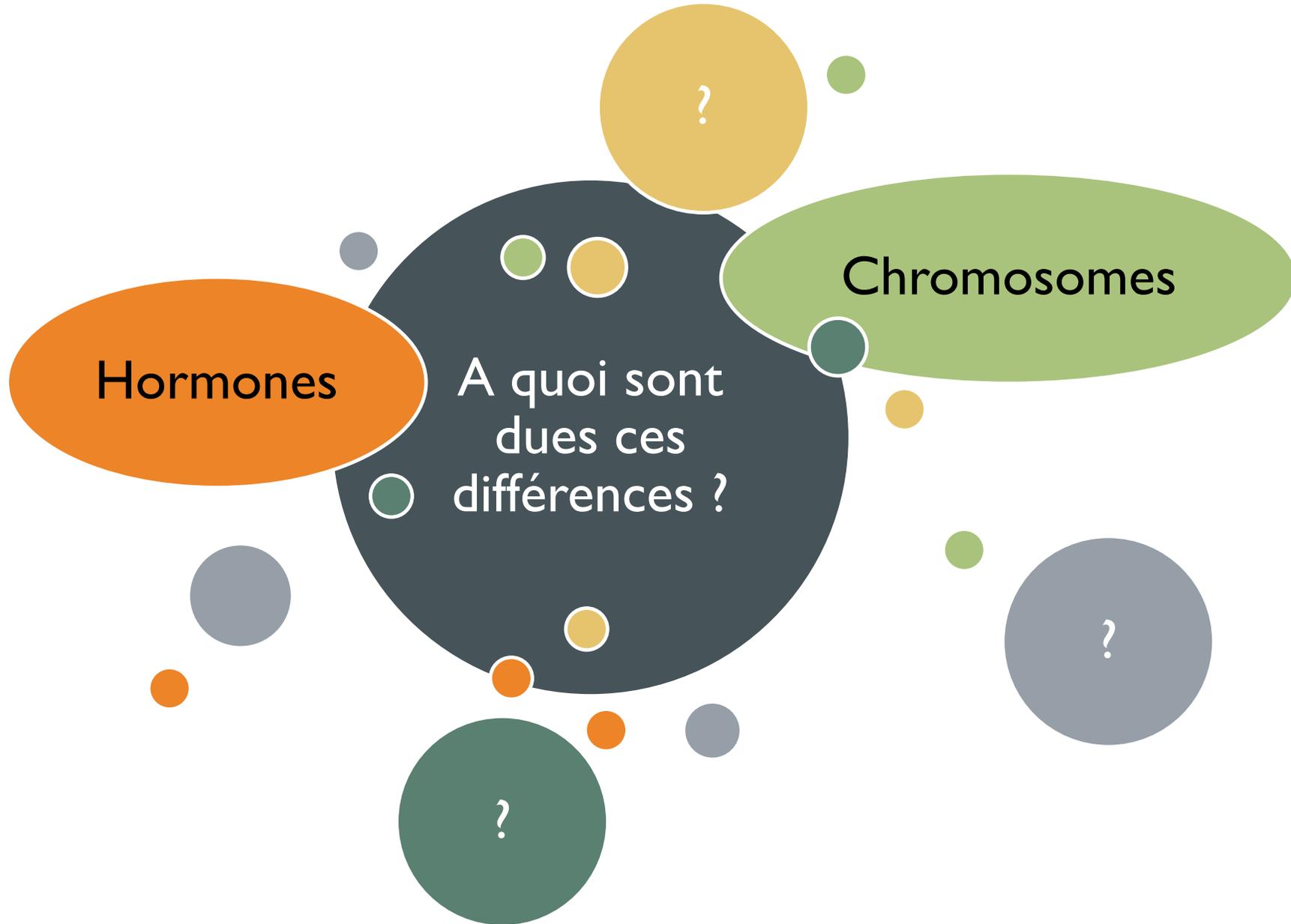
Les dogmes hormones sexuelles mâles et femelles ?

	Femmes	Hommes
Testostérone	0,3–3,0 nmol/L	8,2–34,6 nmol/L
Progestérone	0.47 - 85 nmol/L	0.47 - 1.57 nmol/L
Œstradiol	0,11 - 2,2 nmol/L	0,08 et 0,18 nmol/L
LH	2 – 75 UI/L	1-7 UI/L
FSH	2-30 UI/L	3-15 UI/L
Ocytocine	4,53 pg/mL	1,53 pg/mL
Prolactine	100 - 500 mUI/L	85 – 325 mU/L
AMH	2,45 et 5,95 ng/mL	3,1 à 5,3 ng/mL

Brian J. Prendergast^a, Kenneth G. Onishi^a, Irving Zucker^{b,c,*} 2014

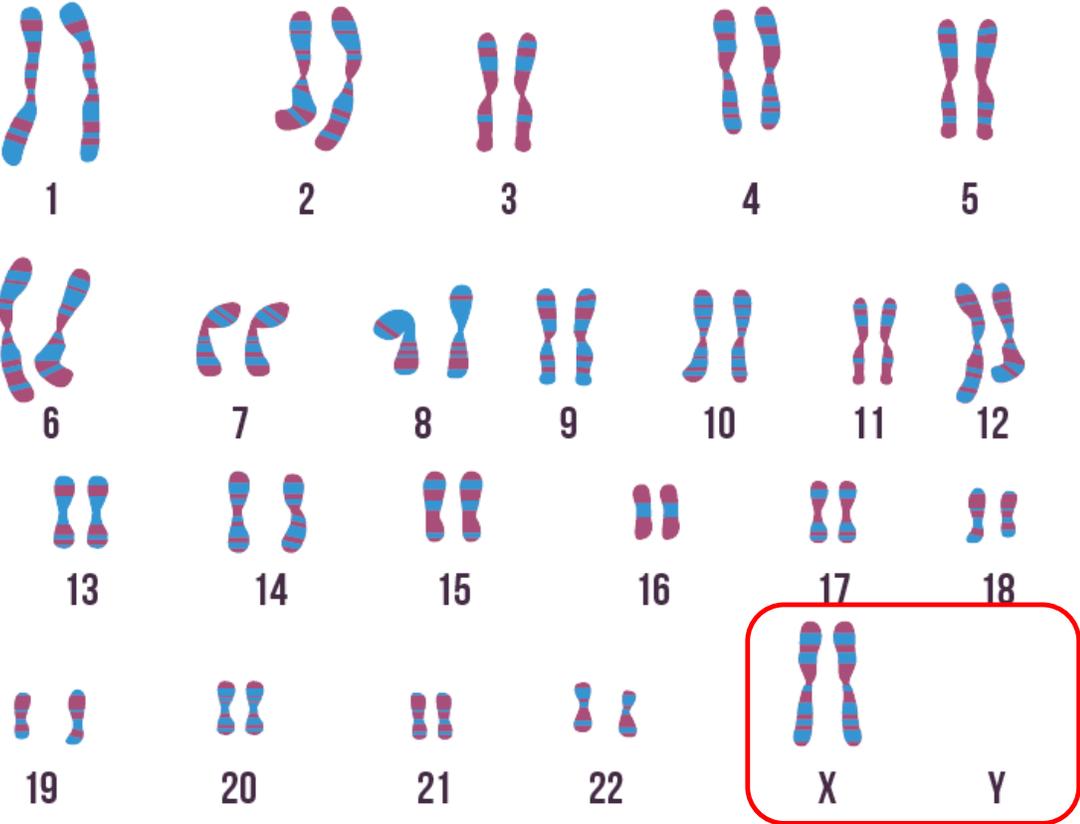
“In a meta-analysis of 293 articles, behavioral, morphological, physiological, and molecular traits were monitored in male mice and females tested without regard to estrous cycle stage; variability was not significantly greater in females than males for any endpoint and was substantially greater in males for several traits.”



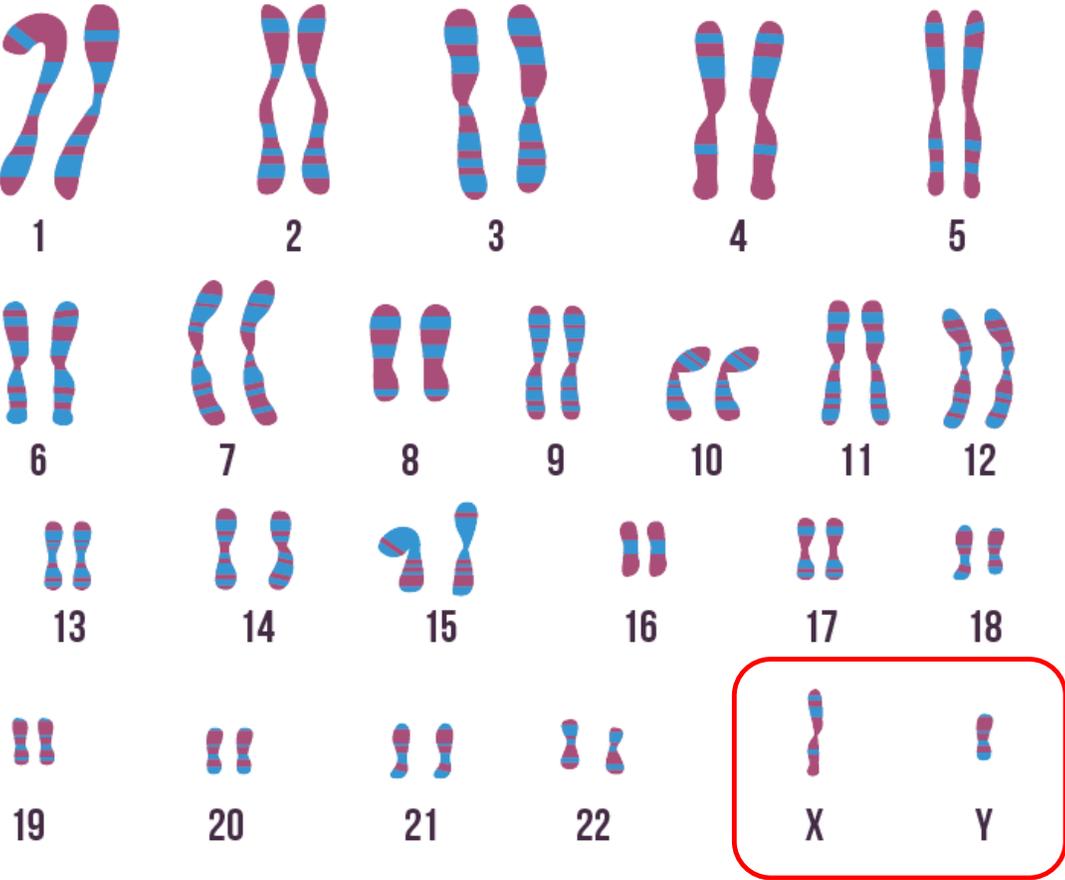


Les chromosomes X et Y

Femme



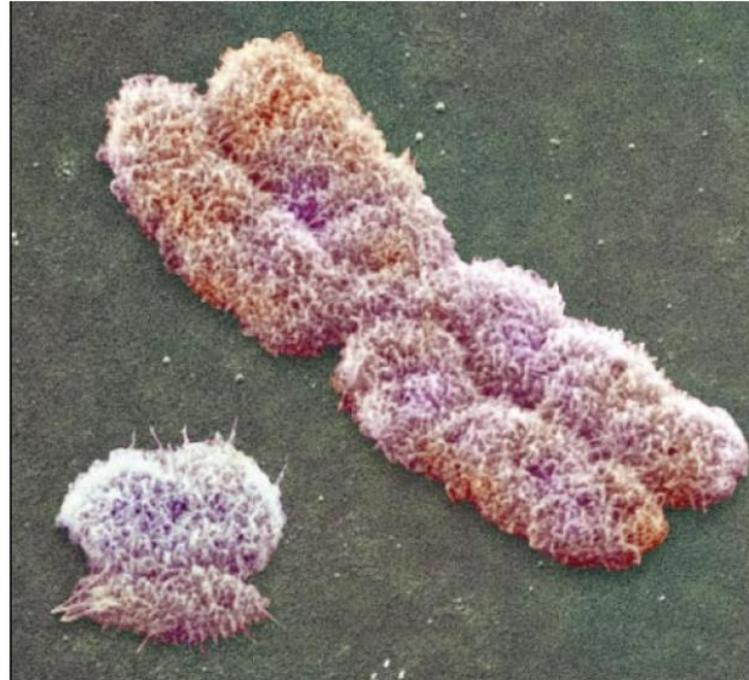
Homme



Que trouve-t-on sur ces chromosomes ?

Une centaine de gènes

- gène Sry de détermination testiculaire
- croissance et taille de l'individu
- quelques gènes de fonctions cellulaires basales



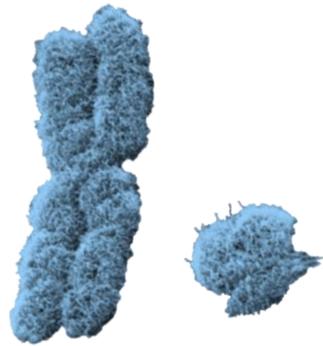
Y

X

Une millier de gènes

- de très nombreuses fonctions cellulaires
- souvent connus par des mutations entraînant des pathologies (hémophilie, daltonisme, myopathies)
- spermatogénèse et fertilité masculine

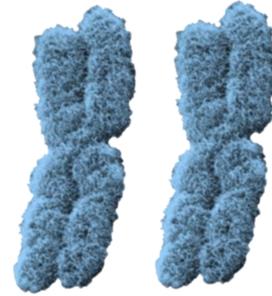
Homme



Xm

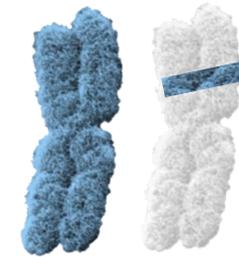
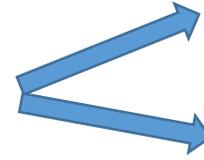
Yp

Femme
« Mécanisme de compensation de dose »

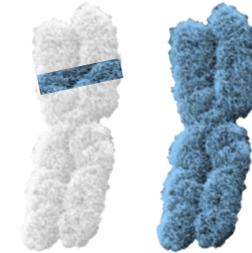


Xm

Xp

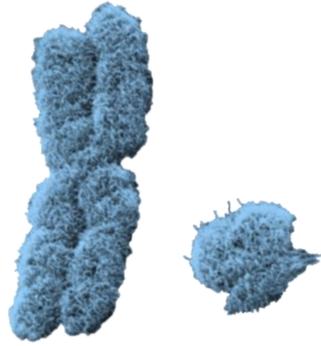


Xm



Xp

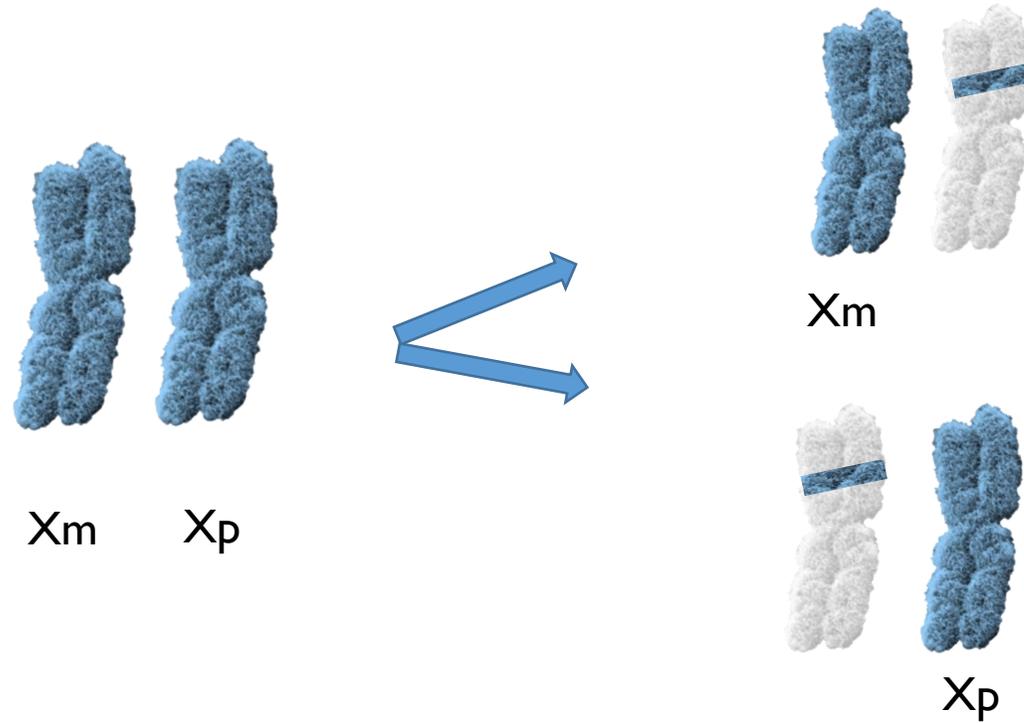
Homme



Mary F. Lyon
(1925-2014)

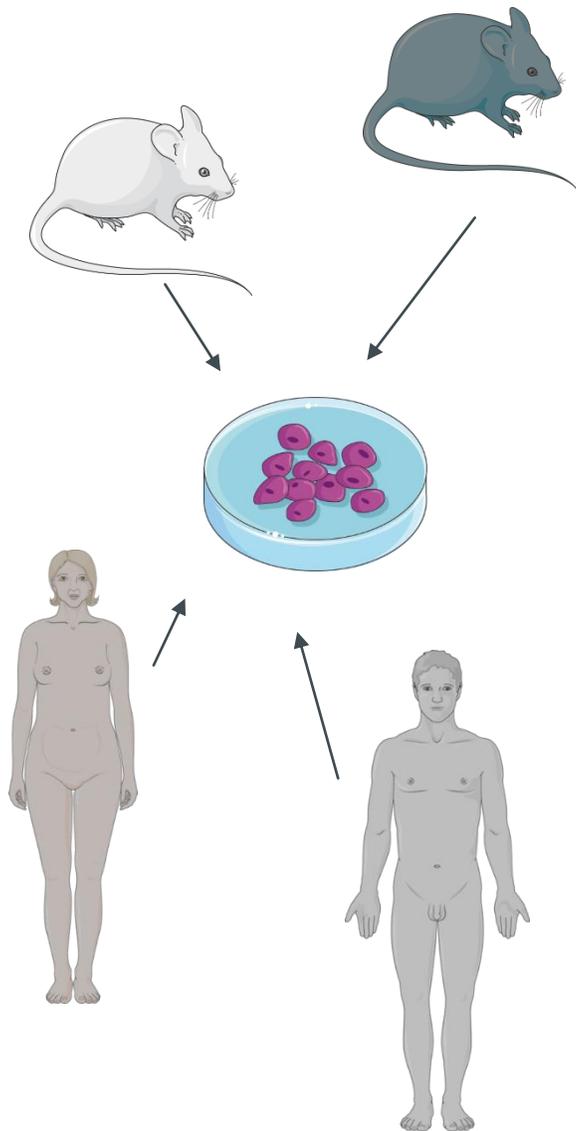
Femme

« Mécanisme de compensation de dose »



- Inactivation d'un des deux X (sauf 10-20% gènes)
- Pendant embryogénèse
- Aléatoire
- Sauf dans gamètes

Les cellules en culture ont aussi un sexe !



Am J Physiol Cell Physiol 306: C3–C18, 2014.
First published November 6, 2013; doi:10.1152/ajpcell.00281.2013.

Do you know the sex of your cells?

Kalpita Shah, Charles E. McCormack, and Neil A. Bradbury
Department of Physiology and Biophysics, Chicago Medical School, Rosalind Franklin University of Medicine and Science,
North Chicago, Illinois

Review

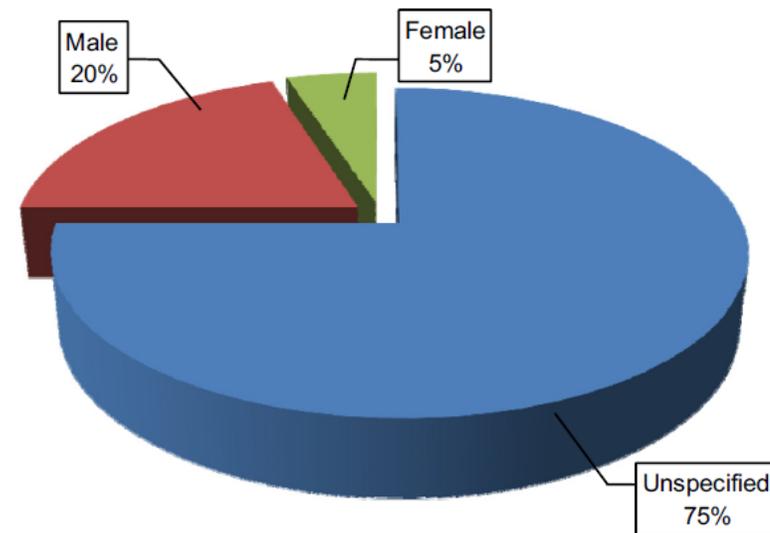


Fig. 1. Distribution of studies by sex, published in *AJP-Cell Physiology* in 2013. Shown is the percentage of articles describing the sex of cells derived from male subjects, female subjects, or unreported ($n = 100$ articles randomly selected from *AJP-Cell Physiology* manuscripts published in 2013).



Consider

Design studies that take sex into account, or explain why it isn't incorporated



Collect

Tabulate sex-based data



Characterize

Analyze sex-based data



Communicate

Report and publish sex-based data

The 4 Cs in integrating sex as a variable in biomedical research. Photo: US National Institutes of Health

Le site français du programme européen
pour la recherche et l'innovation



Eligibility: Gender Equality Plan



Award Criteria: Integration of the gender dimension



Ranking Criteria: Gender balance

In Horizon Europe research applications, gender-equality requirements comprise three aspects, encompassing host-institution eligibility, integration of the gender dimension in the research proposed, and gender balance in the research teams. Photo: N/A

- ❑ Combattre les idées reçues sur la complexité des études chez les femelles et leur variabilité. Trouver des bons modèles femelles pour certaines pathologies.
- ❑ Approche bio-sociale en médecine (Richardson S, 2015). Inégalités de santé ne doivent pas être rapportées qu'à des différences biologiques. Risque de conforter l'idée de différences inhérentes au sexe.
- ❑ Nécessité de réduire le « gender data gap »: déficit de données sur les femelles lors de la collecte des données scientifiques. En biologie comme dans d'autres disciplines scientifiques.

Merci de votre attention !

