Coups de cœur 2012

Ce qui influence la recherche fondamentale en hypertension au Québec

Le Mandat

- Donner un aperçu de la recherche d'impact en hypertension au cours de la dernière année
- Méthodologie
  - Appel aux récipiendaires du Prix du Jeune chercheur de la SQHA
  - Quelle est l'étude qui vous a le plus impressionné en 2012 et pourquoi?

Pierre Moreau

Les antihypertenseurs sont de mieux en mieux utilisés et probablement de plus en plus efficaces et sécuritaires (grâce à toute la recherche faite sur plusieurs décennies).

CMAJ RESEARCH

Changes in the rates of awareness, treatment and control of hypertension in Canada over the past two decades

Finlay A. McAlister MD MSc, Kathryn Wilkins MSc, Michel Joffres MD PhD, Frans H.H. Leenen MD PhD, George Fodor MD PhD, Marianne Gee MSc, Mark S. Tremblay PhD, Robin Walker MSc, Helen Johansen PhD, Norm Campbell MD

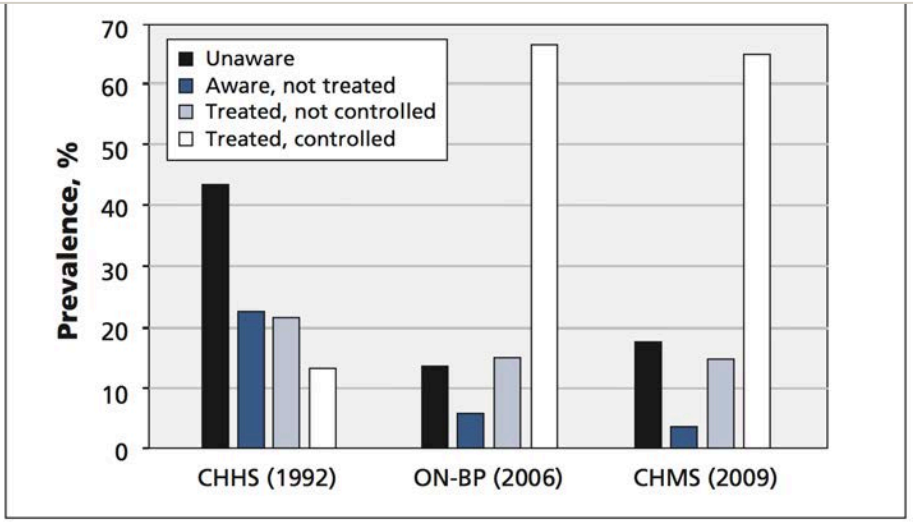


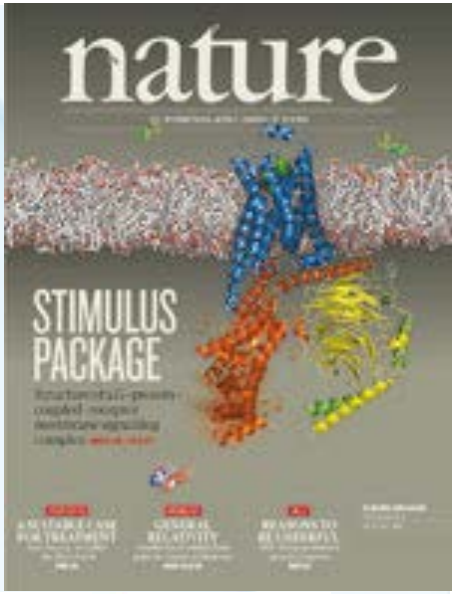
Figure 1: Rates of hypertension awareness, treatment and control among Canadians with hypertension from 1992 to 2009. CHHS = Canadian Heart Health Survey, ON-BP = Ontario Survey on the Prevalence and Control of Hypertension, CHMS = Canadian Health Measures Survey.

Pierre Moreau

IMPACT

Il reste encore de la place pour une grande proportion de la population, ce qui justifie de poursuivre les efforts en recherche dans le domaine de l'hypertension.

Michel Bouvier



Crystal structure of the β_2 adrenergic receptor–Gs protein complex

Søren G. F. Rasmussen[1,2]*, Brian T. DeVree[3]*, Yaozhong Zou[1], Andrew C. Kruse[1], Ka Young Chung[1], Tong Sun Kobilka[1], Foon Sun Thian[1], Pil Seok Chae[4], Els Pardon[5,6], Diane Calinski[3], Jesper M. Mathiesen[1], Syed T. A. Shah[7], Joseph A. Lyons[7], Martin Caffrey[7], Samuel H. Gellman[4], Jan Steyaert[5,6], Georgios Skiniotis[8], William I. Weis[1,9], Roger K. Sunahara[3] & Brian K. Kobilka[1]

G protein–coupled receptors (GPCRs) are responsible for the majority of cellular responses to hormones and neurotransmitters as well as the senses of sight, olfaction and taste. The paradigm of GPCR signalling is the activation of a heterotrimeric GTP binding protein (G protein) by an agonist–occupied receptor. The β_2 adrenergic receptor (β_2AR) activation of Gs, the stimulatory G protein for adenylyl cyclase, has long been a model system for GPCR signalling. Here we present the crystal structure of the active state ternary complex composed of agonist–occupied monomeric β_2AR and nucleotide–free Gs heterotrimer. The principal interactions between the β_2AR and Gs involve the amino– and carboxy–terminal α–helices of Gs, with conformational changes propagating to the nucleotide–binding pocket. The largest conformational changes in the β_2AR include a 14 Å outward movement at the cytoplasmic end of transmembrane segment 6 (TM6) and an α–helical extension of the cytoplasmic end of TM5. The most surprising observation is a major displacement of the α–helical domain of Gαs relative to the Ras–like GTPase domain. This crystal structure represents the first high–resolution view of transmembrane signalling by a GPCR.

Michel Bouvier

- La conformation active du récepteur β_2-adrénergique ne peut être atteinte qu'en présence de la protéine G_s qu'il active. L'agoniste seul n'est pas suffisant. Ceci indique que l'effecteur qui est activé par le récepteur contribue autant que le l'agoniste à la conformation active du récepteur. Des conformations actives distinctes pourraient être atteintes pour différents effecteurs engagés par le récepteur.

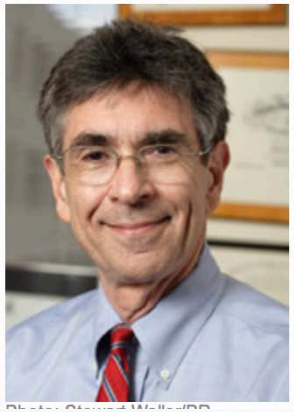
The Nobel Prize in Chemistry 2012
Robert J. Lefkowitz, Brian K. Kobilka

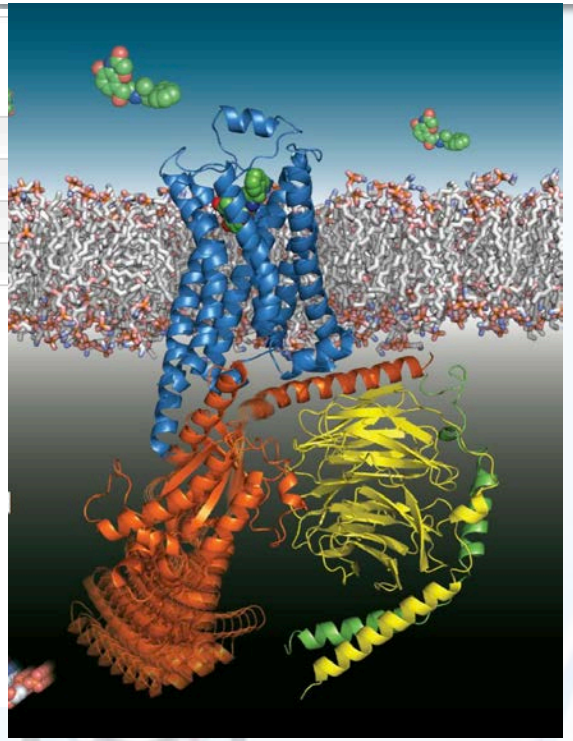
The Nobel Prize in Chemistry 2012

Nobel Prize Award Ceremony

Robert J. Lefkowitz

Brian K. Kobilka





Conformations différentes

Effets différents

Michel Bouvier

IMPACT

- Un grand potentiel pour le développememt de médicaments ayant un profil de sélectivité thérapeutique amélioré.

Anne-Monique Nuyt

Un papier qui lie le microbiome, le syndrome métabolique et qui pourrait pousser l'hypertension hors des remparts des maladies dites « non-transmissibles ».

Published in final edited form as:
Nature. ; 482(7384): 179–185. doi:10.1038/nature10809.

Inflammasome-mediated dysbiosis regulates progression of NAFLD and obesity

Jorge Henao-Mejia[1,*], **Eran Elinav**[1,*], **Cheng-Cheng Jin**[1,2,*], **Liming Hao**[3], **Wajahat Z. Mehal**[4], **Till Strowig**[1], **Christoph A. Thaiss**[1], **Andrew L. Kau**[5,6], **Stephanie C. Eisenbarth**[7], **Michael J. Jurczak**[4], **Joao-Paulo Camporez**[4], **Gerald I. Shulman**[4,9], **Jeffrey I. Gordon**[5], **Hal M. Hoffman**[8], and **Richard A. Flavell**[1,9,**]

[1]Department of Immunobiology, Yale University School of Medicine, New Haven, CT 06520

[2]Department of Cell Biology, Yale University School of Medicine, New Haven, CT 06520

[3]Department of Pathology, Yale University School of Medicine, New Haven, CT 06520

[4]Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520

[5]Center for Genome Sciences and Systems Biology, Washington University School of Medicine, St Louis, MO 63108

[6]Division of Allergy and Immunology, Department of Internal Medicine, Washington University School of Medicine, St Louis, MO 63108

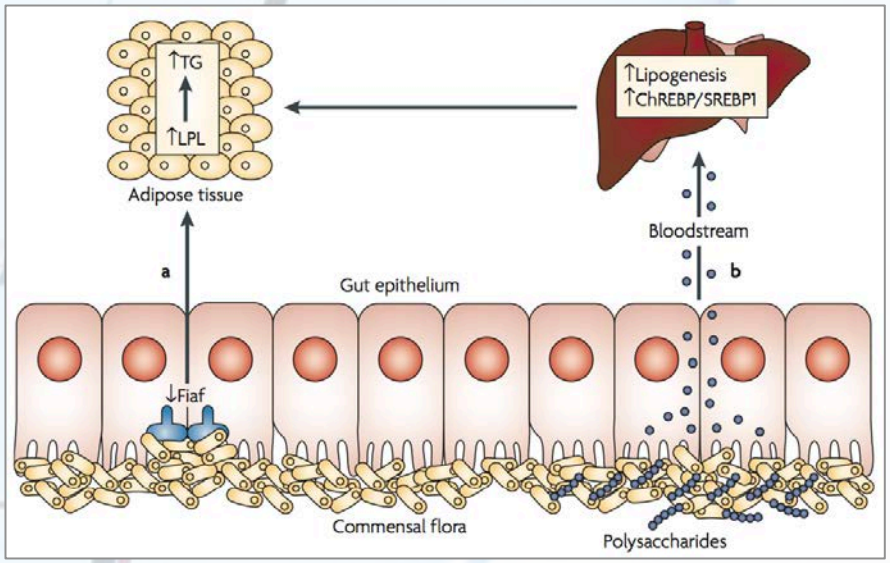
[7]Department of Laboratory Medicine, Yale University School of Medicine, New Haven, CT 06520

[8]Department of Pediatrics, Rady Children's Hospital San Diego, University of California at San Diego, La Jolla, CA 92093

[9]Howard Hughes Medical Institute

Abstract

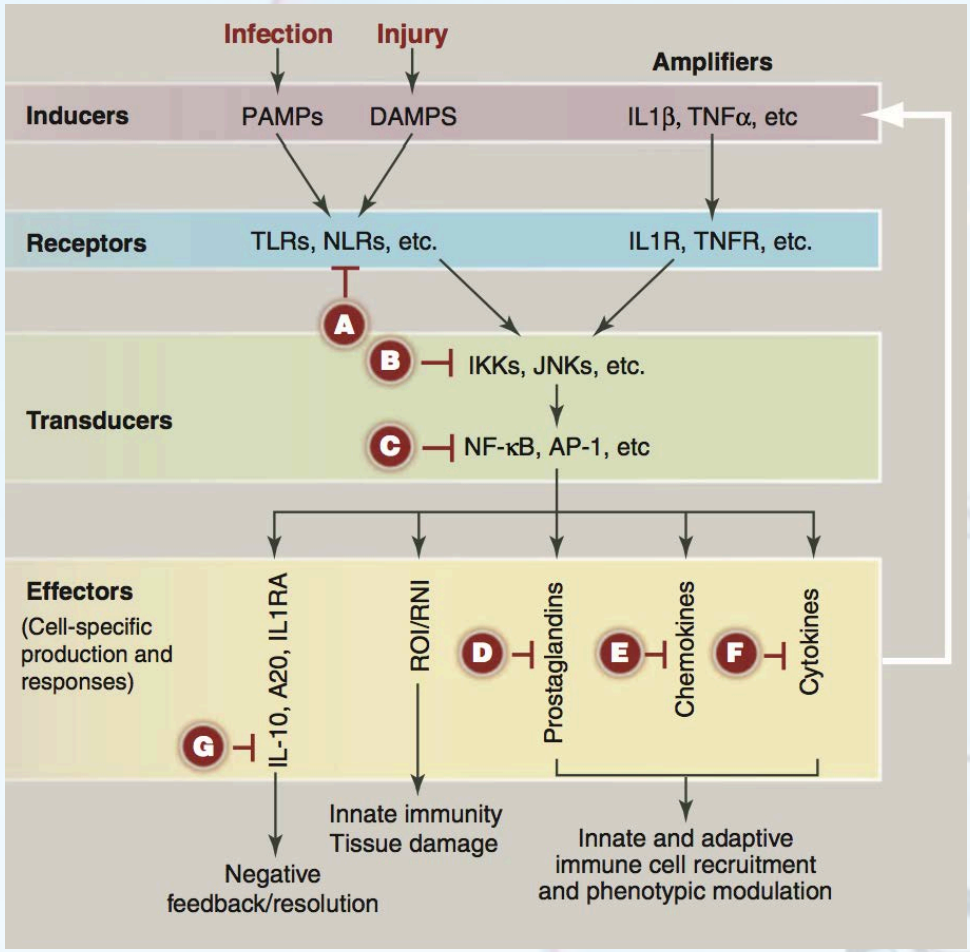
Non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome and the leading cause of chronic liver disease in the Western world. Twenty percent of NAFLD individuals develop chronic hepatic inflammation (non-alcoholic steatohepatitis, NASH) associated with cirrhosis, portal hypertension and hepatocellular carcinoma, yet causes of progression from NAFLD to NASH remain obscure. Here, we show that the NLRP6 and NLRP3 inflammasomes and the effector protein IL-18 negatively regulate NAFLD/NASH progression, as



Microbiome: flore commensale

Anne-Monique Nuyt

Un papier qui lie le microbiome, le syndrome métabolique et qui pourrait pousser l'hypertension hors des remparts des maladies dites « non-transmissibles ».



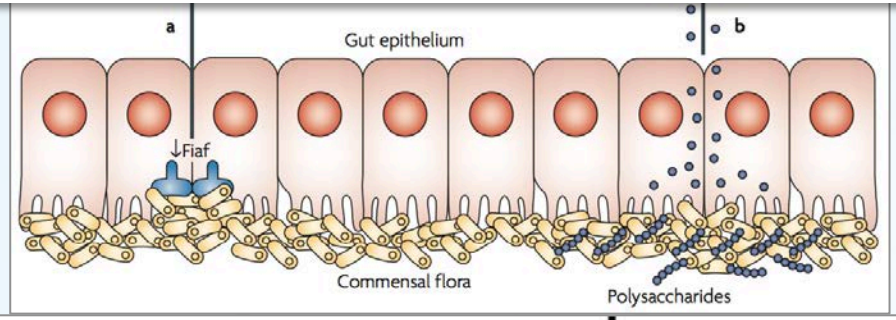
PAMPs: pathogen- associated molecular patterns

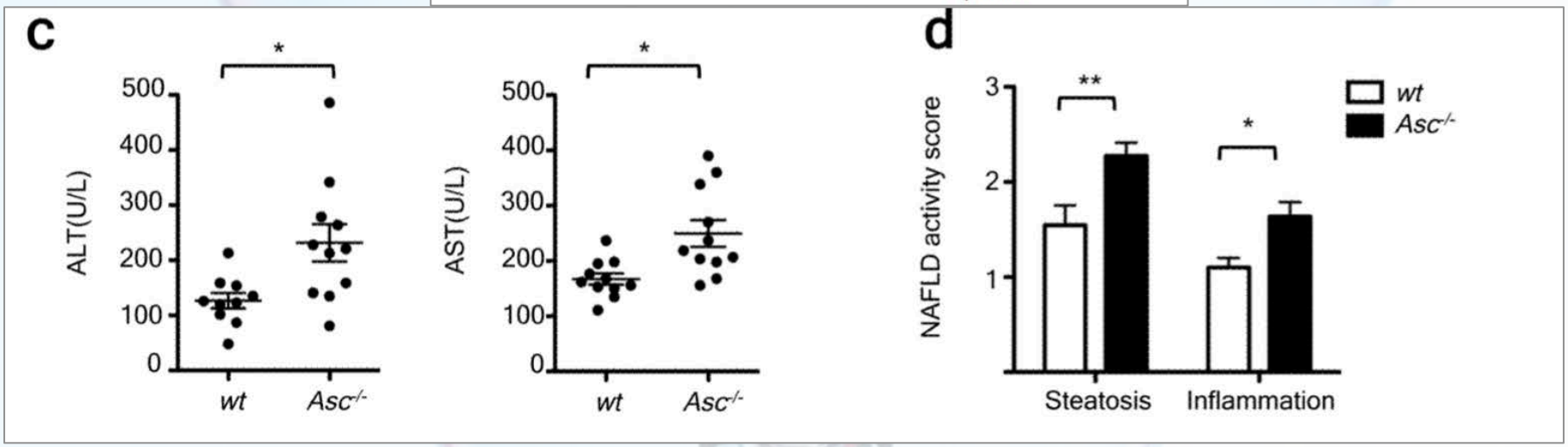
DAMPS: damage-associated molecular patterns

	Example Target(s)	Example Drug(s)
A	TLRs, inflammasome	Neutralizing Ab (TLRs), Caspase I inhibitor
B	IKK, JNK, JAK, MAPK, etc	Small molecule kinase inhibitors
C	NFκB, AP-1, 'Epigenome'	GR ligands, HMT/HDM inhibitors
D	Cox2	NSAIDs
E	MCP-1/Ccr2	Neutralizing Abs, small molecule inhibitors
F	TNFα, IL1β	Neutralizing Abs
G	Negative feedback/ resolution	Resolution enhancers (e.g., resolvins)

Anne-Monique Nuyt

- Si on invalide l'inflammasome ($Asc^{-/-}$)
  - On altère significativement la flore du mirobiome avec moins de lactobacilles bénéfiques et plus de bactéroidètes néfastes
  - on augmente la sévérité de la stéatose hépatique (*NAFLD: non alcoholic fatty liver disease*) chez les souris nourries avec une diète riche en gras.

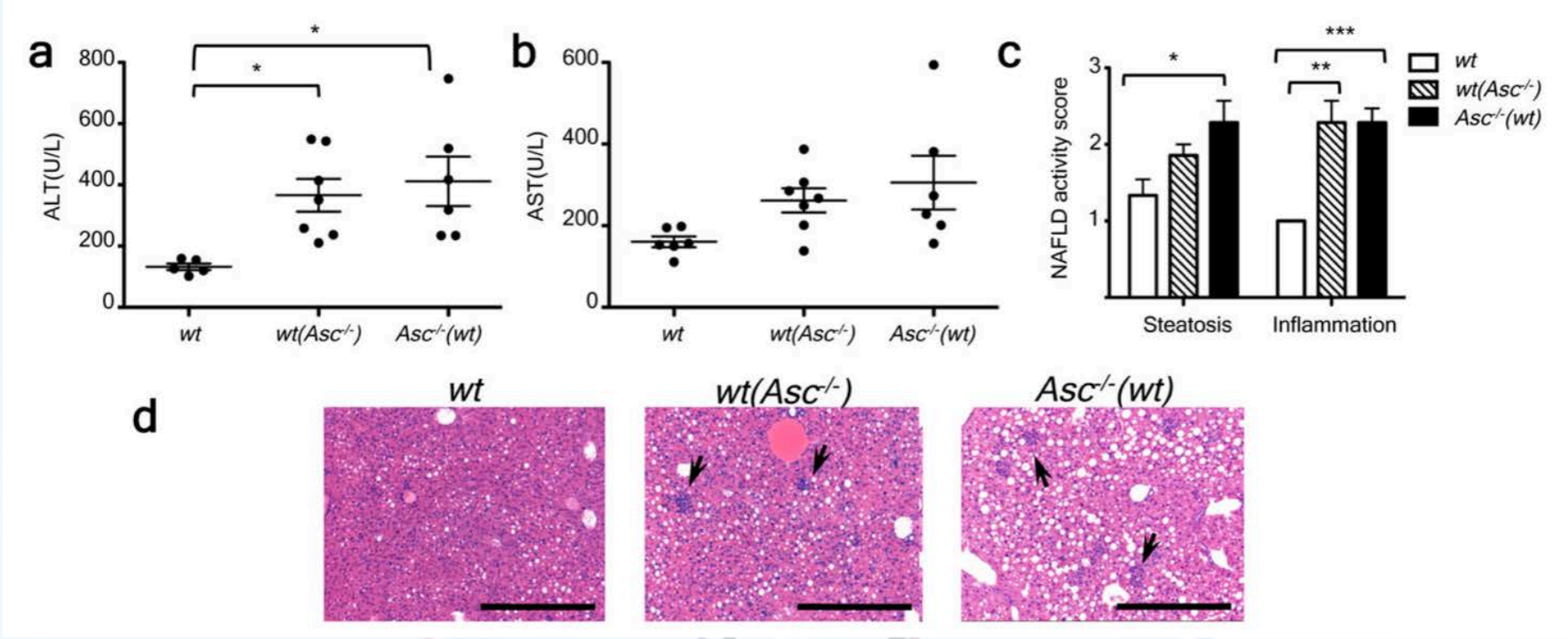




Anne-Monique Nuyt

L'hypersensibilité à la diète riche en gras est transmissible!

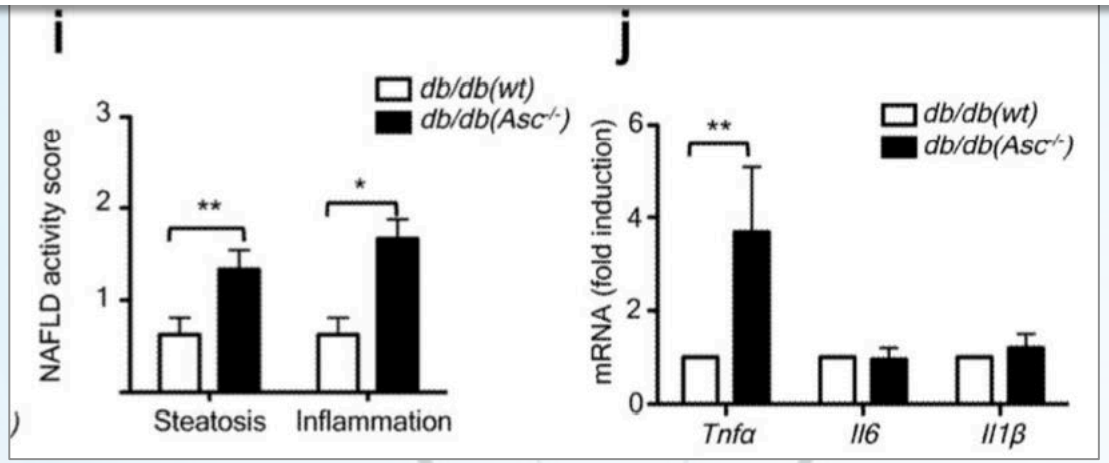
Les souris sauvage (WT) sont à risque de développer la stéatose hépatique induite par la diète si elles sont maintenues dans la même cage que les souris Asc$^{-/-}$.

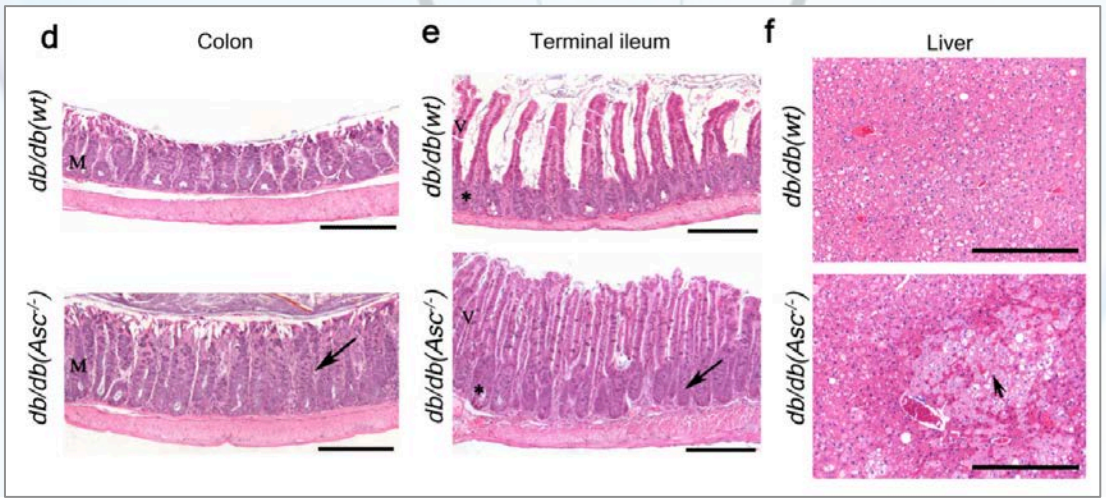


Anne-Monique Nuyt

On savait que les souris déficiente en récepteur de leptine (db/db) développe spontanément un stage précoce de la maladie hépatique, même avec une diète normale.

Si les souris db/db partage leur vie avec des souris $Asc^{-/-}$, elles aussi adoptent le microbiome et la sensibilité hépatique des souris $Asc^{-/-}$.





Anne-Monique Nuyt

IMPACT

- Ultimement, il faudra peut-être faire disparaitre cette ségrégation entre les maladies transmissibles et non-transmissibles.
- Notre microbiome pourrait nous caractériser autant que nos gènes.

Marc Servant

Conditional Targeting of Tumor Necrosis Factor Receptor–Associated Factor 6 Reveals Opposing Functions of Toll-Like Receptor Signaling in Endothelial and Myeloid Cells in a Mouse Model of Atherosclerosis

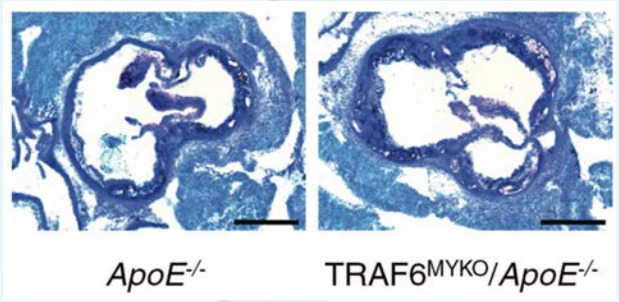
Apostolos Polykratis, PhD; Geert van Loo, PhD; Sofia Xanthoulea, PhD;
Martin Hellmich, PhD; Manolis Pasparakis, PhD

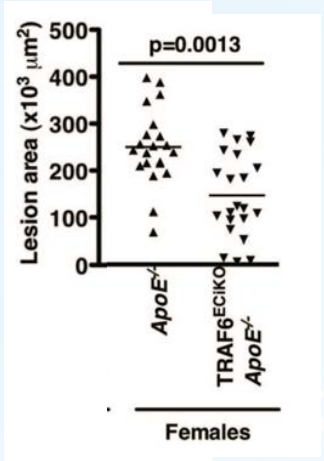
Circulation. 2012; 126: 1739-1751

- Certains récepteurs de surface appartenant à la famille des TLR reconnaissent des déterminants moléculaires des pathogènes (ex: LPS) conduisant à une réponse inflammatoire essentielle pour la prise en charge de l'envahisseur.
- Les lipides modifiés, peuvent engendrer des réponses inflammatoires via ces récepteurs et induire l'apparition de plaques athéromateuses.
- Un des effecteurs essentiels des TLR et de l'inflammasome est la protéine TRAF6.
- La présente étude visait donc à vérifier et comprendre le rôle de TRAF6 dans l'athérogenèse.

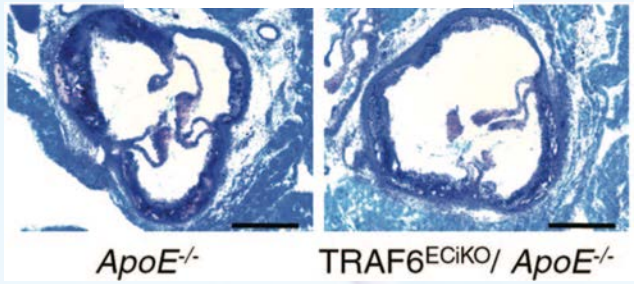
Marc Servant

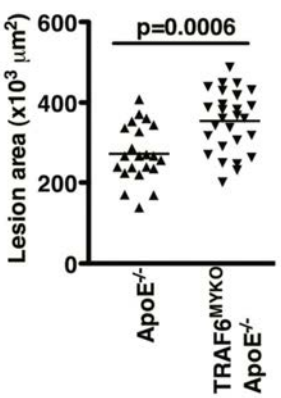
A. Endo TRAF6 KO



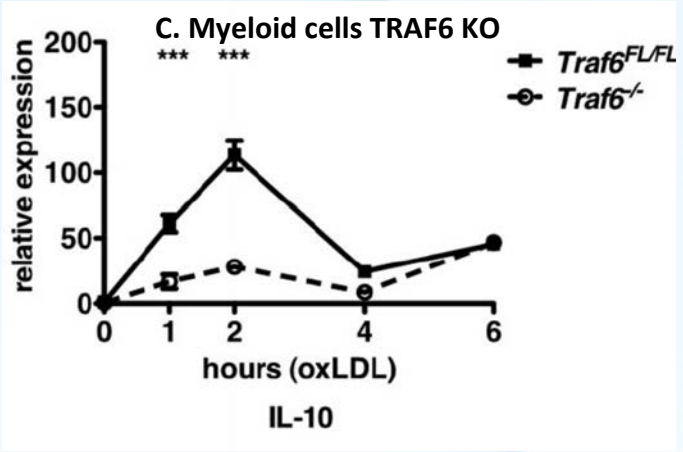


B. Myeloid cells TRAF6 KO

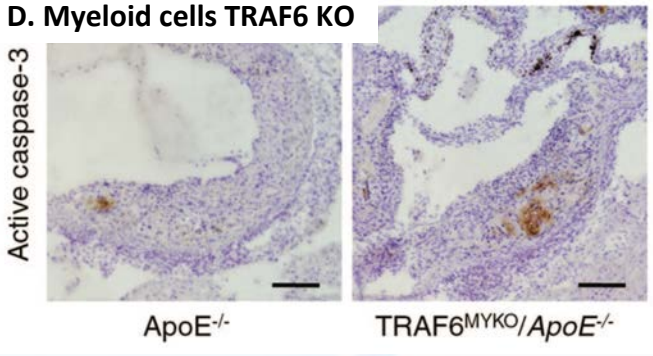




C. Myeloid cells TRAF6 KO



D. Myeloid cells TRAF6 KO



Le *knock-down* spécifique de TRAF6 dans l'endothélium diminue le développement de la plaque athéromateuse dans le modèle ApoE-/- sous diète riche **(A)**. Cependant, la délétion de TRAF6 au niveau ces cellules myléoïdes exacerbe l'apparition des plaques **(B)**, un effet en partie dû à l'incapacité de ces cellules à produire une cytokine anti-inflammatoire en réponse au LDLoxydé **(C)** et une augmentation de la sensibilité de ces cellules à l'apoptose **(D)**.

Marc Servant

IMPACT

- Cette étude interroge les effets bénéfiques d'une utilisation future des antagonistes des TLR de façon systémique comme agents anti-athérosclérotique chez l'humain.
- Une approche ciblant spécifiquement les cellules endothéliales auraient un meilleur potentiel thérapeutique.

Yan Burelle

LETTER *Nature* **485**, 179–180 (10 May 2012)

doi:10.1038/nature10992

Mitochondrial DNA that escapes from autophagy causes inflammation and heart failure

Takafumi Oka[1], Shungo Hikoso[1], Osamu Yamaguchi[1], Manabu Taneike[1,2], Toshihiro Takeda[1], Takahito Tamai[1], Jota Oyabu[1], Tomokazu Murakawa[1], Hiroyuki Nakayama[3], Kazuhiko Nishida[1,2], Shizuo Akira[4,5], Akitsugu Yamamoto[6], Issei Komuro[1] & Kinya Otsu[1,2]

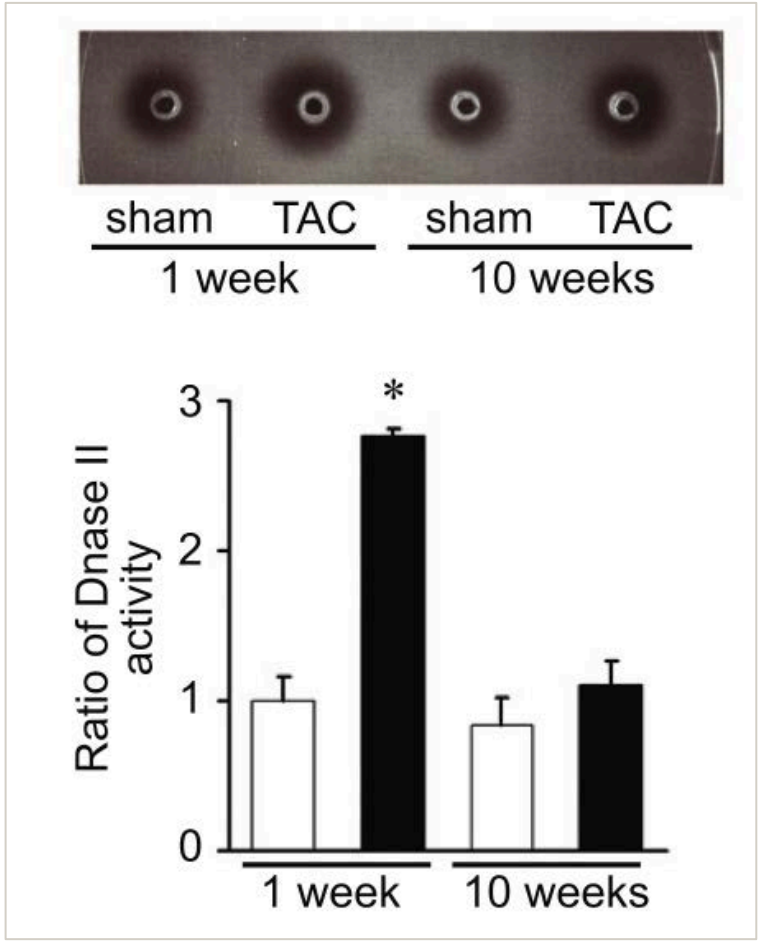
Dans cette étude, les auteurs démontrent que:

1. L'expression de la DNase II, une enzyme lysosomiale dégradant d'ADN, est augmentée dans le cœur au cours du remodelage post-infarctus.

2. L'ablation de la DNase II entraîne une incapacité à dégrader l'ADN mitochondrial normalement livrée aux lysosomes.

3. L'ADN mitochondrial est reconnu comme de l'ADN bactérien par TLR9 induisant ainsi une réponse inflammatoire qui précipite l'insuffisance cardiaque.

Augmentation de l'activité de la Dnase II et accumulation d'ADN dans les autophasosomes et lysosomes



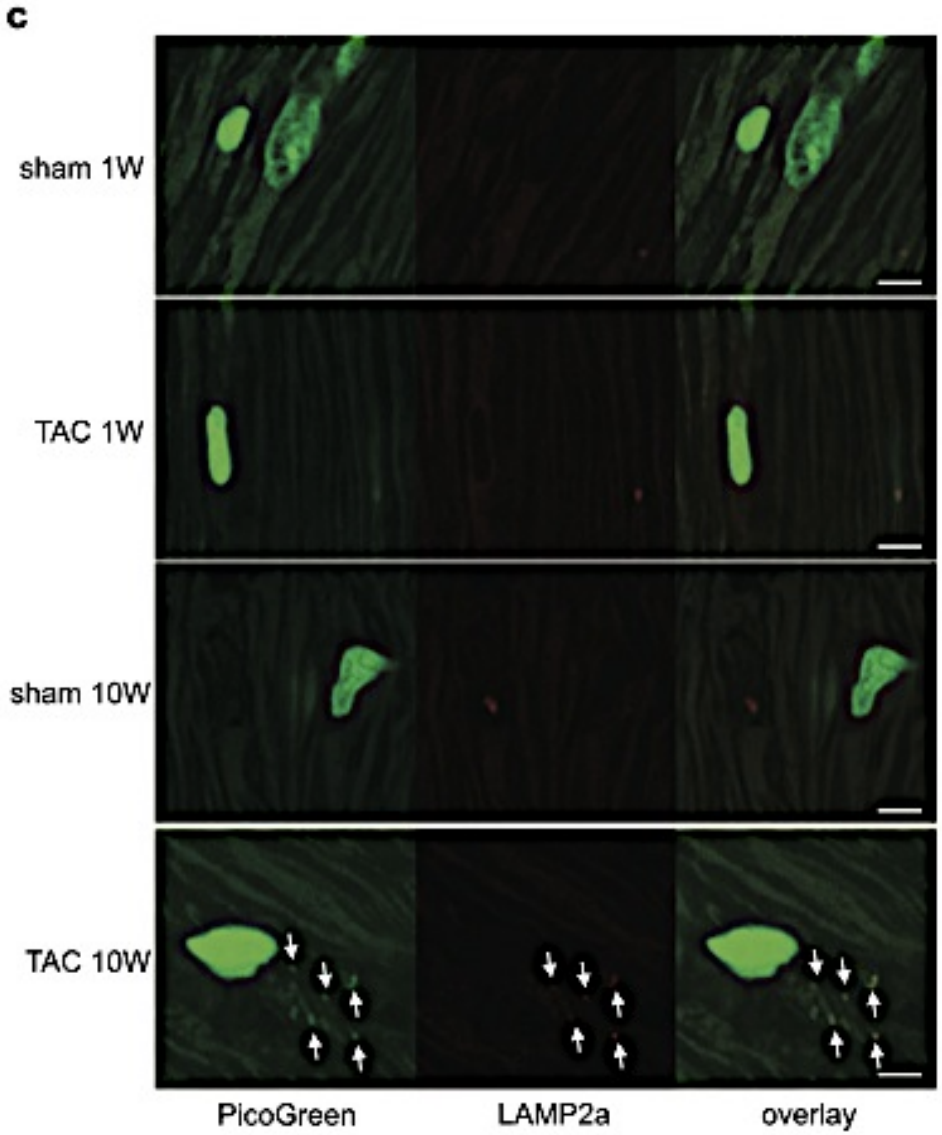
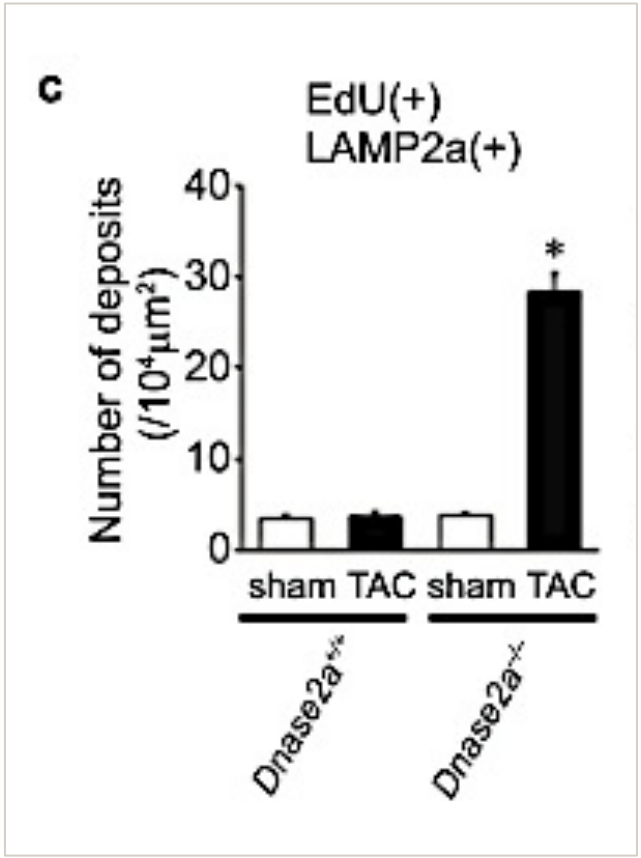
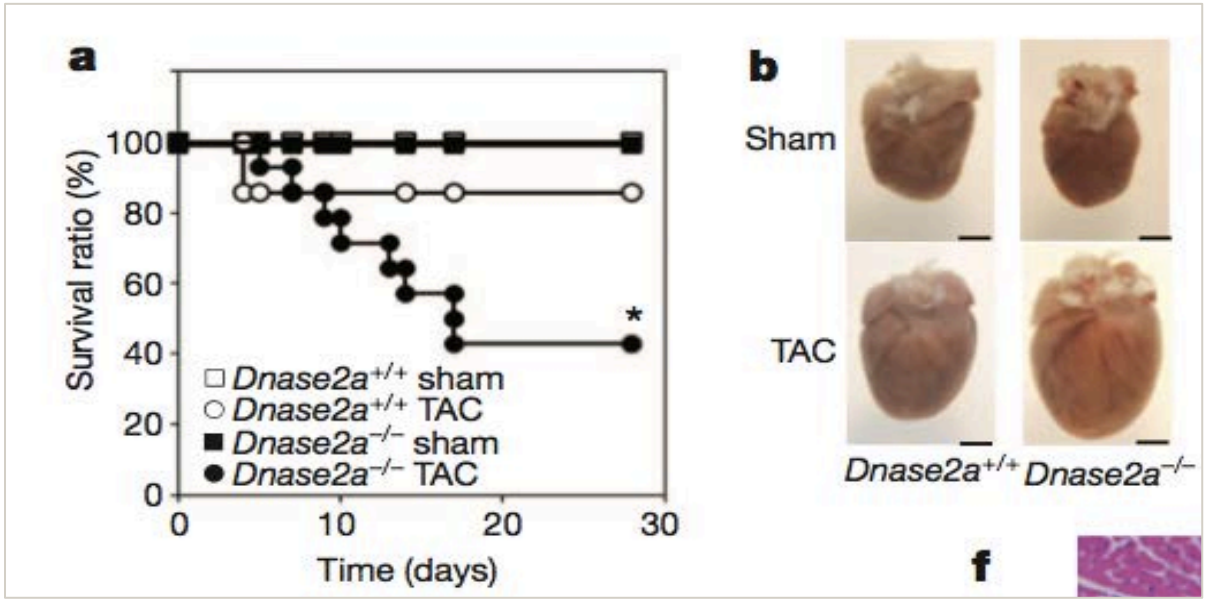


Figure S1

L'ablation de la Dnase II entraine une accumulation d'ADN mitochondrial dans les autophagosomes/lysosomes et précipite l'insuffisance cardiaque





L’ablation de TLR9 diminue l’inflammation et améliore le phénotype cardiaque chez les souris déficientes en DNase II.

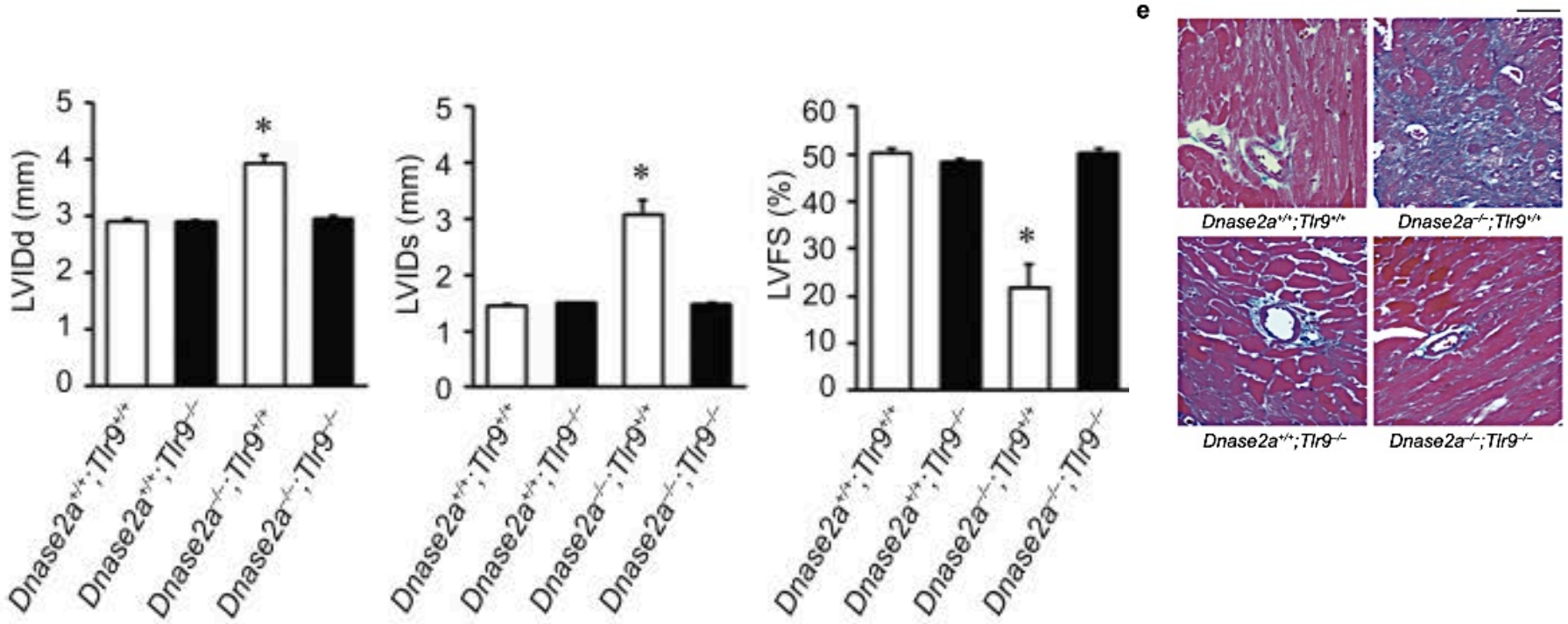


Figure S9

Yan Burelle

IMPACT

L'inflammation chronique et les anomalies métaboliques couplées à des dysfonctions mitochondriales sont des phénomènes fréquemment observés dans plusieurs états pathologiques. Cet article démontre de belle façon le rôle pro-inflammatoire de l'ADNmt qui peux se retrouver en circulation dans bon nombre de ces états.

Mohsen Agharazii

http://www.kidney-international.org original article

see commentary on page 1149

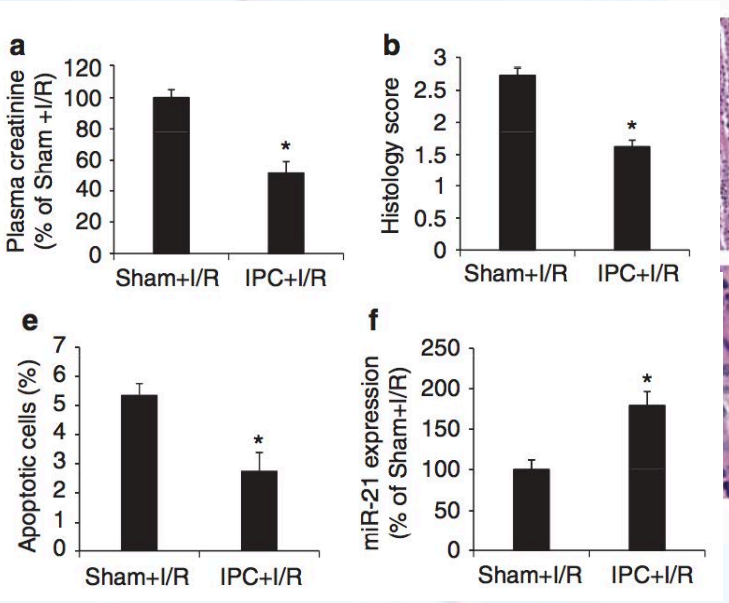
Delayed ischemic preconditioning contributes to renal protection by upregulation of miR-21

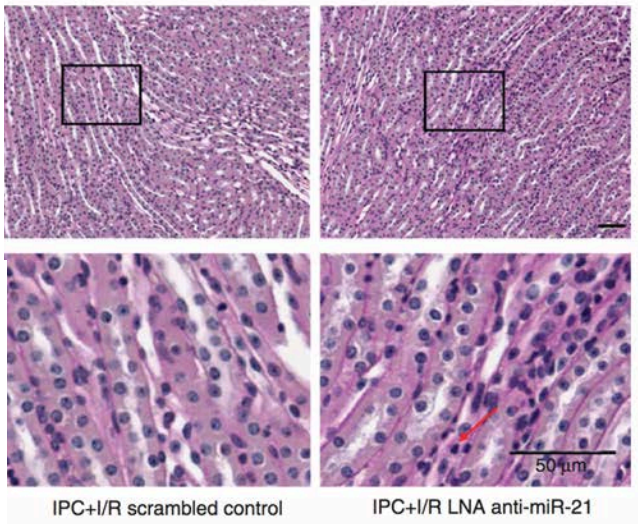
Xialian Xu[1,2], Alison J. Kriegel[2], Yong Liu[2], Kristie Usa[2], Domagoj Mladinov[2], Hong Liu[1], Yi Fang[1], Xiaoqiang Ding[1] and Mingyu Liang[2]

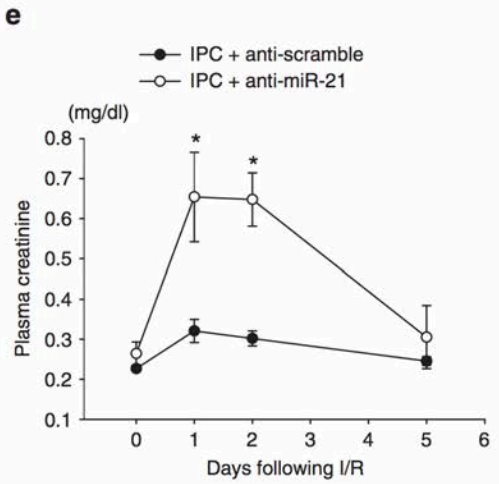
[1]Division of Nephrology, Shanghai Medical College, Fudan University, Zhongshan Hospital, Shanghai, PR China and [2]Department of Physiology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

Mohsen Agharazii

- Le préconditionnement ischémique du rein
  - protège le rein des dommages causées par une iscémie prolongée ischémiques (histologie, apoptose, et clairance de la créatinine)
  - induit l'expression du microARN-21
- L'inhibition (knock-down) du microARN-21 prévient l'effet protecteur du préconditionnement ischémique







Mohsen Agharazii

IMPACT

- Un autre exemple du rôle émergent des microRNA en physiopathologie et en clinique.
- Le concept de « preconditionning » est applicable dans plusieurs contextes
  - résection partielle d'une tumeur au niveau rein (nécessitant une ischémie prévisible de tout le rein pendant la chirurgie)
  - greffe rénale avec une situation ischémique prévisible.

Guy Rousseau

- On sait que le tissu gras des individus obèses est un site inflammatoire (niveaux faibles mais chroniques).
- On sait aussi que les acides gras oméga-3 génèrent des métabolites avec des effets anti-inflammatoires: les résolvines et lipoxines.
- Quel est le role de ces métabolites dans la pathologie inflammatoire adipeuse dans l'obésité?

Published July 27, 2012, doi:10.4049/jimmunol.1201272

The Journal of Immunology

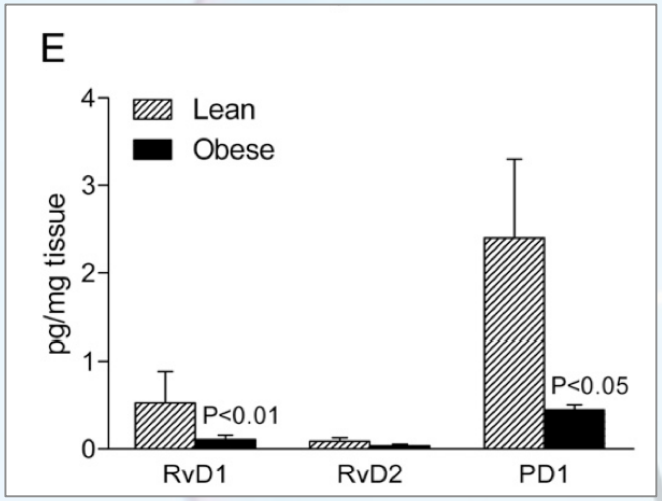
Resolvin D1 and Resolvin D2 Govern Local Inflammatory Tone in Obese Fat

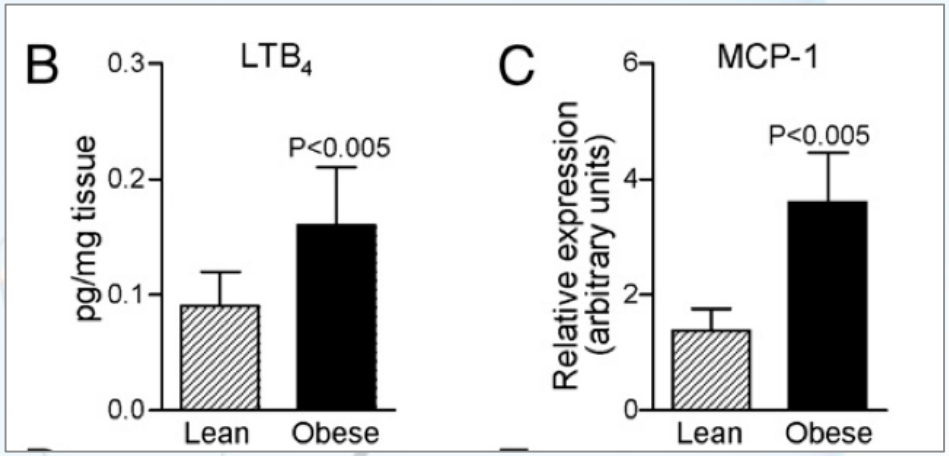
Joan Clària,[1] Jesmond Dalli, Stephanie Yacoubian, Fei Gao, and Charles N. Serhan

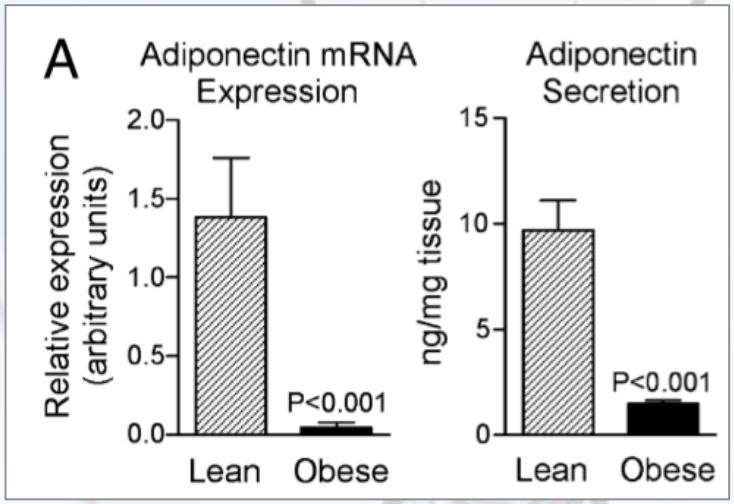
The unprecedented increase in the prevalence of obesity and obesity-related disorders is causally linked to a chronic state of low-grade inflammation in adipose tissue. Timely resolution of inflammation and return of this tissue to homeostasis are key to reducing obesity-induced metabolic dysfunctions. In this study, with inflamed adipose, we investigated the biosynthesis, conversion, and actions of Resolvins D1 (RvD1, 7*S*,8*R*,17*S*-trihydroxy-4*Z*,9*E*,11*E*,13*Z*,15*E*,19*Z*-docosahexaenoic acid) and D2 (RvD2, 7*S*,16*R*,17*S*-trihydroxy-4*Z*,8*E*,10*Z*,12*E*,14*E*,19*Z*-docosahexaenoic acid), potent anti-inflammatory and proresolving lipid mediators (LMs), and their ability to regulate monocyte interactions with adipocytes. Lipid mediator-metabololipidomics identified RvD1 and RvD2 from endogenous sources in human and mouse adipose tissues. We also identified proresolving receptors (i.e., ALX/FPR2, ChemR23, and GPR32) in these tissues. Compared with lean tissue, obese adipose showed a deficit of these endogenous anti-inflammatory signals. With inflamed obese adipose tissue, RvD1 and RvD2 each rescued impaired expression and secretion of adiponectin in a time- and concentration-dependent manner as well as decreasing proinflammatory adipokine production including leptin, TNF-α, IL-6, and IL-1β. RvD1 and RvD2 each reduced MCP-1 and leukotriene B_4-stimulated monocyte adhesion to adipocytes and their trans-adipose migration. Adipose tissue rapidly converted both resolvins (Rvs) to novel oxo-Rvs. RvD2 was enzymatically converted to 7-oxo-RvD2 as its major metabolic route that retained adipose-directed RvD2 actions. These results indicate, in adipose, D-series Rvs (RvD1 and RvD2) are potent proresolving mediators that counteract both local adipokine production and monocyte accumulation in obesity-induced adipose inflammation. *The Journal of Immunology*, 2012, 189: 000–000.

Guy Rousseau

Le tissu adipeux de souris obèses montre un déficit de médiateurs anti-inflammatoires (résolvines) et une accumulation de médiateurs pro-inflammatoires (leucotriènes B4 et monocyte chemoattractant protein-1).

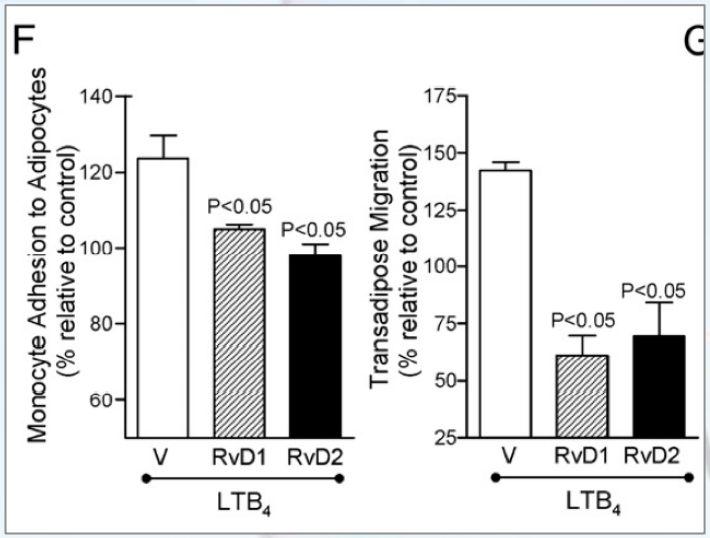


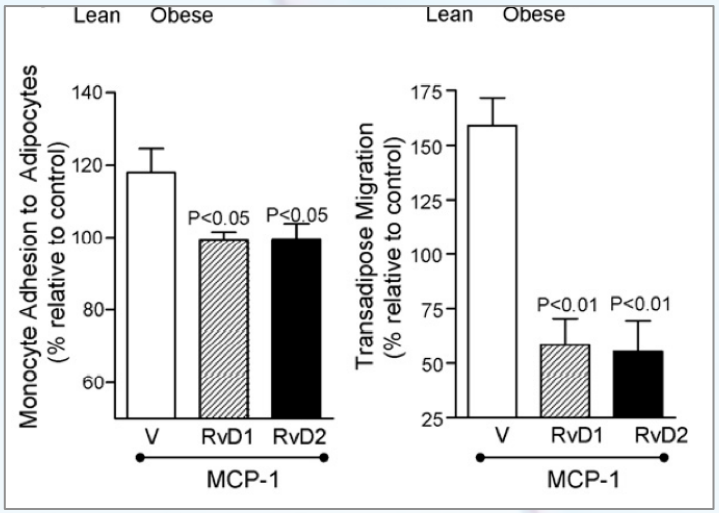


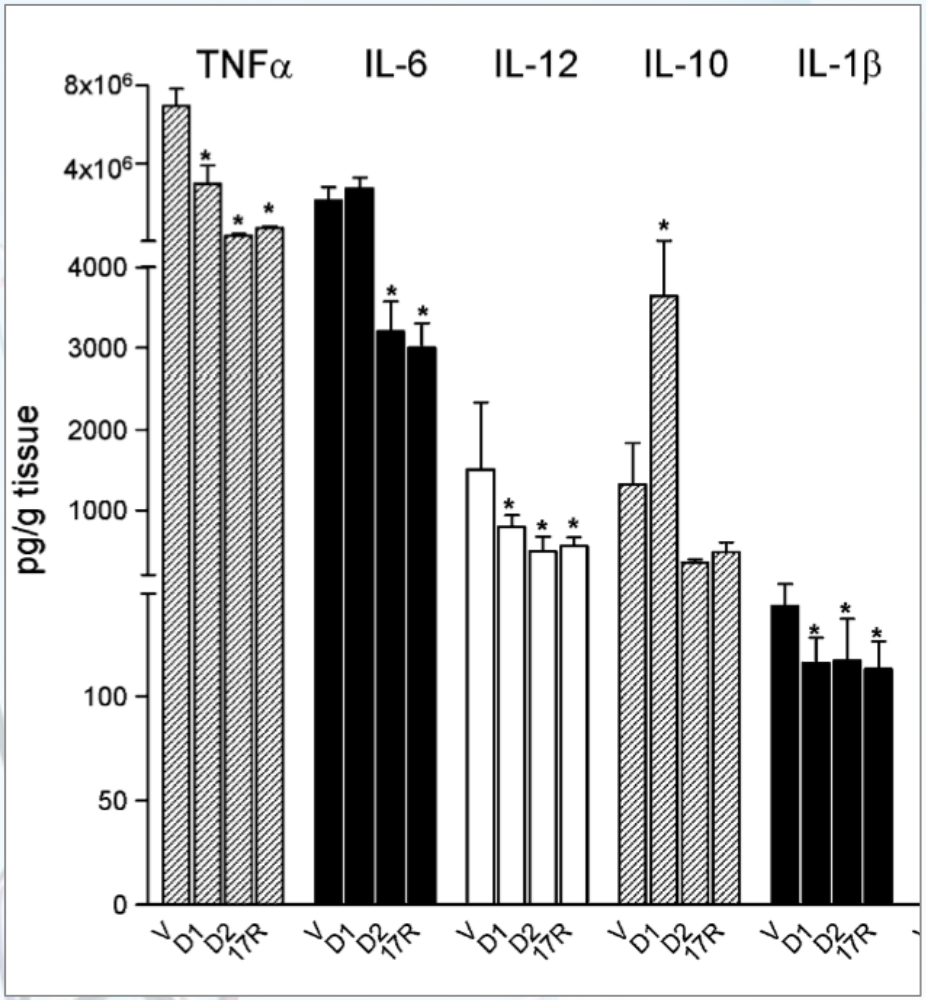


Guy Rousseau

Pourtant les résolvines peuvent contrecarrer l'action des médiateurs inflammatoires et diminuer la sécrétion adipokines pro-inflammatoires.







Guy Rousseau

IMPACT

- Les métabolites des acides gras oméga-3 pourraient avoir un rôle important dans l'inflammation associée à l'obésité.

Julie Lavoie

Cell Metab. 2007 December ; 6(6): 506–512.

Increased energy expenditure, dietary fat wasting and resistance to diet-induced obesity in mice lacking renin

Nobuyuki Takahashi[1,2,*], **Feng Li**[1], **Kunjie Hua**[3], **Jianbei Deng**[3], **Chih-Hong Wang**[1], **Robert R. Bowers**[4], **Timothy J. Bartness**[4], **Hyung-Suk Kim**[1], and **Joyce B. Harp**[3]

1*Department of Pathology and Laboratory Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599 USA*

2*Department of Cell and Molecular Physiology, The University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599 USA*

3*Department of Nutrition, The University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599 USA*

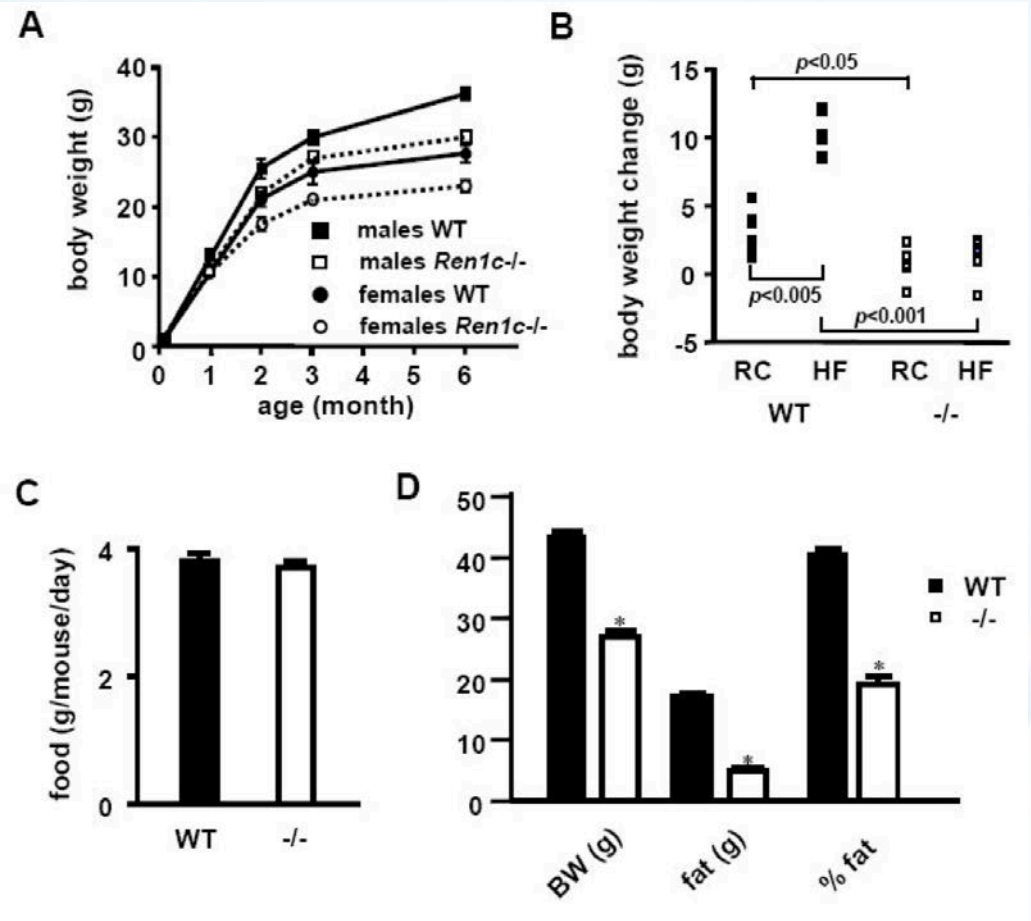
4*Department of Biology, Neurobiology and Behavior Program, Center for Behavioral Neuroscience, Georgia State University, Atlanta, GA, 30302 USA*

SUMMARY

An overactive renin angiotensin system is associated with obesity and the metabolic syndrome. However, mechanisms behind it are unclear. Cleaving angiotensinogen to angiotensin I by renin is a rate-limiting step of angiotensin II production, but renin is suggested to have angiotensin-independent effects. We generated mice lacking renin (*Ren1c*) using embryonic stem cells from C57BL/6 mouse, a strain prone to diet-induced obesity. *Ren1c-/-* mice are lean, insulin sensitive, and resistant to diet-induced obesity without changes in food intake and physical activity. The lean phenotype is likely due to a higher metabolic rate, and gastrointestinal loss of dietary fat. Most of the metabolic changes in *Ren1c-/-* mice were reversed by angiotensin II administration. These results support a role for angiotensin II in the pathogenesis of diet-induced obesity and insulin resistance.

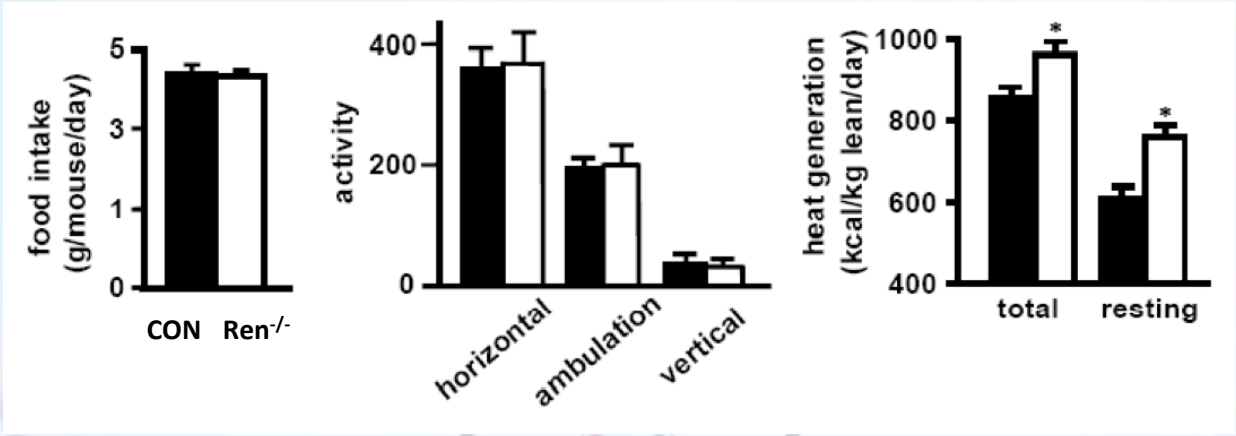
Julie Lavoie

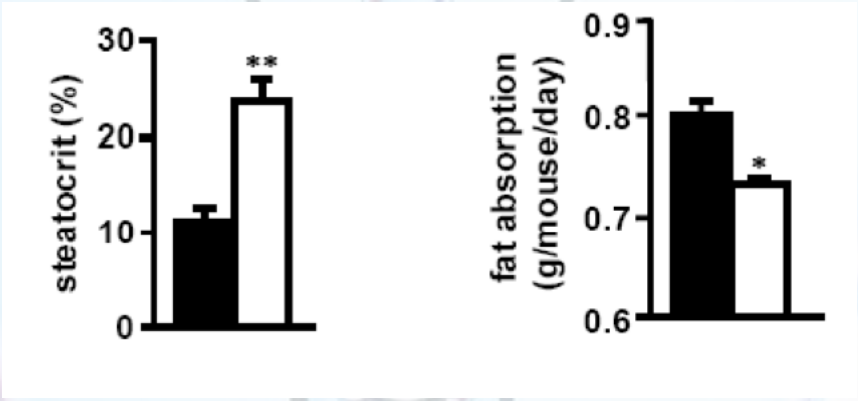
Les souris déficientes en rénine sont plus minces et plus résistantes à l'obésité que les souris témoins.



Julie Lavoie

Les souris déficientes en rénine sont aussi actives mais génèrent plus de chaleur et absorbent moins le gras de la diète.





Julie Lavoie

IMPACT

Les inhibiteurs de la rénine pourraient avoir des effets intéressants pour le contrôle du poids chez les personnes obèses hypertendues.

Denis deBlois

2009

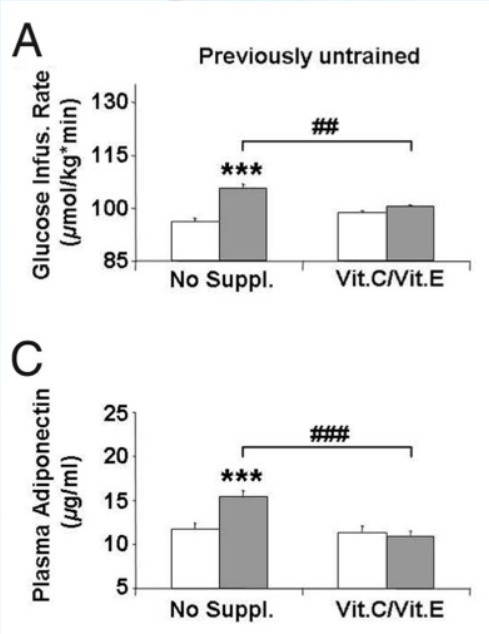
PNAS

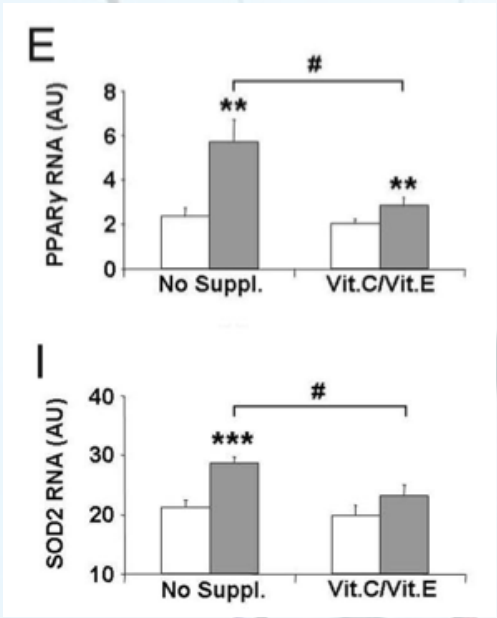
Antioxidants prevent health-promoting effects of physical exercise in humans

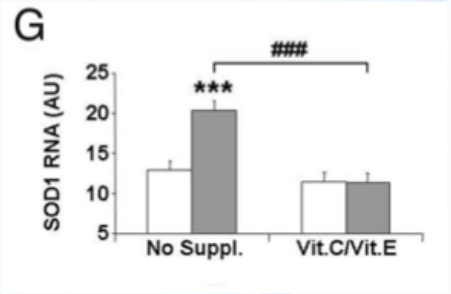
Michael Ristow[a,b,1,2], Kim Zarse[a,2], Andreas Oberbach[c,2], Nora Klöting[c], Marc Birringer[a], Michael Kiehntopf[d], Michael Stumvoll[c], C. Ronald Kahn[e], and Matthias Blüher[c,2]

[a]Department of Human Nutrition, Institute of Nutrition, University of Jena, Jena D-07743, Germany; [b]German Institute of Human Nutrition, Potsdam-Rehbrücke D-14558, Germany; [c]Department of Medicine, University of Leipzig, Leipzig D-04103, Germany; [d]Institute of Clinical Chemistry and Laboratory Medicine, University of Jena, Jena D-07743, Germany; and [e]Research Division, Joslin Diabetes Center, Harvard Medical School, Boston, MA 02215

Contributed by C. Ronald Kahn, March 31, 2009 (sent for review March 14, 2009)







Denis deBlois

- *Knock-out* combiné de SOD1/2/3/4/5 chez *C. Elegans*
- Quel effet sur la survie et la résistance aux stress environnementaux?

Superoxide dismutase is dispensable for normal animal lifespan

PNAS | April 10, 2012 | vol. 109 | no. 15 | 5785–5790

Jeremy Michael Van Raamsdonk and Siegfried Hekimi[1]

Department of Biology, McGill University, Montreal, QC, Canada H3A 1B1

Edited by Iva Greenwald, Columbia University, New York, NY, and approved March 1, 2012 (received for review October 3, 2011)

Reactive oxygen species (ROS) are toxic oxygen-containing molecules that can damage multiple components of the cell and have been proposed to be the primary cause of aging. The antioxidant enzyme superoxide dismutase (SOD) is the only eukaryotic enzyme capable of detoxifying superoxide, one type of ROS. The fact that SOD is present in all aerobic organisms raises the question as to whether SOD is absolutely required for animal life and whether the loss of SOD activity will result in decreased lifespan. Here we use the genetic model organism *Caenorhabditis elegans* to generate an animal that completely lacks SOD activity (*sod-12345* worms). We show that *sod-12345* worms are viable and exhibit a normal lifespan, despite markedly increased sensitivity to multiple stresses. This is in stark contrast to what is observed in other genetic model organisms where the loss of a single *sod* gene can result in severely decreased survival. Investigating the mechanism underlying the normal lifespan of *sod-12345* worms reveals that their longevity results from a balance between the prosurvival signaling and the toxicity of superoxide. Overall, our results demonstrate that SOD activity is dispensable for normal animal lifespan but is required to survive acute stresses. Moreover, our findings indicate that maintaining normal stress resistance is not crucial to the rate of aging.

oxidative stress | reactive oxygen species-mediated signaling | free radical theory of aging | *sod-2*

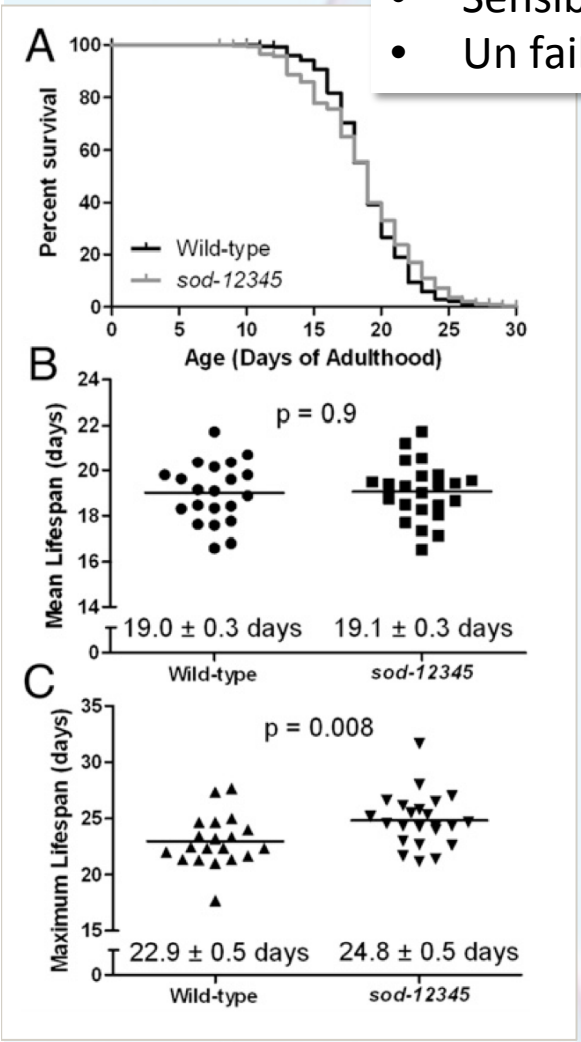
important for survival, deletion of either cytop
chondrial *sod* genes in yeast (8–11), flies (12–14)
17) results in decreased lifespan (Table 1). In co
of individual *sod* genes has been found to have
rimental effect on lifespan in the roundworm
elegans (18–22) (Table 1).

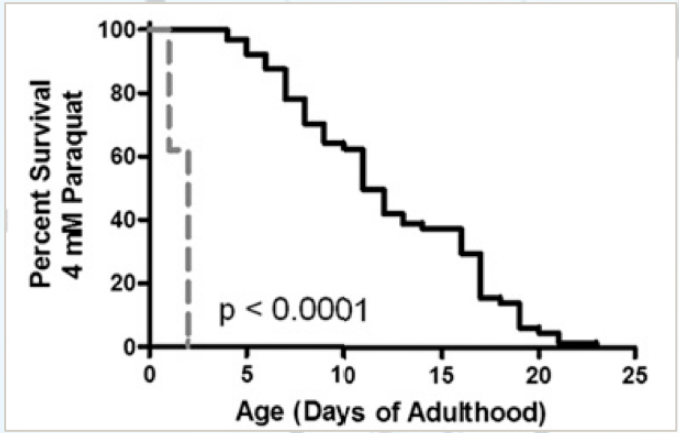
One explanation for the ability of *C. elegans* t
for the loss of *sod* genes might be the numbe
present. Yeast and flies both have two SODs, one
one mitochondrial. In addition to the cytoplasmic
drial SODs, mice also express an extracellular SO
C. elegans has five *sod* genes. *sod-1*, *sod-2*, and *so*
mary cytoplasmic, mitochondrial, and extracell
respectively, whereas *sod-3* and *sod-5* are inducibl
and cytoplasmic *sod* genes, respectively. Thus, it is
loss of individual SODs is compensated for by
these additional *sod* genes. In fact, up-regulation of
has been observed in individual *sod* deletion muta

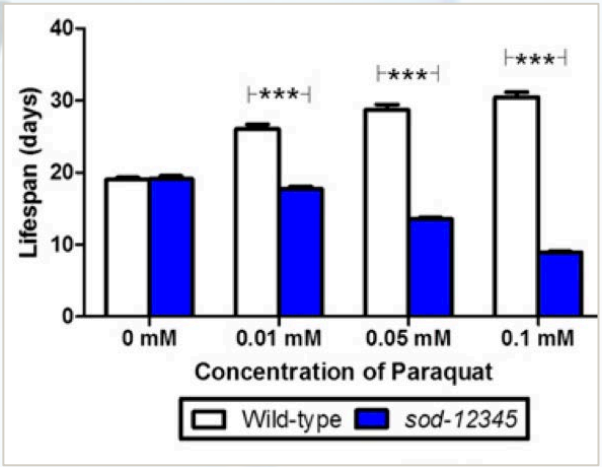
To determine whether the presence of additio
C. elegans masks a detrimental effect of *sod* ge
lifespan, we generated a *sod* quintuple mutant th
sod genes (*sod-12345* worms). *sod-12345* worms w
viable and fertile but exhibited multiple alteration
rates. Despite having markedly increased sensiti
stresses, the lifespan of *sod-12345* worms was no
wild-type worms. Overall, this suggests that SO

Denis deBlois

- Pas de changement de survie moyenne.
- Les plus vieux sont des KO !
- Sensibilité accrue aux stress environnementaux (pro-oxydant et autres)
- Un faible stress oxydant est bénéfique pour les WT!

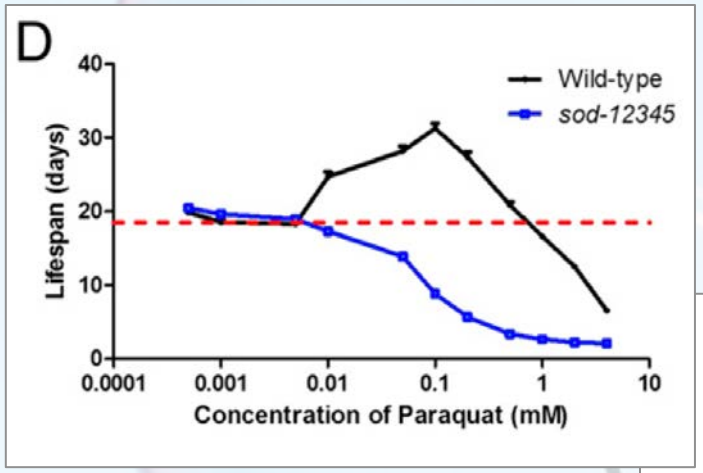


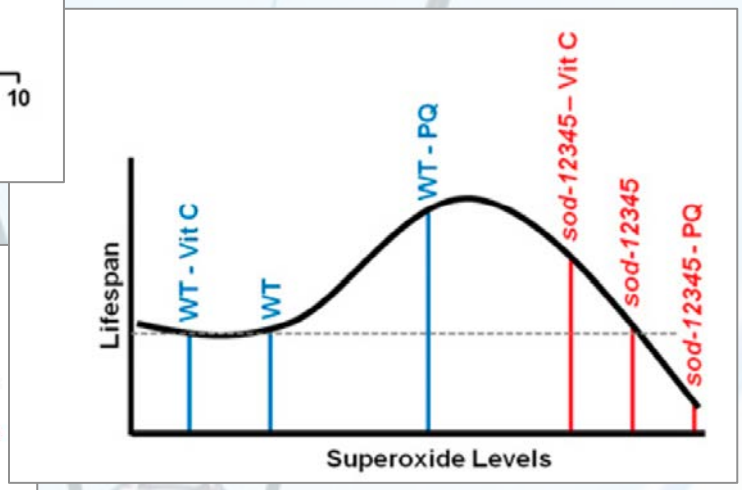


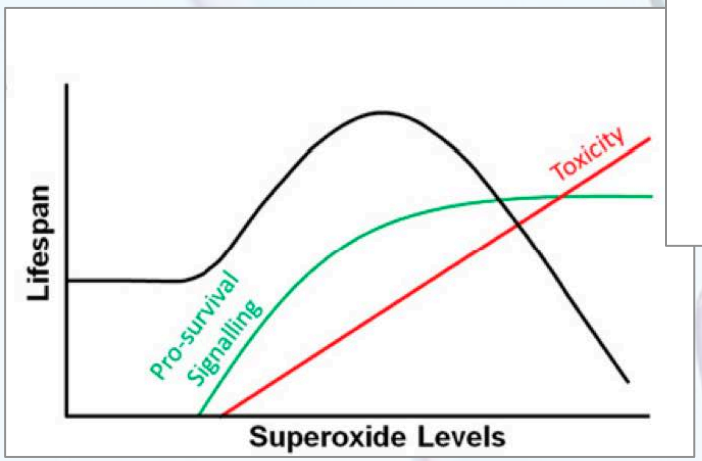


Denis deBlois

- KO : sensibilité accrue aux stress pro-oxydant
- Les sauvages (WT): effet bénéfique d'un faible stress oxydant!







Denis deBlois

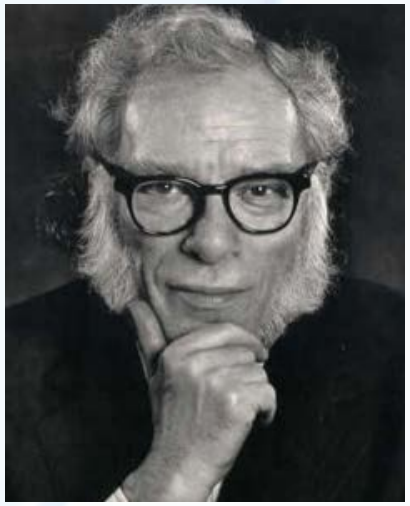
IMPACT

Pour le stress oxydant comme pour le cocktail qui s'en vient:
La modération a bien meilleur goût.

Expect the unexpected

« The most exciting phrase to hear in science, the one that heralds the most discoveries, is not « Eureka! » but « That's funny... »

Isaac Asimov




Bonne année 2013
Du succès dans vos études!