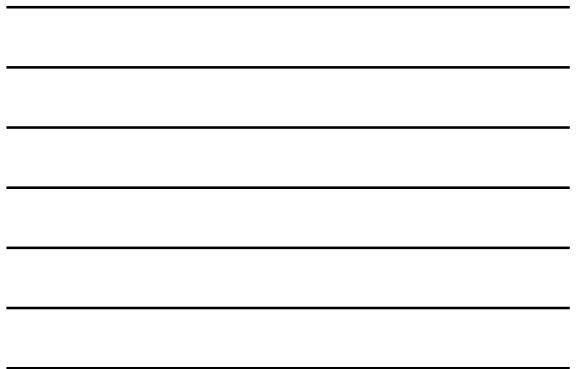
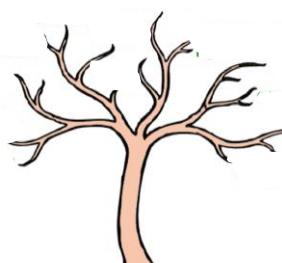


# Gut microbes and cardiometabolic risk factors : *Akkermansia* as novel target ?



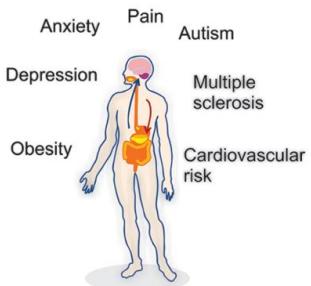
# Gut microbiota and diseases



The tree diagram illustrates the complex relationship between the gut microbiota (the pink parts) and the host (the brown parts). The roots are at the bottom, labeled "Gut Microbiota". The trunk and branches represent the microbiota, which extends upwards and outwards, symbolizing its influence and interaction with the host's body.



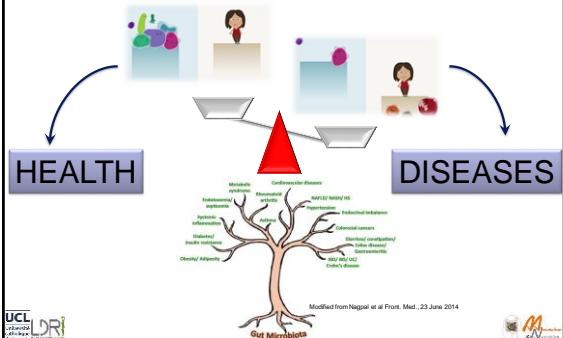
## When gut microbes talk to organs



Montiel-Castro et al Front. Integr. Neurosci. 2016

LDRIM

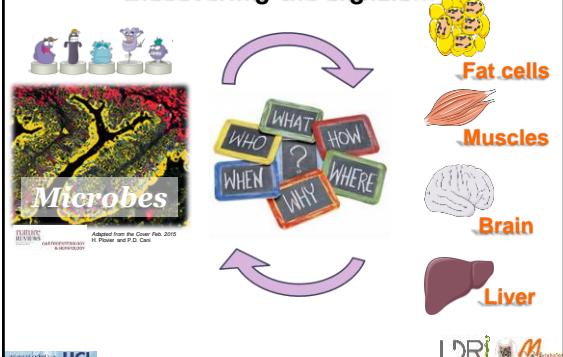
## FACT: Gut microbes are different during metabolic disorders



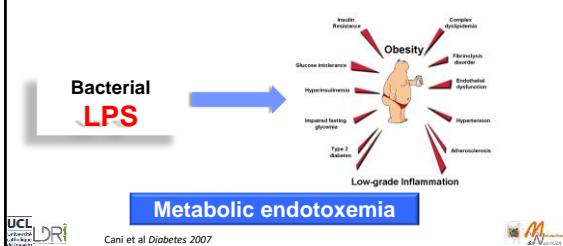
UCL LDRIM

M

## How do microbes interact with host cells? Discovering the signals...



## Gut microbiota derived compounds acting as triggering factors?



UCL DRI

Cani et al Diabetes 2007



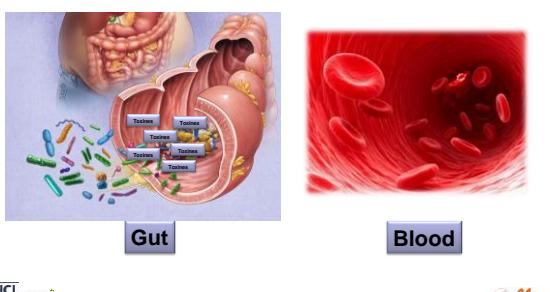
## Leaky gut syndrome



UCL DRI



## Bacterial toxins stay in the Healthy gut



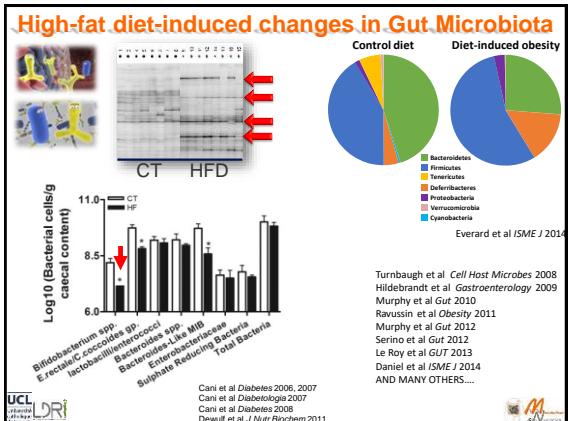
UCL DRI



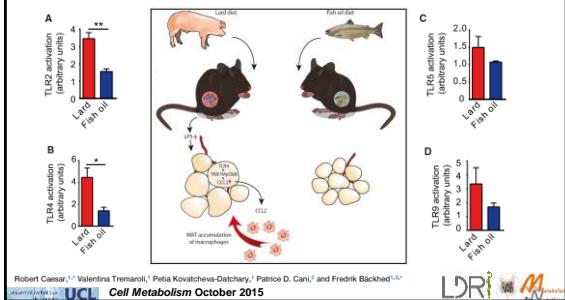
## Leaky gut syndrome Or Gut permeability



# Causal role of the gut microbiota ?



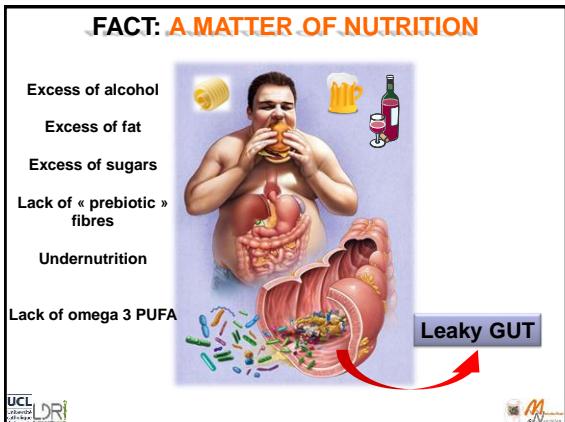
## Gut microbiota derived compounds acting as triggering factors? Fatty acids composition is crucial!



Robert Caesar,<sup>1,\*</sup> Valentina Tremaroli,<sup>1</sup> Petia Kovatcheva-Datchary,<sup>1</sup> Patrice D. Cani,<sup>2</sup> and Fredrik Backhed<sup>1,3,\*</sup>

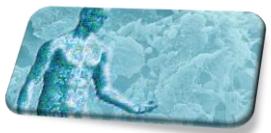
Cell Metabolism October 2015

UCL LDRIM



## More than 20 years ago in Belgium at UCL Brussels....

## The prebiotic concept



 UCL UDR



The prebiotic concept was born more than 20 years ago!

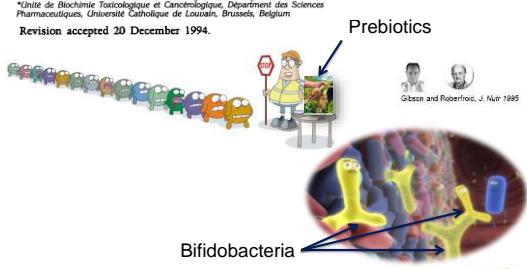
## Dietary Modulation of the Human Colonic Microbiota: Introducing the Concept of Prebiotics

GLENN R. GIBSON AND MARCEL B. ROBERFROID\*

MRC Dunn Clinical Nutrition Centre, Cambridge, United Kingdom and  
\*Unité de Biochimie Toxicologique et Cancérologique, Département des Sciences

Received: November 22, December 1994

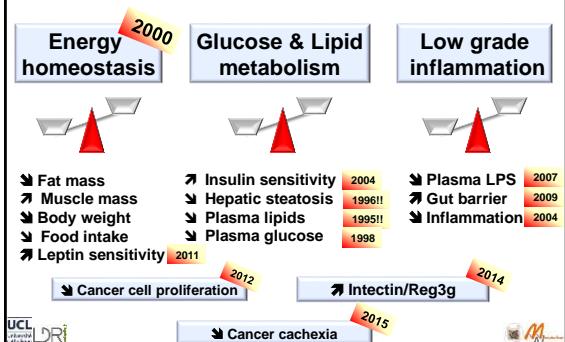
Revision accepted 20 December 1994.



 UCL LDRI



## **Non-comprehensive list of targets of prebiotic-induced microbiota modulation**



 UCL  
University College London



## Serendipity, the case: « Akkermansia »



UNIVERSITY COLLEGE LONDON



## Prebiotic feeding changes numerous taxa and functions

# Responses of Gut Microbiota and Glucose and Lipid Metabolism to Prebiotics in Genetic Obese and Diet-Induced Leptin-Resistant Mice

**ORIGINAL ARTICLE**  
**Microbiome of prebiotic-treated mice reveals novel targets involved in host response during obesity and diabetes**

Everard et al Diabetes 2011

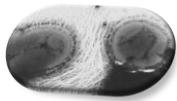
Everard et al / SME J 2014 epub ahead of print April 3rd



Akk



## *Akkermansia muciniphila*

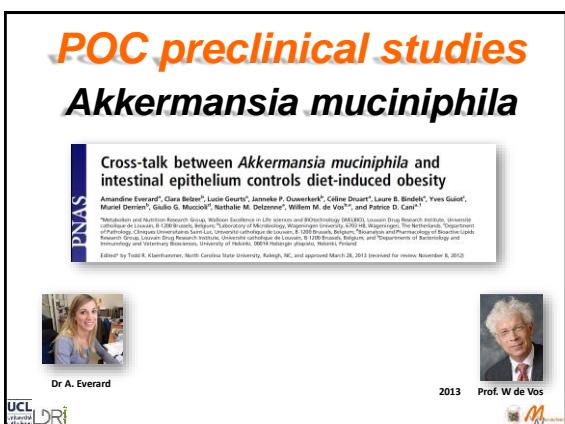
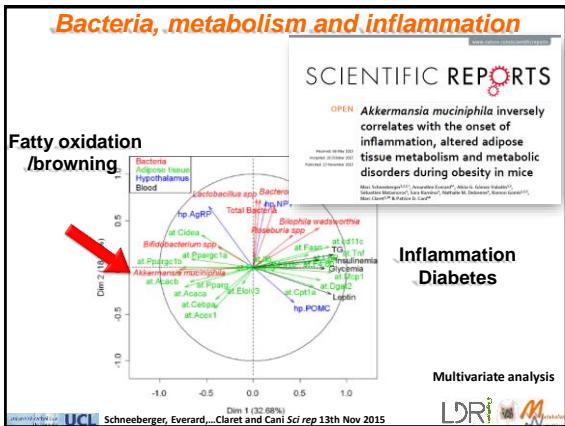
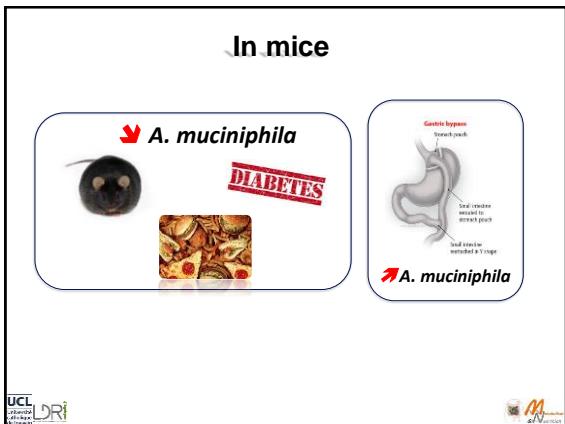


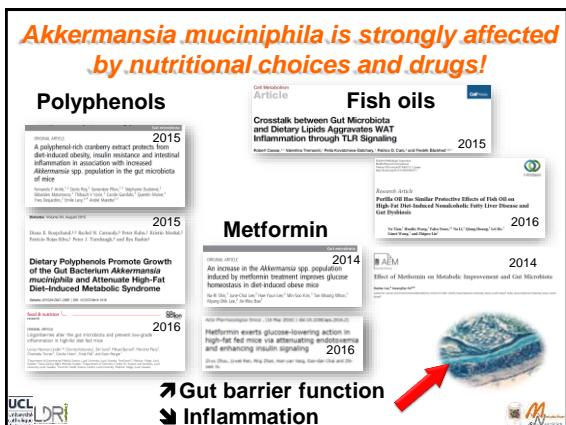
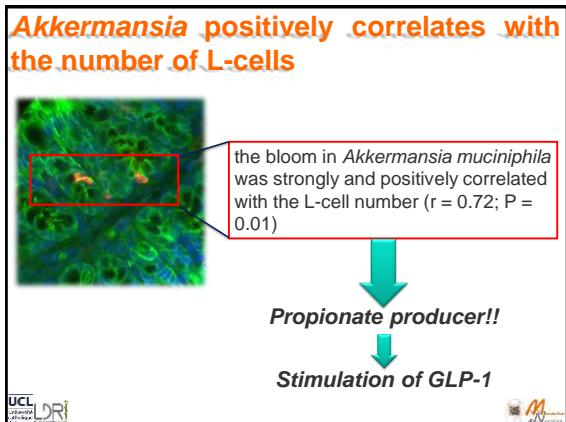
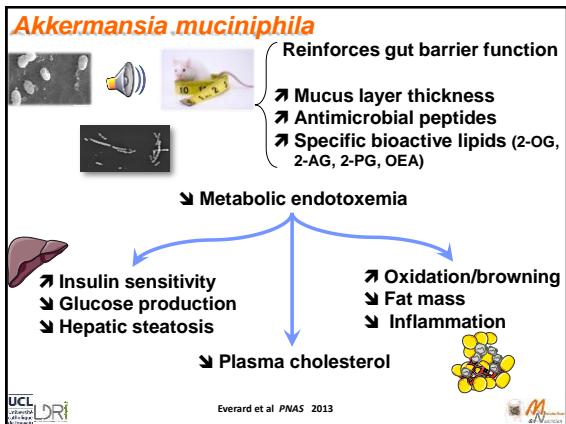
*Isolated in 2004 by*



 UCL LDR







**Akkermansia, obesity and type 2 diabetes**

**nature** International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current issue | Archive | Audio & Video | For Authors

News & Comment > News > 2011 > June > Article

Gut microbe may fight obesity and diabetes

Bacterium helps to regulate metabolism in mice.

Brian Owens

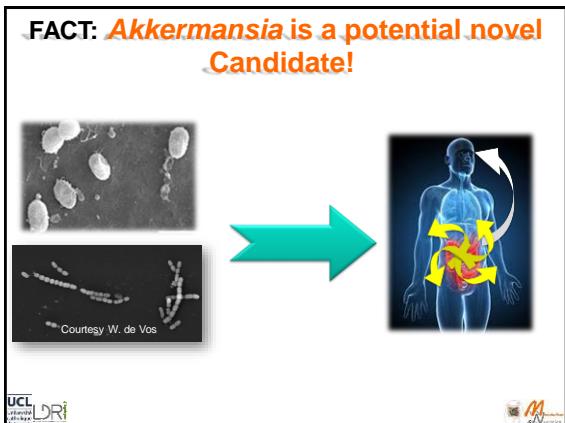
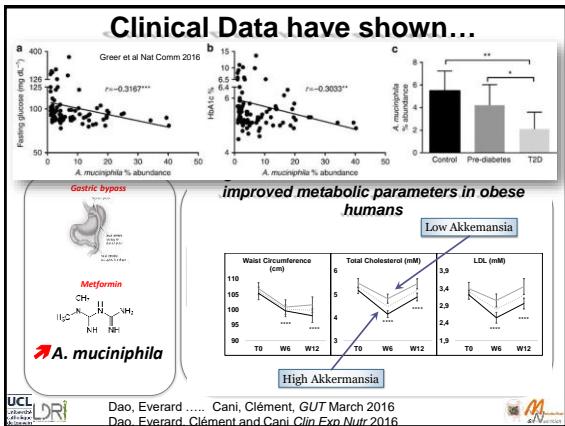
13 May 2011

The gut is home to innumerable different bacteria – a complex ecosystem that has an active role in a variety of bodily functions. In a study published this week in *Proceedings of the National Academy of Sciences*, a team of researchers finds that in mice, *Akkermansia muciniphila* species play a major part in combating obesity and metabolic disorders such as type 2 diabetes.

The bacterium, *Akkermansia muciniphila*, digests mucus and makes up 2–5% of the microbes in a mouse's gut. Mice that have been bred to lack the obese humans and mice, and those with type 2 diabetes, have much lower levels. A team led by Duncan Cani, who studies the interaction between gut bacteria and

In Humans?

**UCL DRI**



# **Akkermansia is a potential novel Candidate!**

# *Akkermansia muciniphila*



 UCL UDR



*But many problems  
remain to be solved  
before a PoC in  
Humans !*

 UCL UDR



## The major issues:

- ✓ Preferred growth medium of *Akkermansia* contains animal-derived compounds (i.e. mucus)! Strongly limits the translational approach for human test...
  - ✓ *Akkermansia* is relatively sensitive to oxygen!
  - ✓ We need to culture *Akkermansia* at a very high level and find a way to store/deliver the bacteria

 UCL  
London  
Digital  
Research  
Institute



**nature  
medicine**

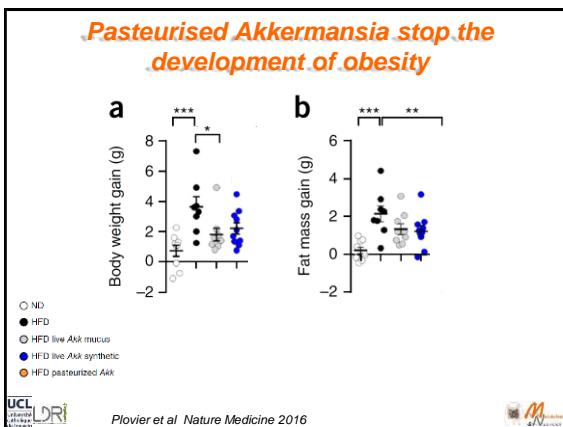
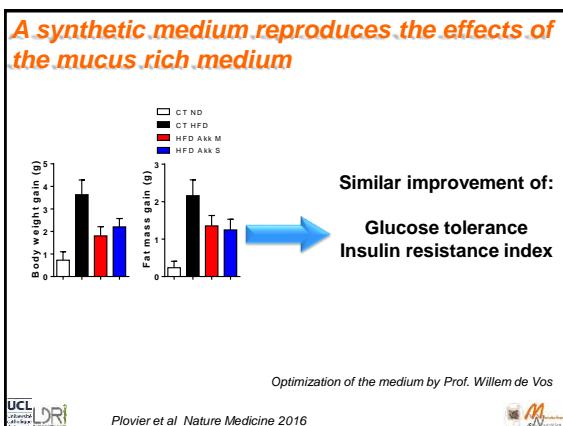
**LETTERS**

A purified membrane protein from *Akkermansia muciniphila* or the pasteurized bacterium improves metabolism in obese and diabetic mice

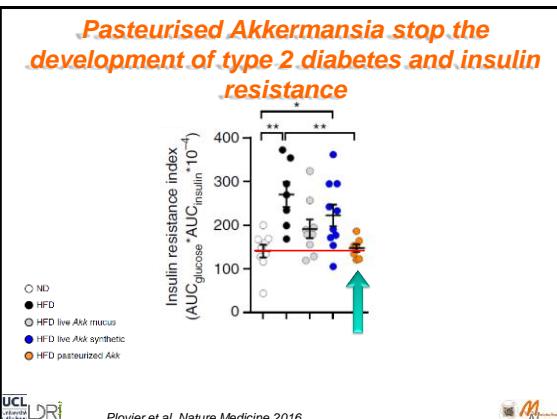
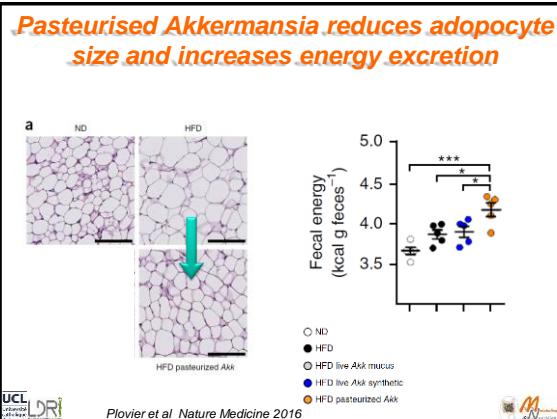
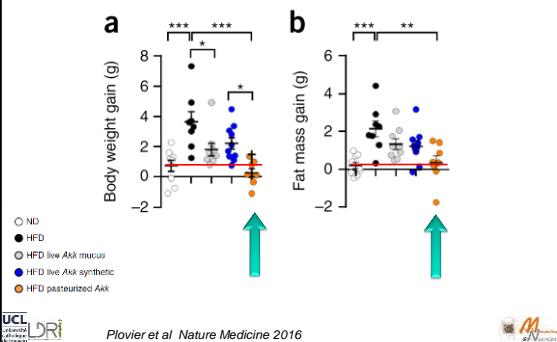
Hubert Plovier<sup>1</sup>, Amandine Everard<sup>1,3</sup>, Céline Druart<sup>1,3</sup>, Clara Depommier<sup>1,3</sup>, Matthias Van Hul<sup>1</sup>, Lucie Geurts<sup>1</sup>, Julien Chilouss<sup>2</sup>, Noora Ottman<sup>2,3</sup>, Thibaut Duparc<sup>4</sup>, Laetitia Lichtenstein<sup>4</sup>, Antonis Myridakis<sup>2</sup>, Nathalie M Delzenne<sup>1</sup>, Judith Klivink<sup>5</sup>, Arunab Bhattacharjee<sup>6</sup>, Kees C H van der Ark<sup>3</sup>, Steven Adlyvink<sup>3</sup>, Laurent O Martinez<sup>3</sup>, Marc-Emmanuel Dumus<sup>2</sup>, Dominique Mater<sup>2</sup>, Audrey Loumaye<sup>3</sup>, Michel P Hermans<sup>6</sup>, Jean-Paul Thissen<sup>6</sup>, Clara Belzer<sup>1</sup>, Willem M de Vos<sup>3,7</sup> & Patrice D Cani<sup>1</sup>

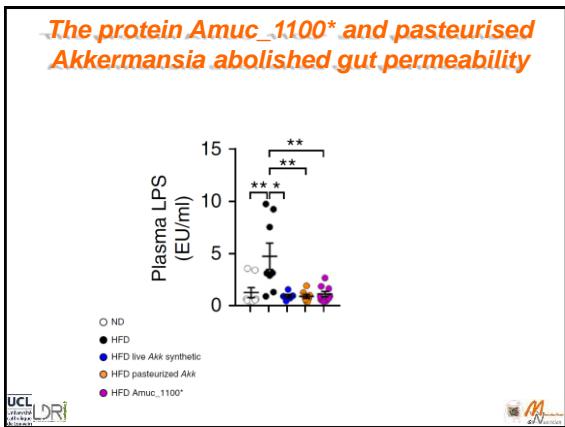
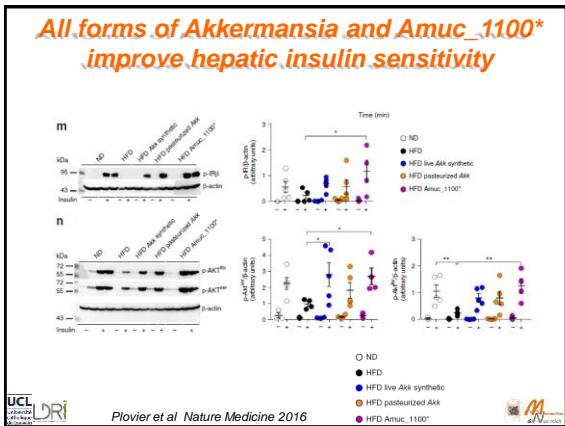
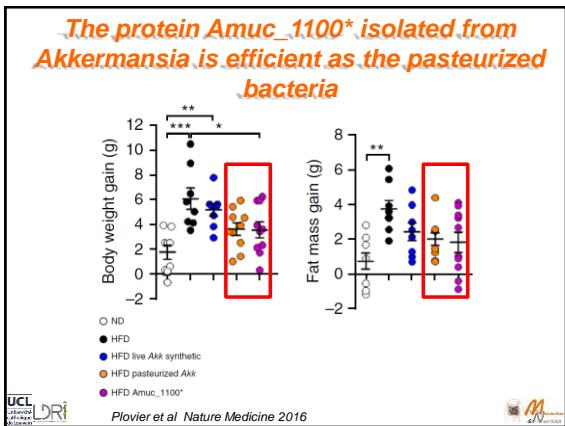
Published 28 November 2016 at 5pm

Hubert Plovier

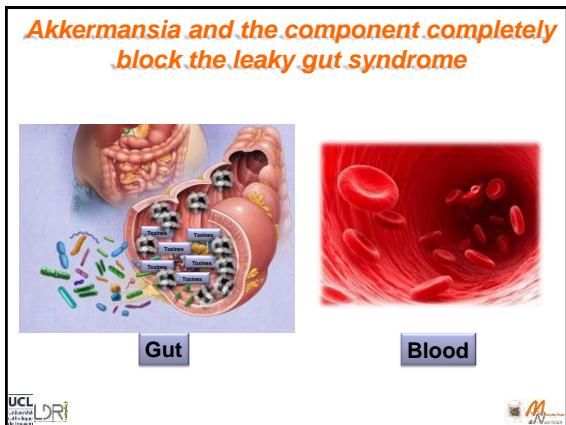
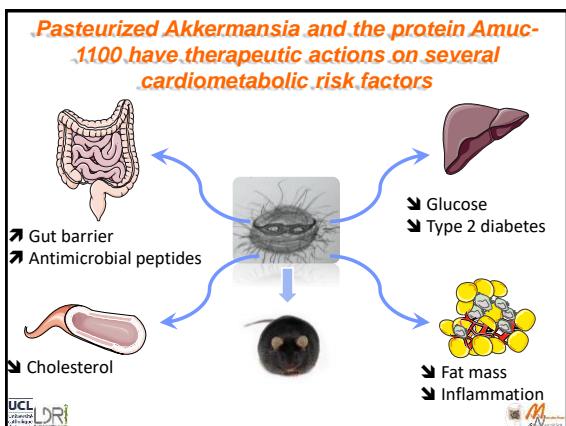
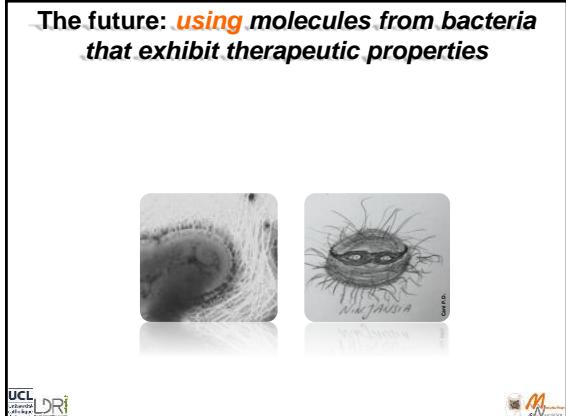


**Pasteurised Akkermansia stop the development of obesity**





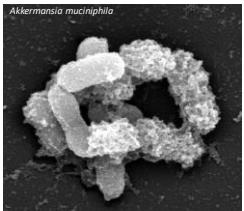
The future: **using molecules from bacteria that exhibit therapeutic properties**



**In humans?**

**First administration of**

***Akkermansia muciniphila***



Louise Hsukenen & Willem M de Vos

**UCL** **DRI**

**M** **Microbes4U**

**PoC in HUMANS**

***Akkermansia* safety and effects on markers of diabetes and cardiometabolic risk factors**

**Microbes4U**

BMI ≥ 25, insulin resistance and metabolic syndrome  
Randomized, single-blind, parallel, placebo-controlled

100 subjects      3 months of treatment

Randomization      Placebo  
Inform-      Live *A. muciniphila* 10<sup>9</sup>/day  
consent      Live *A. muciniphila* 10<sup>9</sup>/day  
                  Heat treated *A.muciniphila* 10<sup>9</sup>/day

**-SAFE-**

**Key Outcomes : Insulin-resistance, inflammation, dyslipidemia, body-weight, type-2 diabetes, gut microbiota, gut barrier function**

**First Spin OFF project**

**ERC-PoC-2016**

**ERC** **Fonds Wallonie Bruxelles** **ClinicalTrials.gov Protocol Record 2015/02/JUL/369**

Prof. Jean-Paul Thissen  
Prof. Michel Hermans  
Prof. Dominique Malter  
Dr. Audrey Lemayre  
Dr. Alexandre Everard  
Dr. Géraldine D'Haese  
Clara Depommier  
Marie de Barys  
Prof. Willem de Vos

**UCL** **DRI**

**fnrs** **UCL** **erc** **ERC-SIG-ENIMGO-2013** and **ERC-PoC-Microbes4U-2016**

**Walloon Excellence in Life Sciences and BIOTechnology** **INSERM, Toulouse, France**

Prof C. Krauf  
Prof R. Bureljin  
**LDRI, UCL, Belgium**  
Prof G. Muccioli  
Prof J-B Demoulain, Dr A. Essaghir  
Prof J-C Renaud, Prof L. Dumoutier  
**IREC**  
Prof Y. Guiot  
Rose-Marie Gobbelis  
**Gothenburg University, Sweden**  
Prof F. Backhed  
Dr S. Robine  
Dr M. Shahman  
Dr M. Johansson

**Former members of Cani's team**  
Dr M. Osto, F. Pierard, M. Van Roye  
O. Rotter, Dr. S. Matamoros, Dr. T. Duparc, A. Bever, Dr G. Trinchese

**IBIBASCO and CIBERDEM**, **Barcelona, Spain**  
Dr M. Claret and his team

**Metabolomic and Molecular Image Lab, INCLIVA, Valencia, Spain**  
Prof. D. Monleon and his team

**Paris Diderot University**  
Dr. S. Luquet  
Prof. C. Magnan  
**Paris Curie Institute**  
Prof. S. Robine  
Prof. K. Lemaire  
Prof. S.W. van der Werve  
Prof. J. van Pelt

**Université de Genève, Hôpitaux universitaires**  
Prof J. Schrenzel  
Prof P. François  
Prof V. Lazarevic

**Wageningen UR ICAN**  
Prof W. de Vos  
Dr. M. Derrien  
Dr. C. Belzer  
Dr. J. Overkirk  
Dr. J. Kleivink

**Pitié-Salpêtrière hospital**  
Prof K. Clément  
Dr Dao and Microbes consortium



---

---

---

---

---

---

---