

« Undernutrition, Juvenile growth and Microbiota »



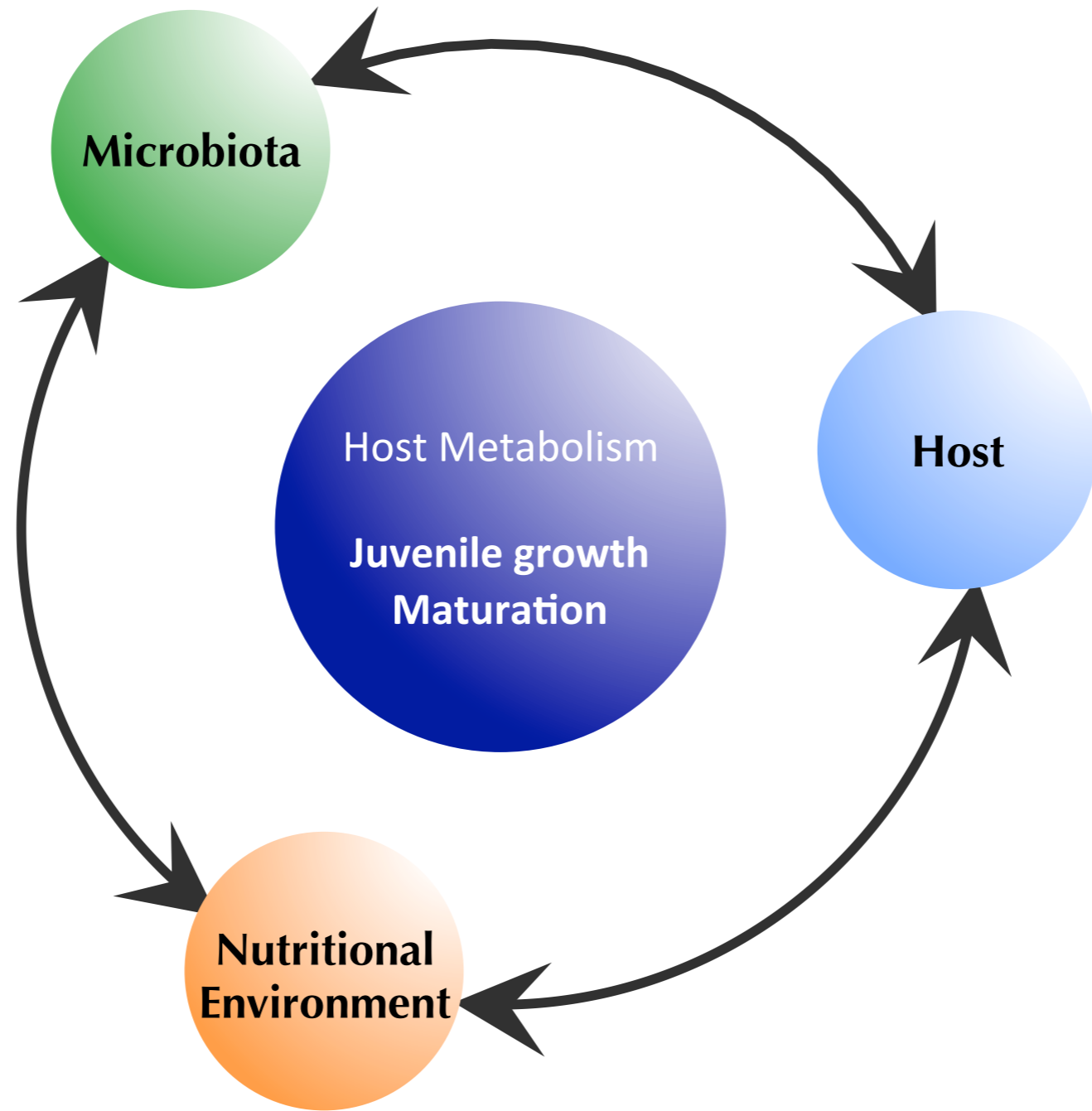
François Leulier

Institut de Génomique Fonctionnelle de Lyon

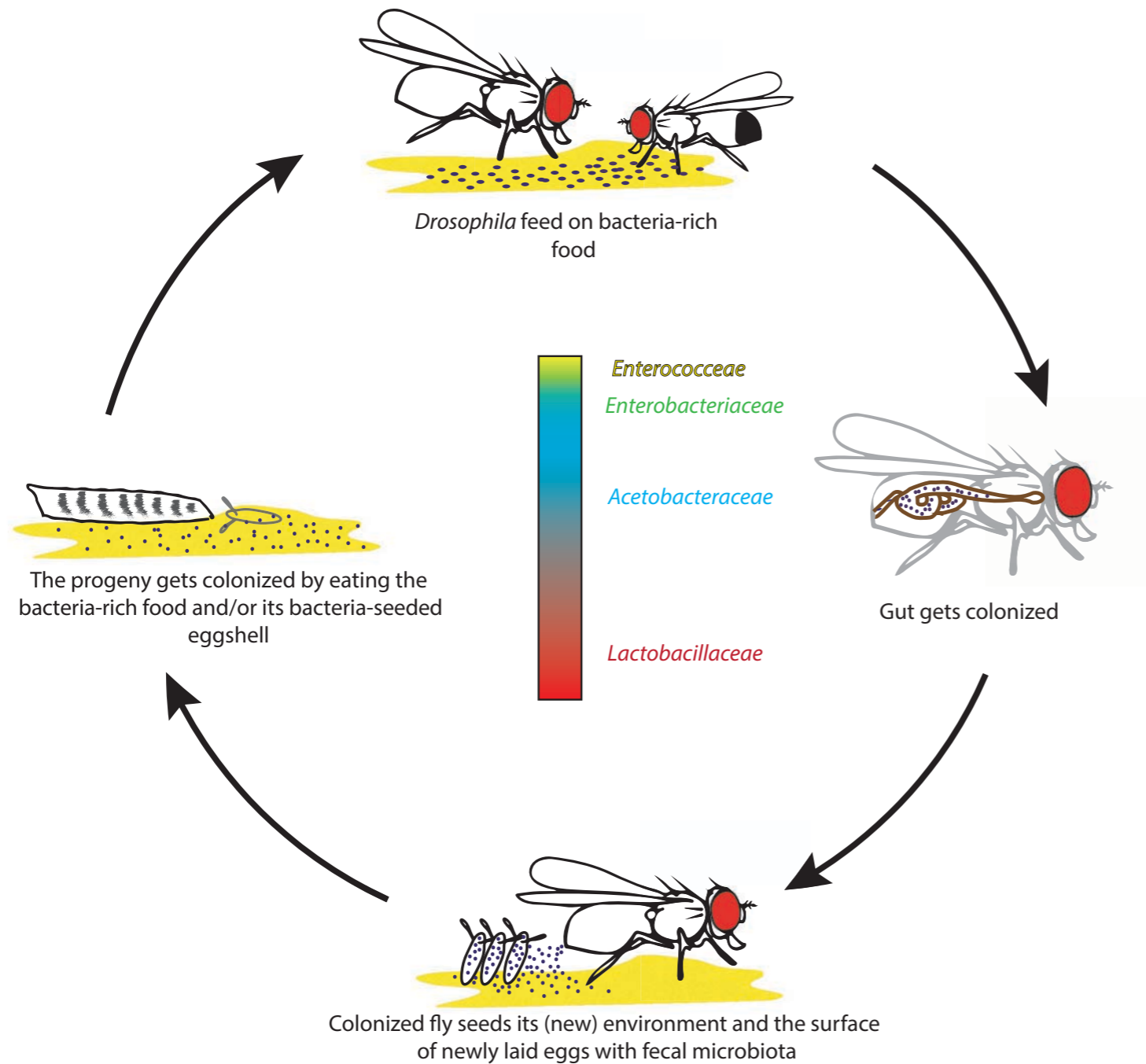
Ecole Normale Supérieure de Lyon

France

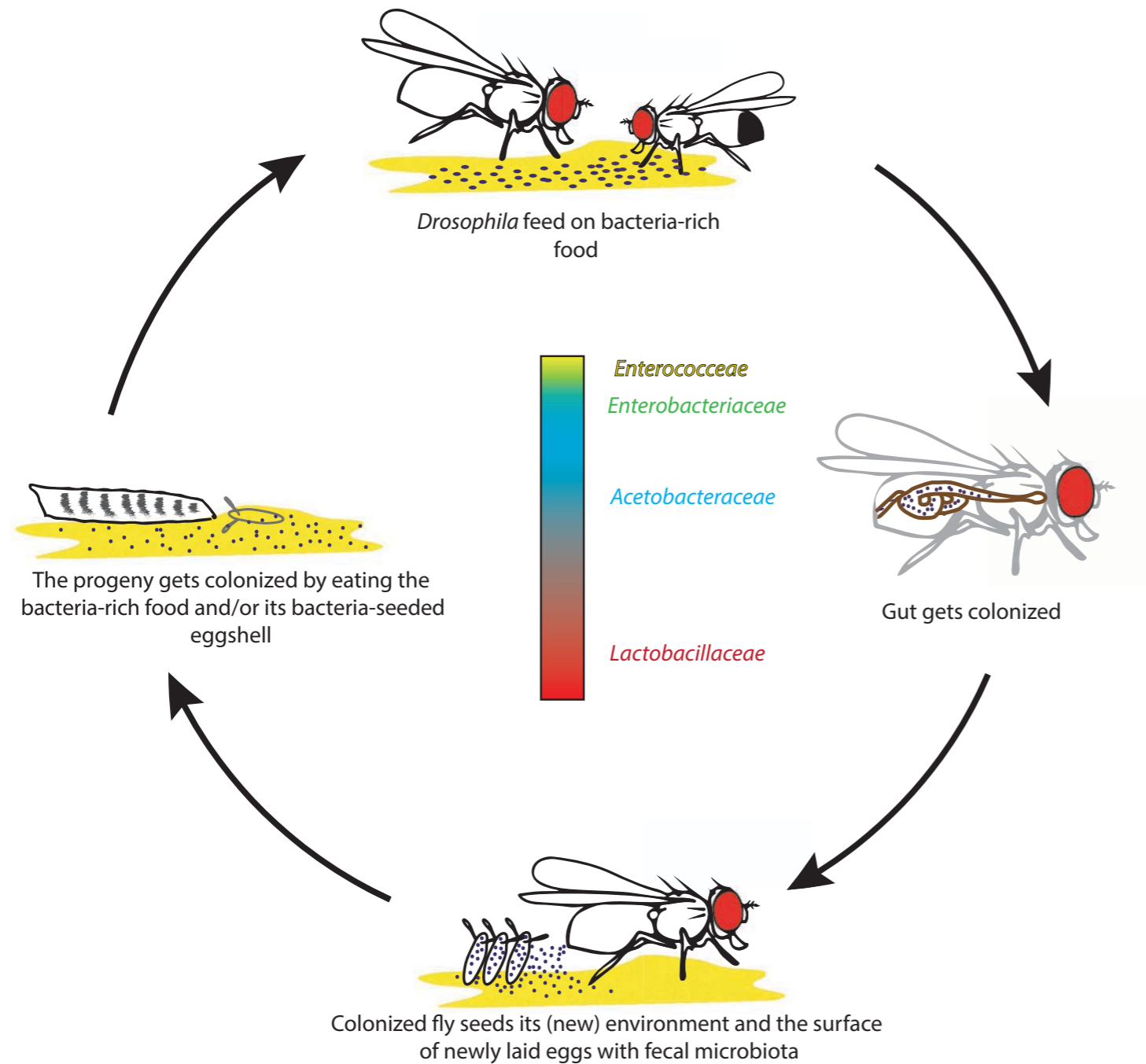




Drosophila melanogaster a host model to study host-nutrition-commensals interactions



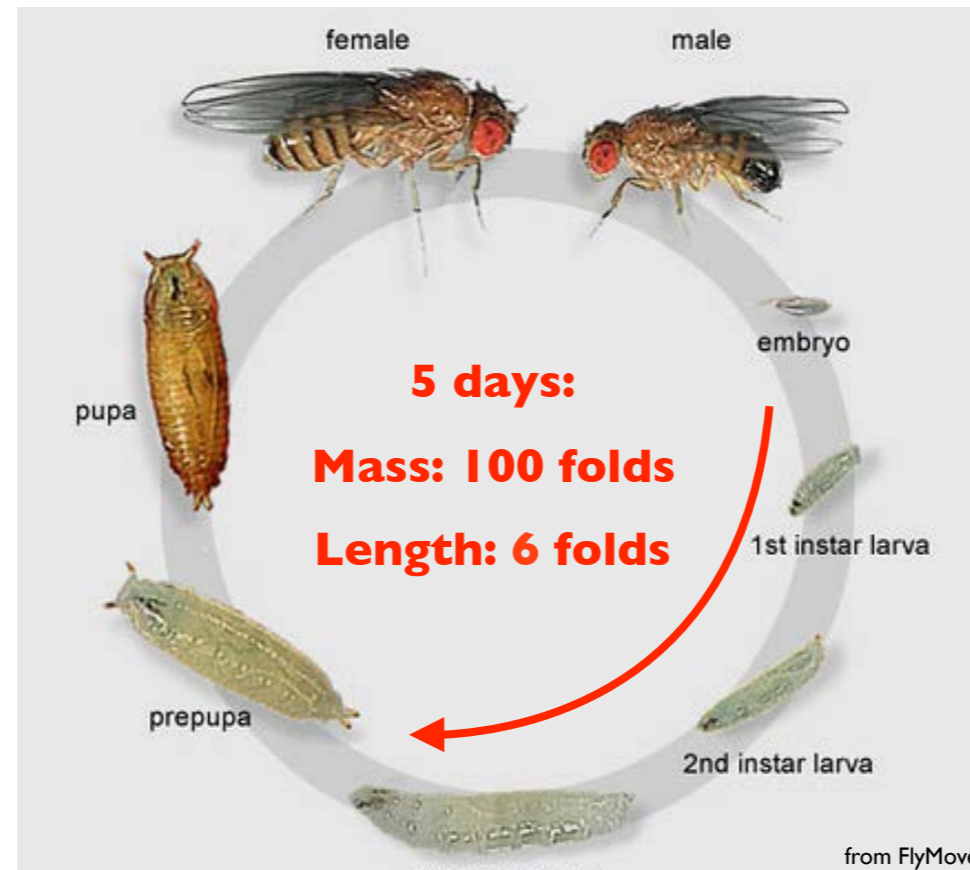
Drosophila melanogaster a host model to study host-nutrition-commensals interactions



Are there mutualists among commensals?

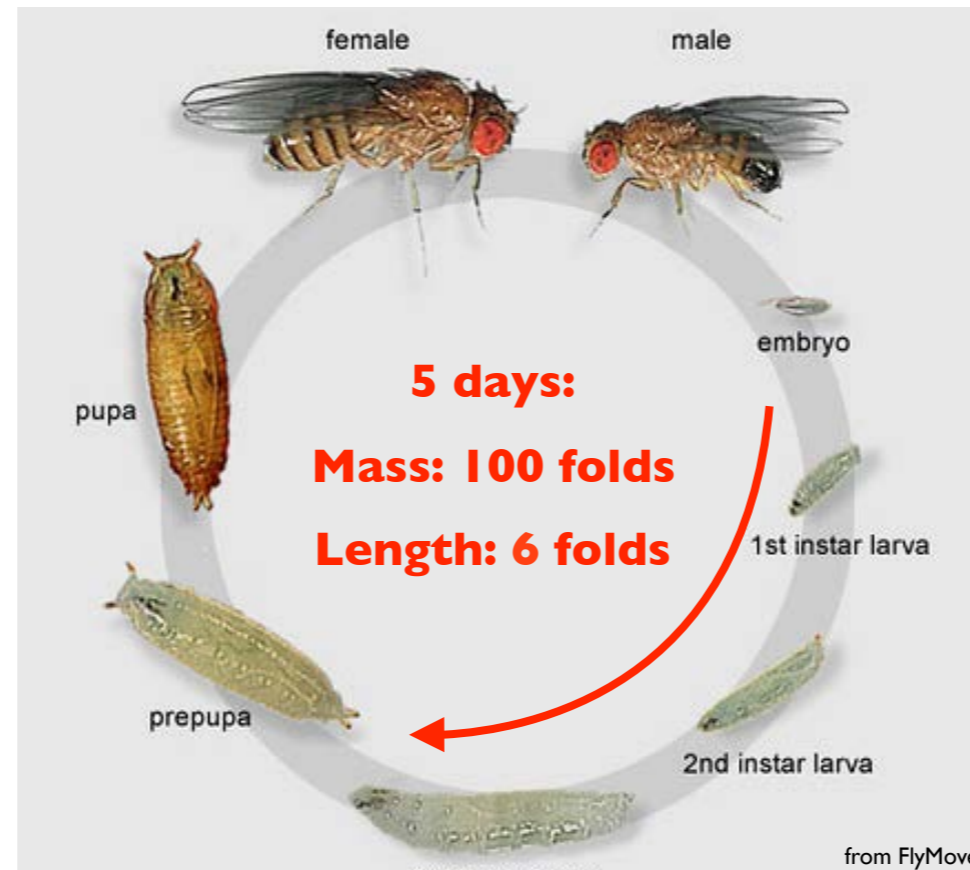
Do commensals influence *Drosophila* juvenile growth?

Laboratory
breeding diet
=
Optimized nutrition



Do commensals influence *Drosophila* juvenile growth?

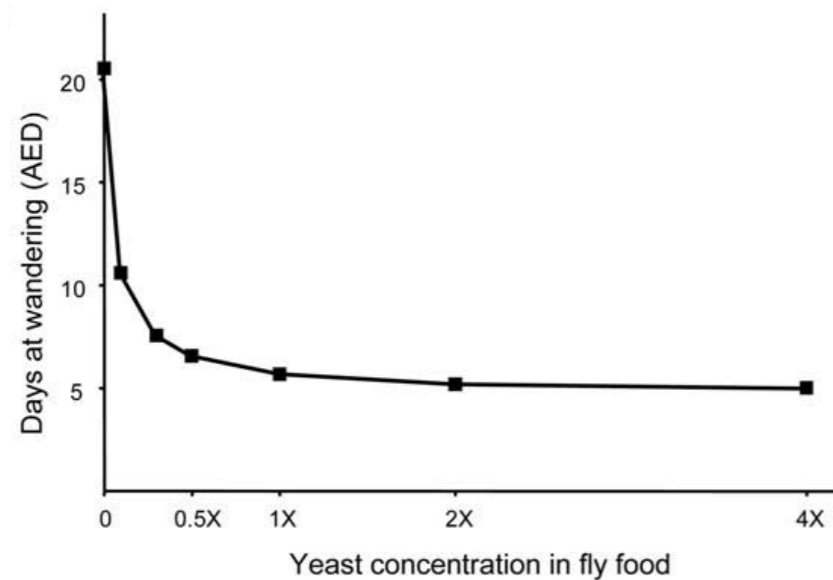
Laboratory
breeding diet
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Optimized nutrition



Chronic undernutrition triggers *Drosophila* stunting

Delayed maturation

Short stature

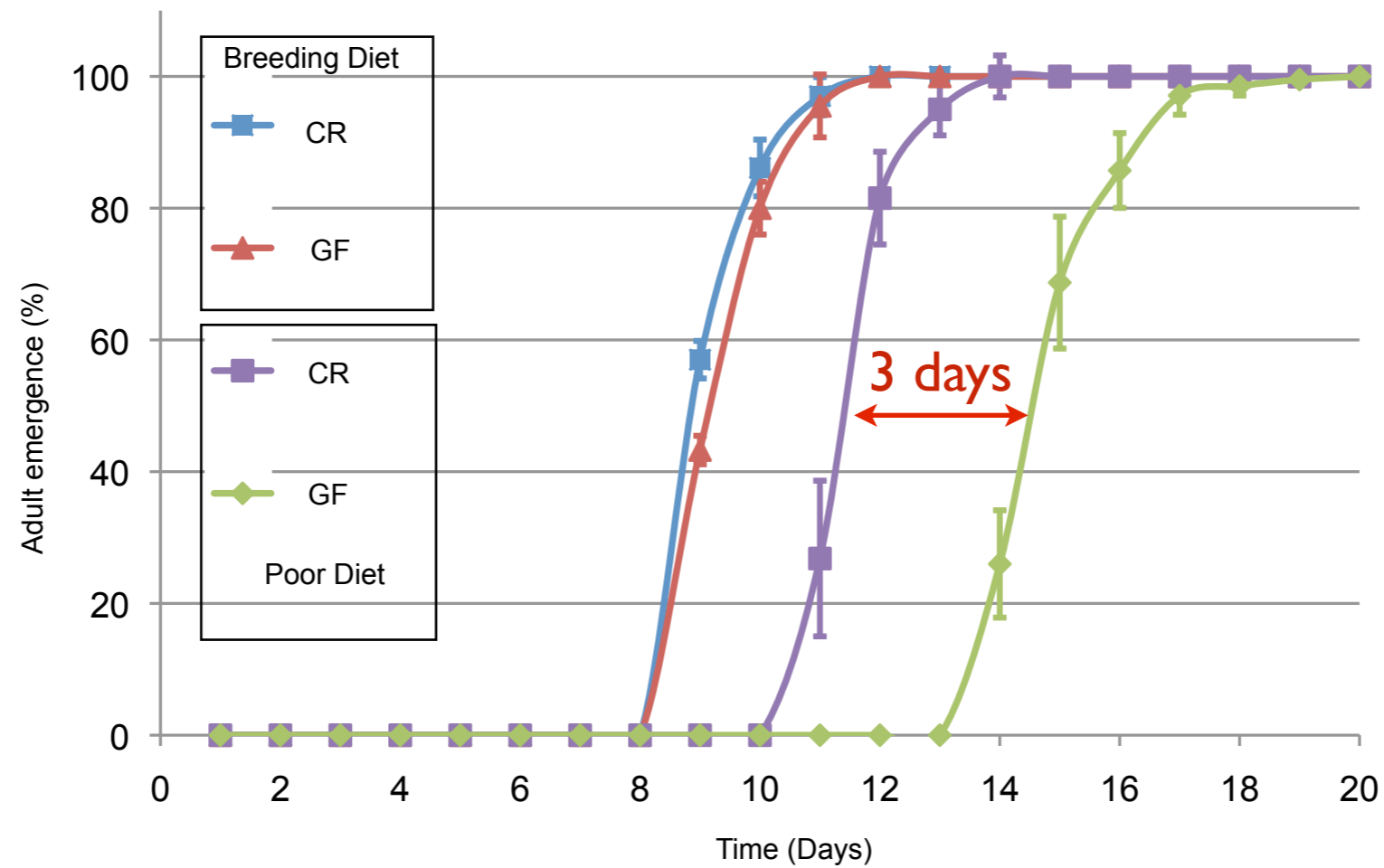


Undernutrition

Normal nutrition



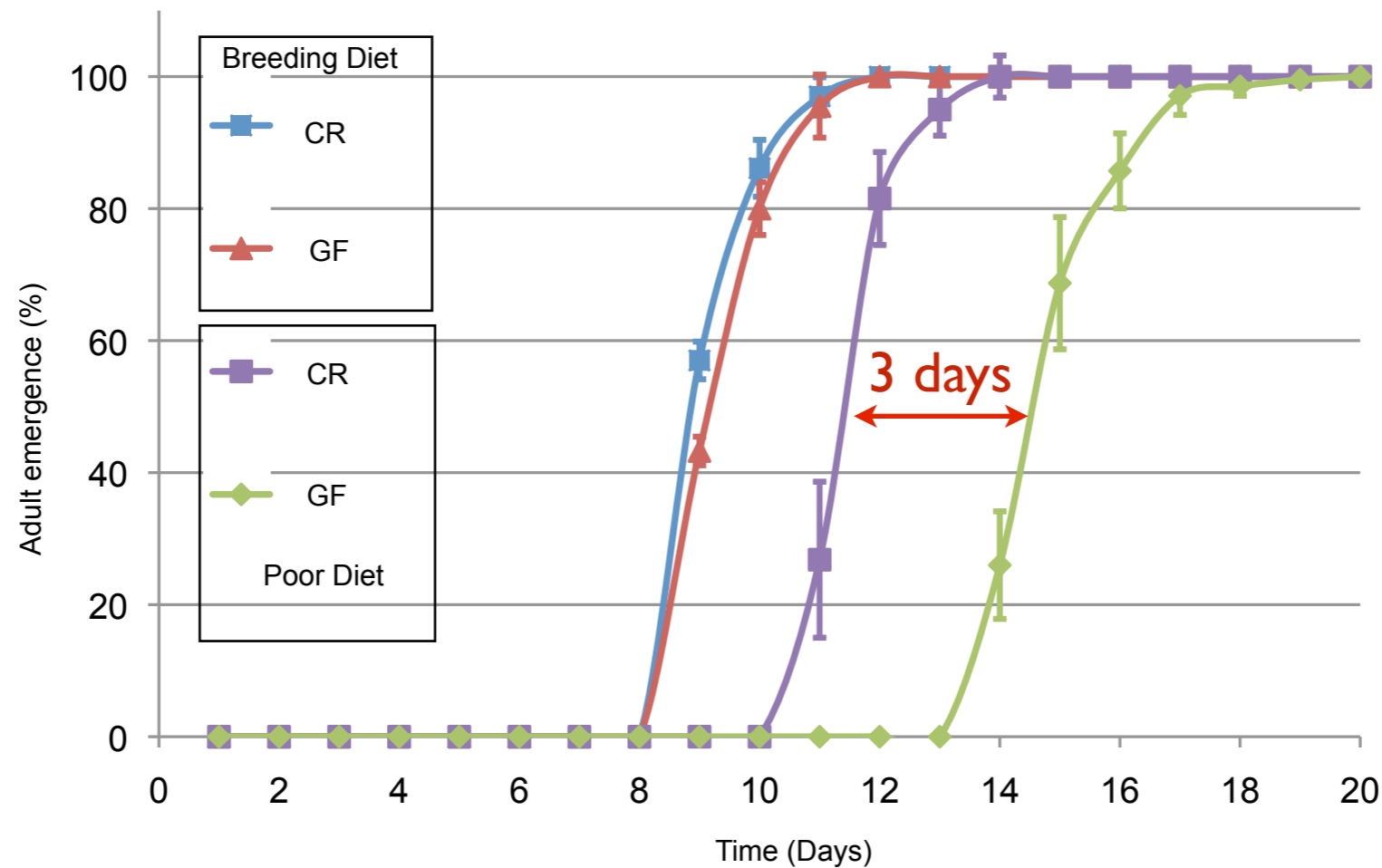
Commensals promote *Drosophila* juvenile growth upon undernutrition



CR: Conventionally reared (+commensals)

GF: Germ-Free

Commensals promote *Drosophila* juvenile growth upon undernutrition



16S rDNA gene profiling

CR yw whole body library

Phylotype	Closest strain	% identity
<i>Enterococcus faecalis</i>	<i>Enterococcus faecalis</i> V583	99%
<i>Lactobacillus plantarum</i>	<i>Lactobacillus plantarum</i> WCFS1	99%
<i>Aerococcus</i> spp.	<i>Aerococcus viridans</i> ATCC11563	97%

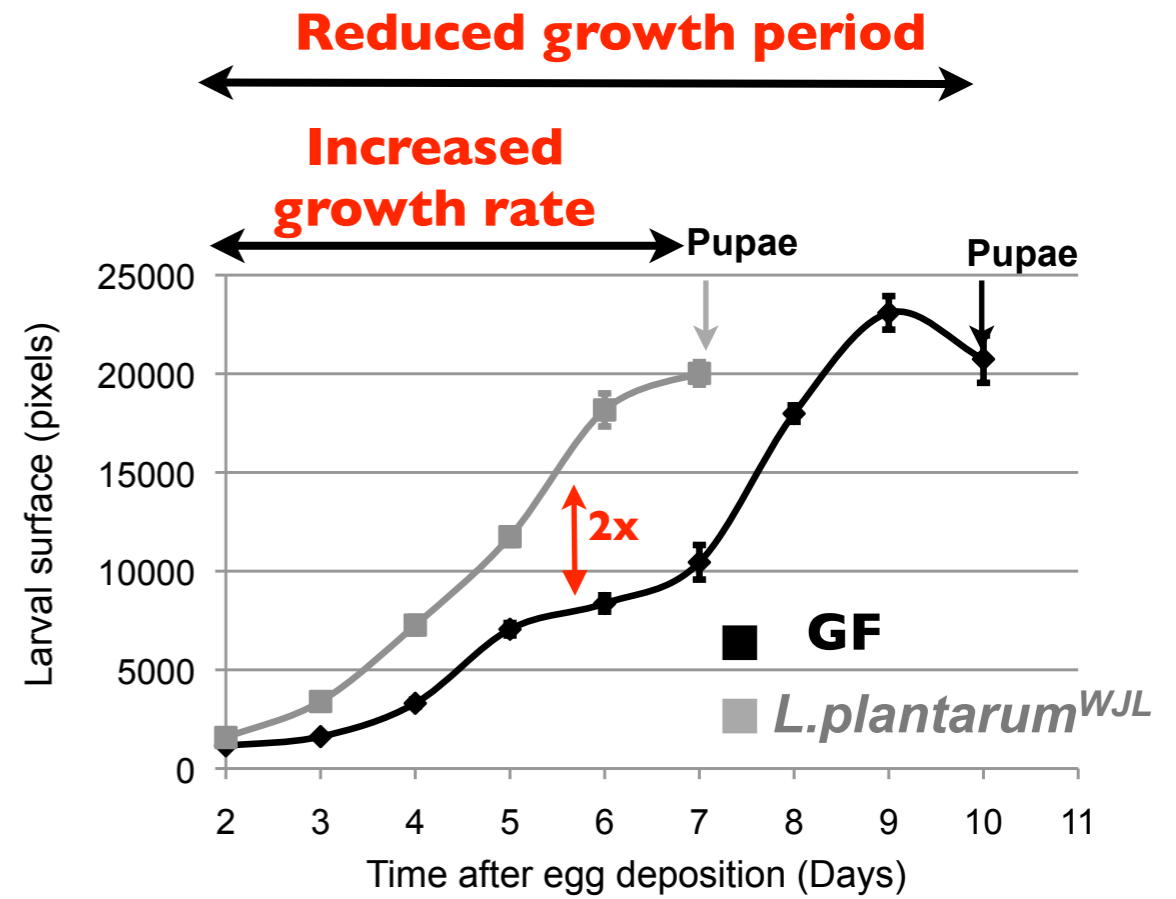
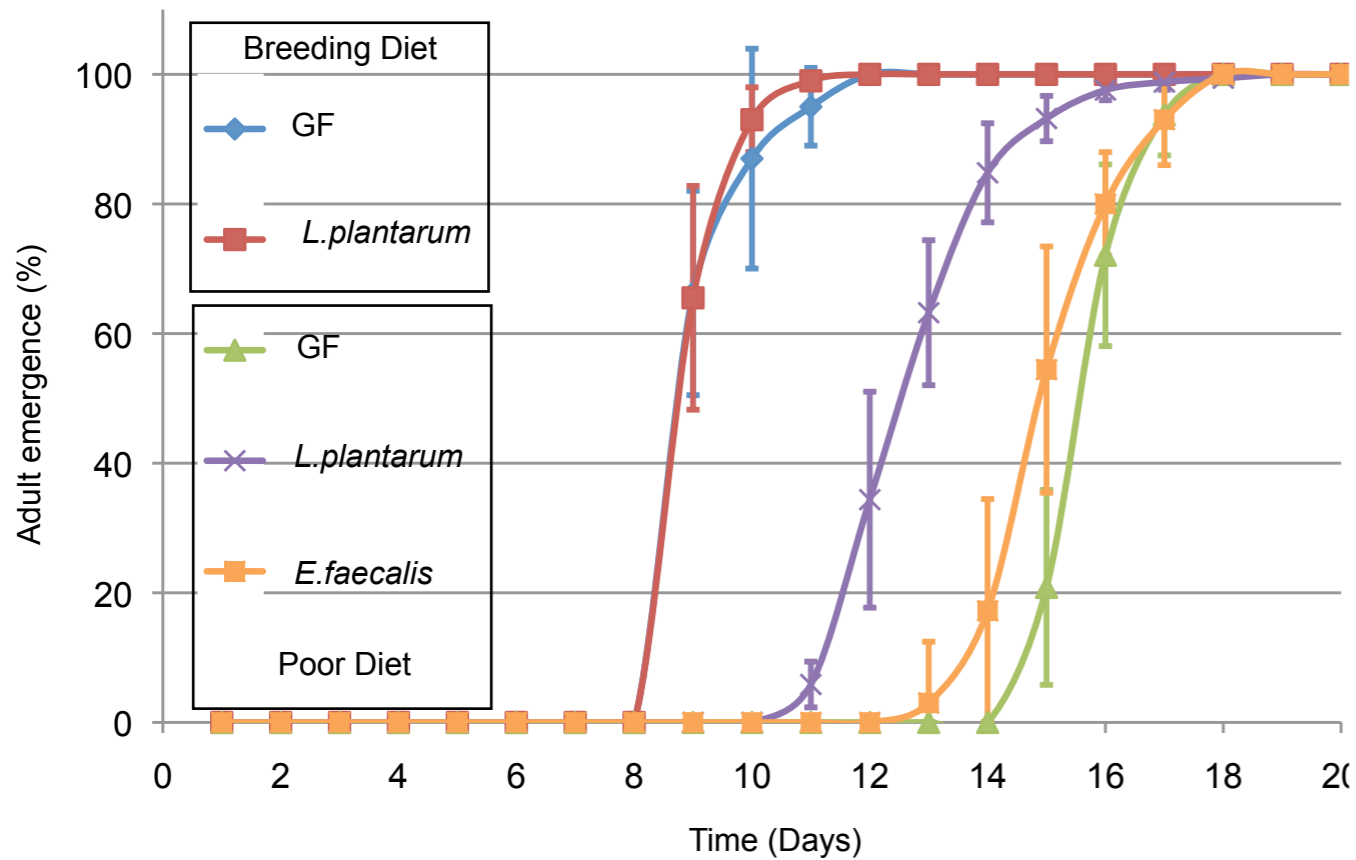
CR yw adult midgut library

Phylotype	Closest strain	% identity
<i>Enterococcus faecalis</i>	<i>Enterococcus faecalis</i> V583	99%
<i>Lactobacillus plantarum</i>	<i>Lactobacillus plantarum</i> WCFS1	99%
<i>Corynebacterium variabile</i>	<i>Corynebacterium variabile</i> DSM20132	98%

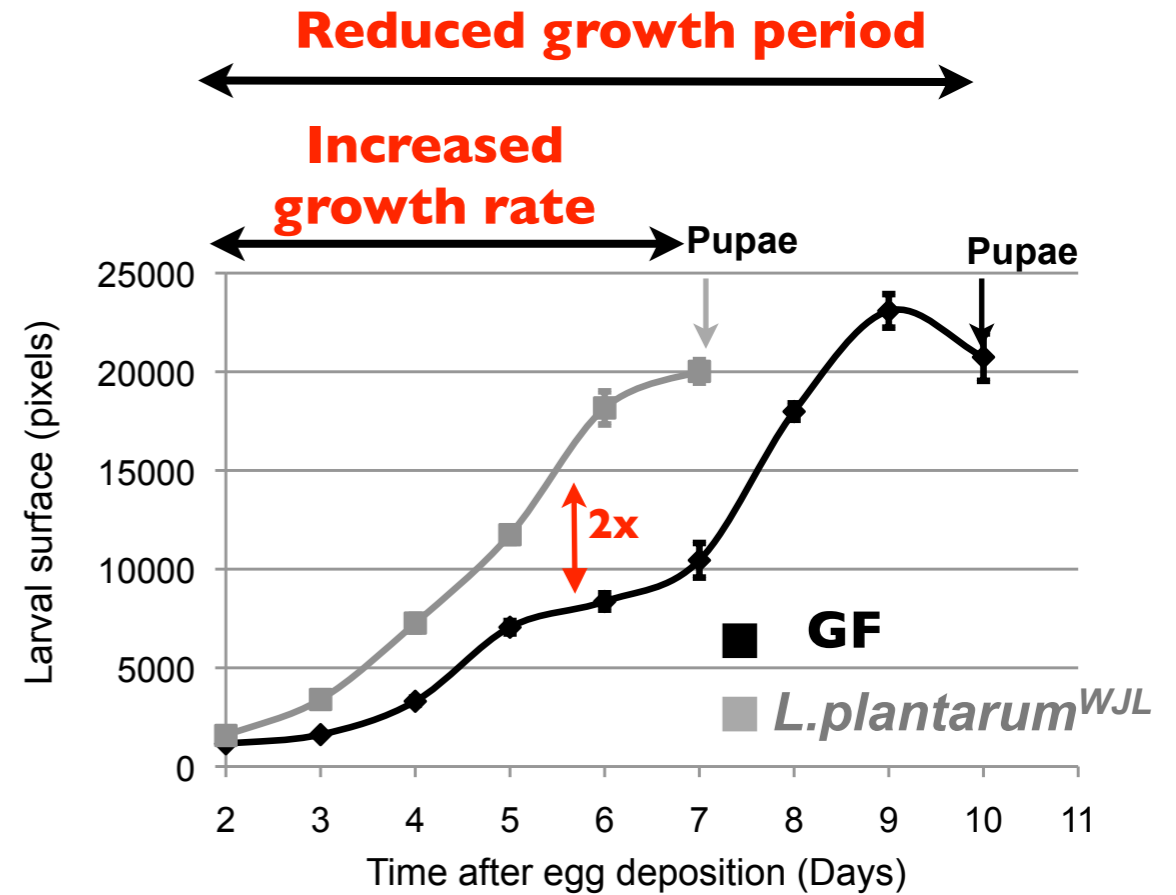
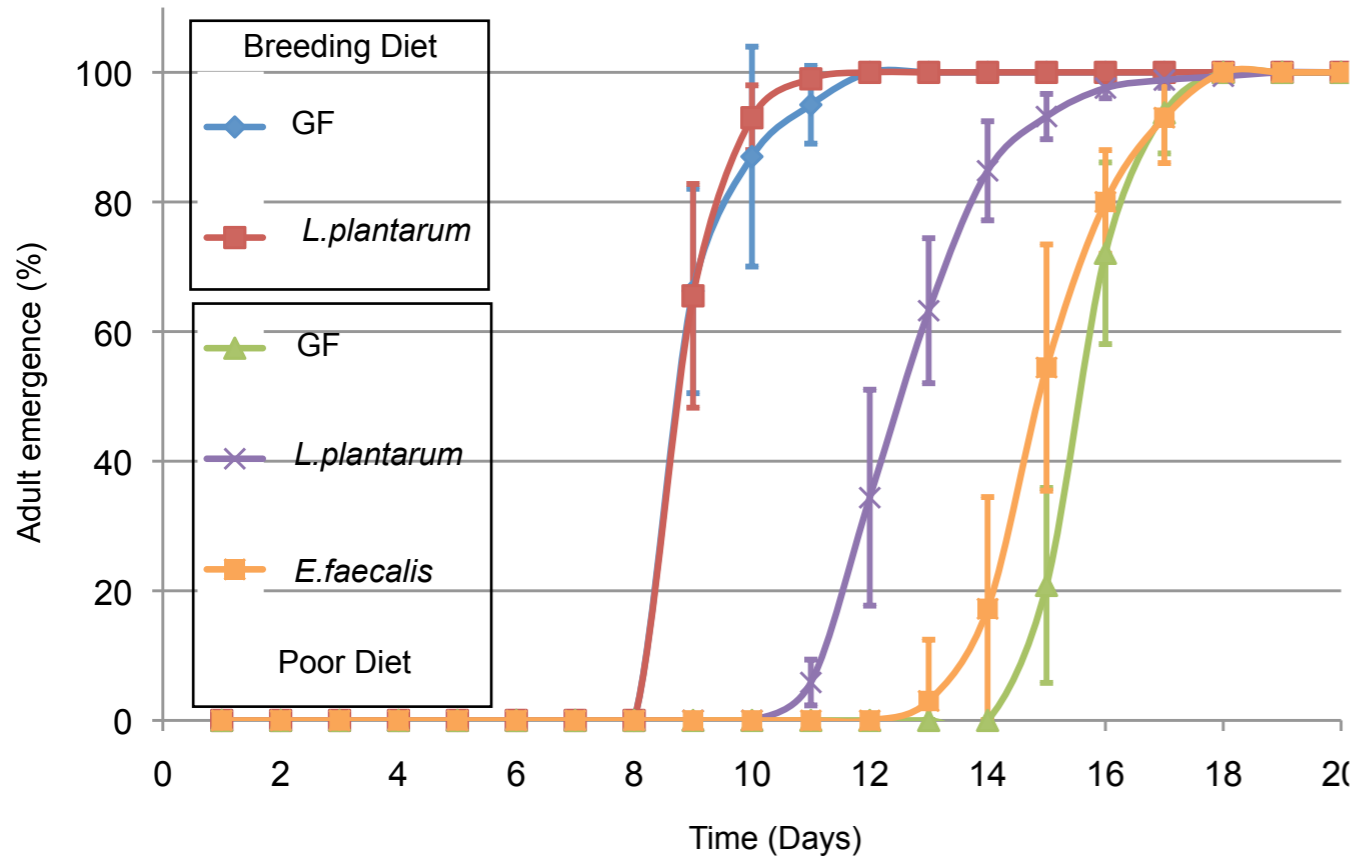
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Mono-association of GF animals with one commensal: *Lactobacillus plantarum* promotes *Drosophila* juvenile growth



Mono-association of GF animals with one commensal: *Lactobacillus plantarum* promotes *Drosophila* juvenile growth



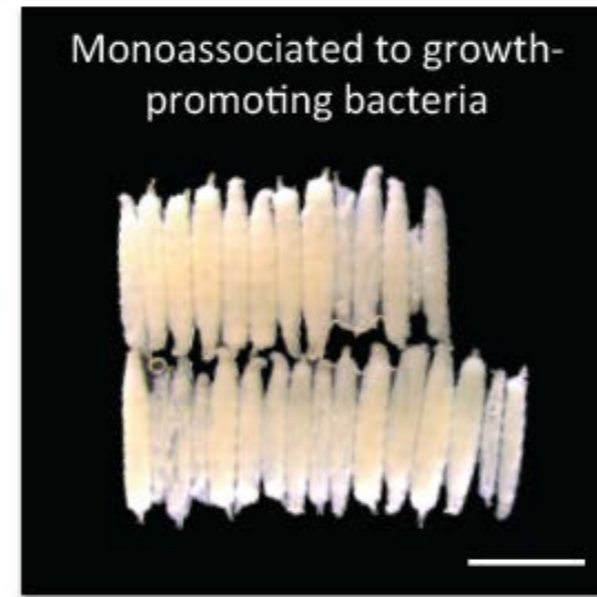
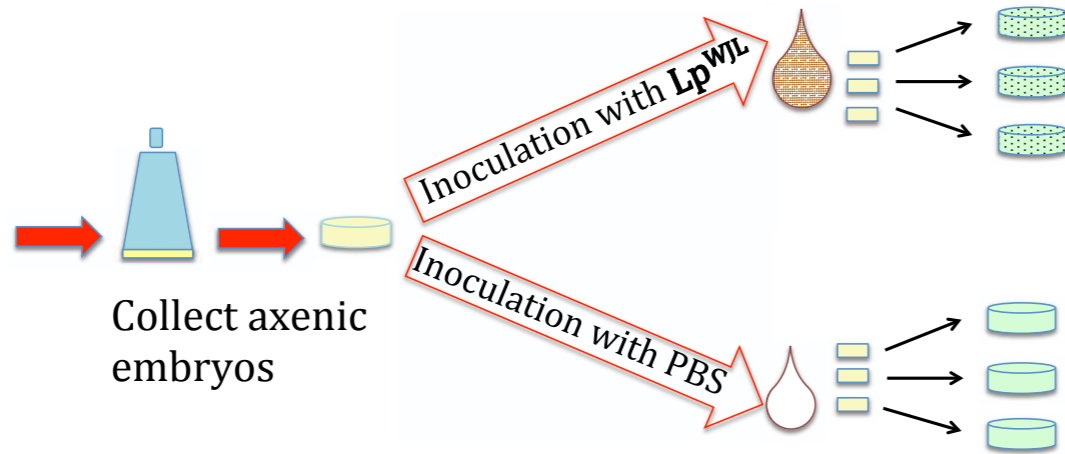
Lactobacillus plantarum^{WJL} = *Drosophila* mutualist

(some strains of *Acetobacter* too)

Selection of growth-promoting Lactobacilli strains (size gain)



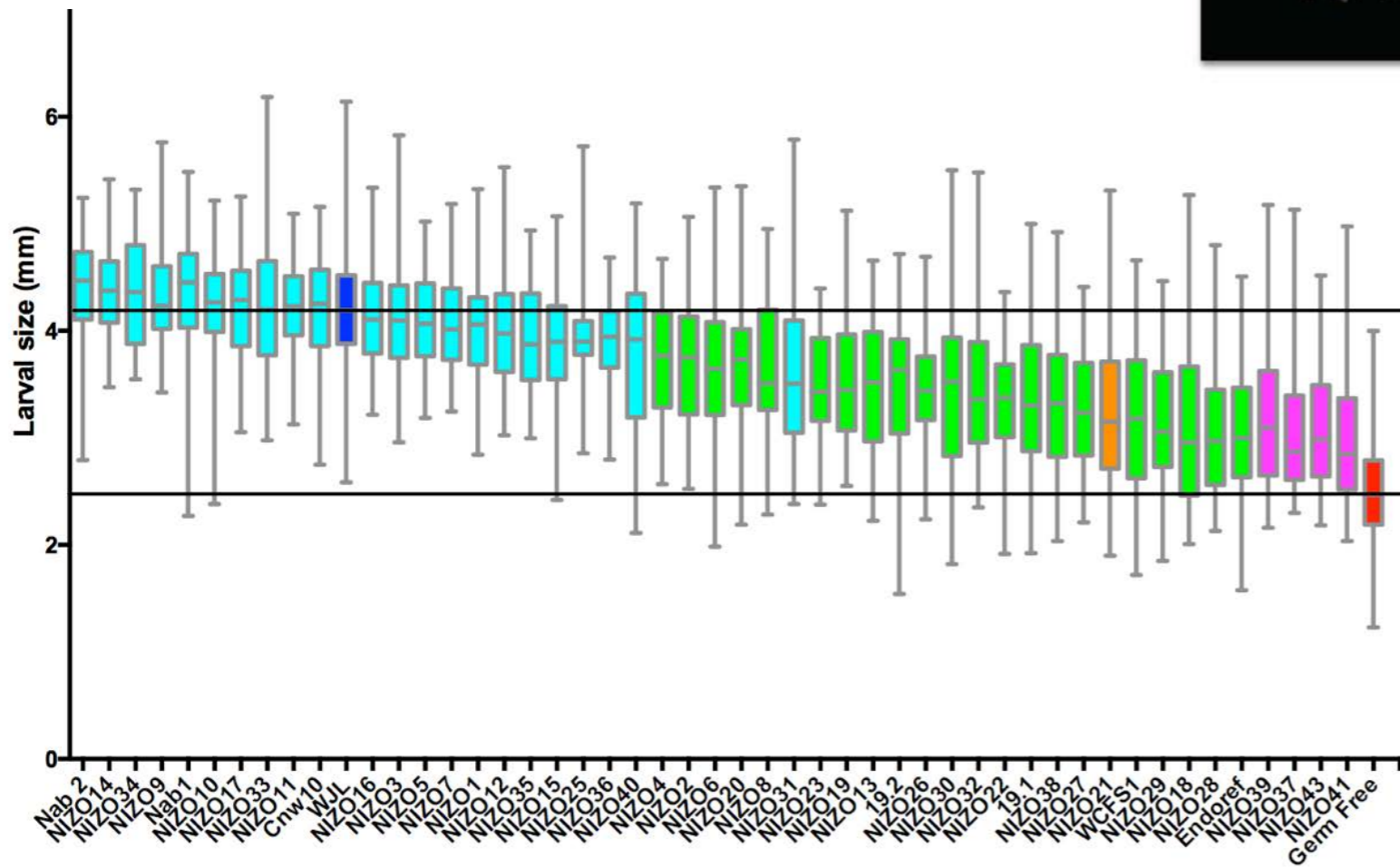
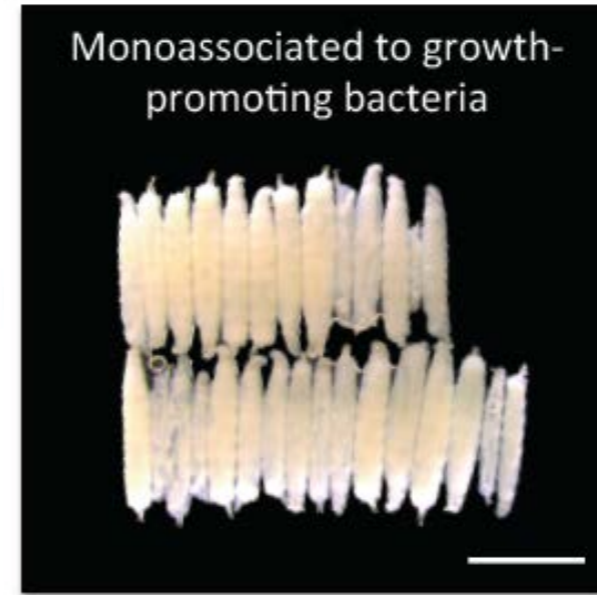
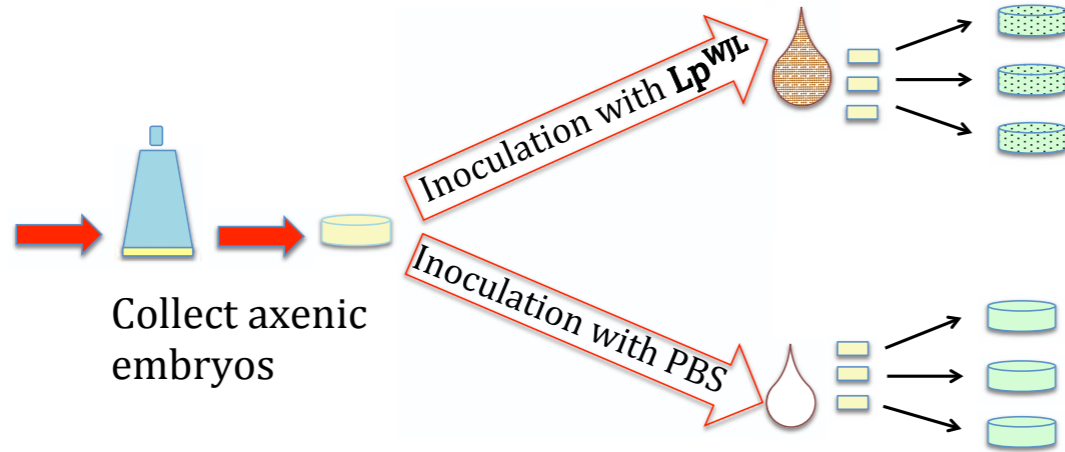
Make germ-free flies



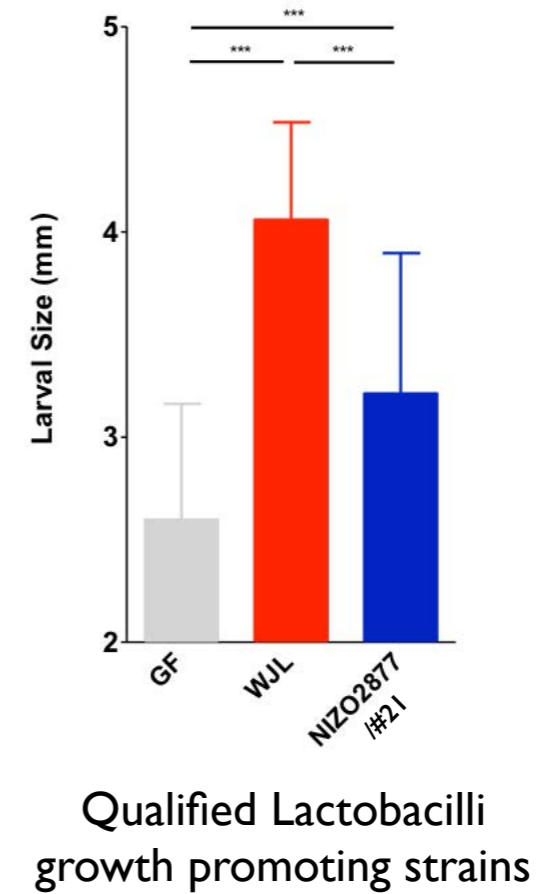
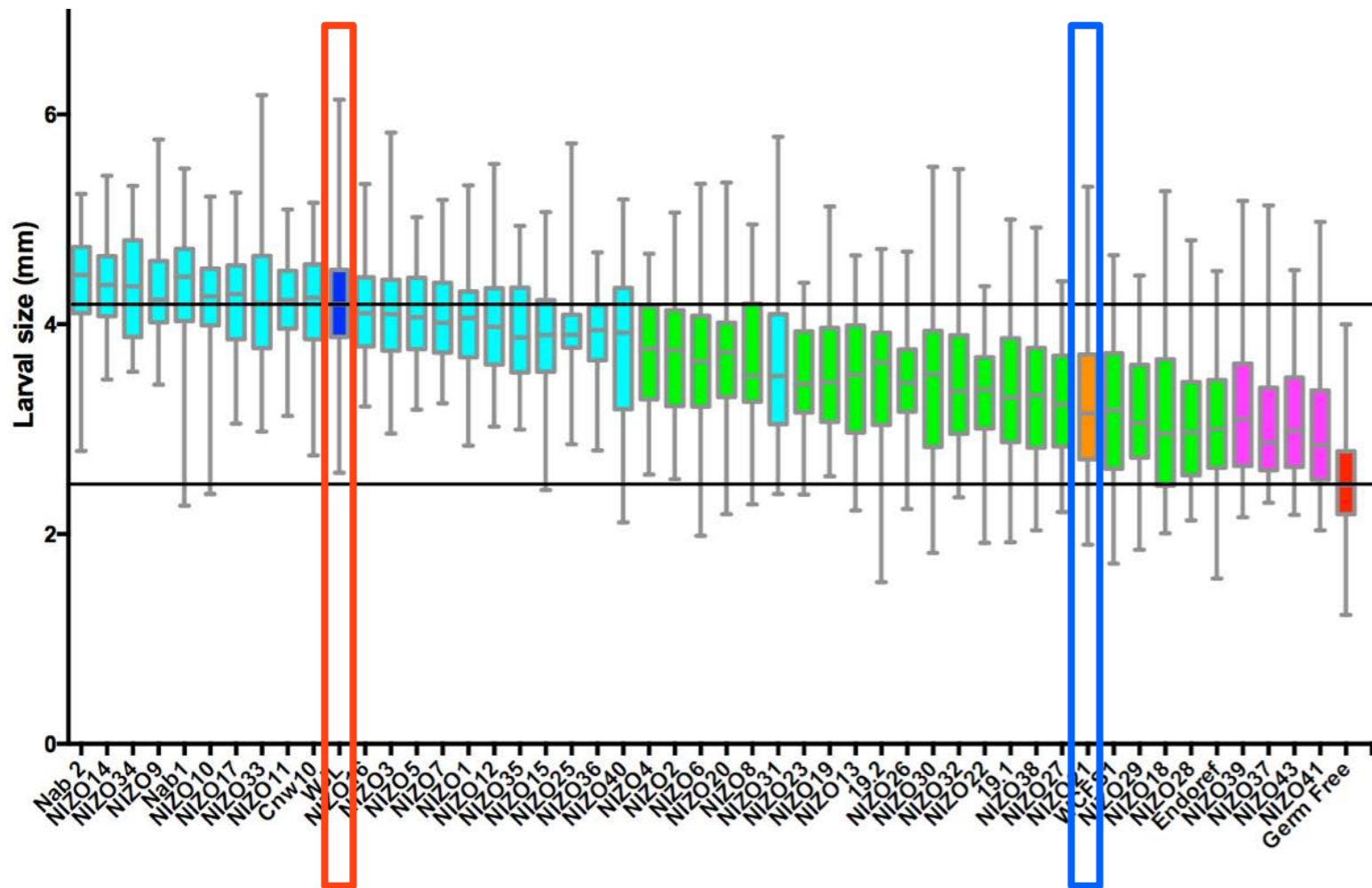
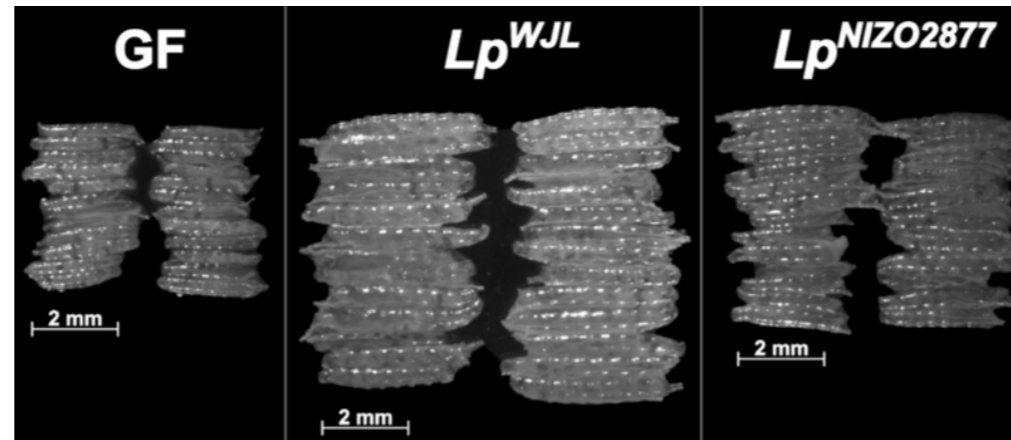
Selection of growth-promoting Lactobacilli strains (size gain)



Make germ-free flies



Selection of growth-promoting Lactobacilli strains (size gain)

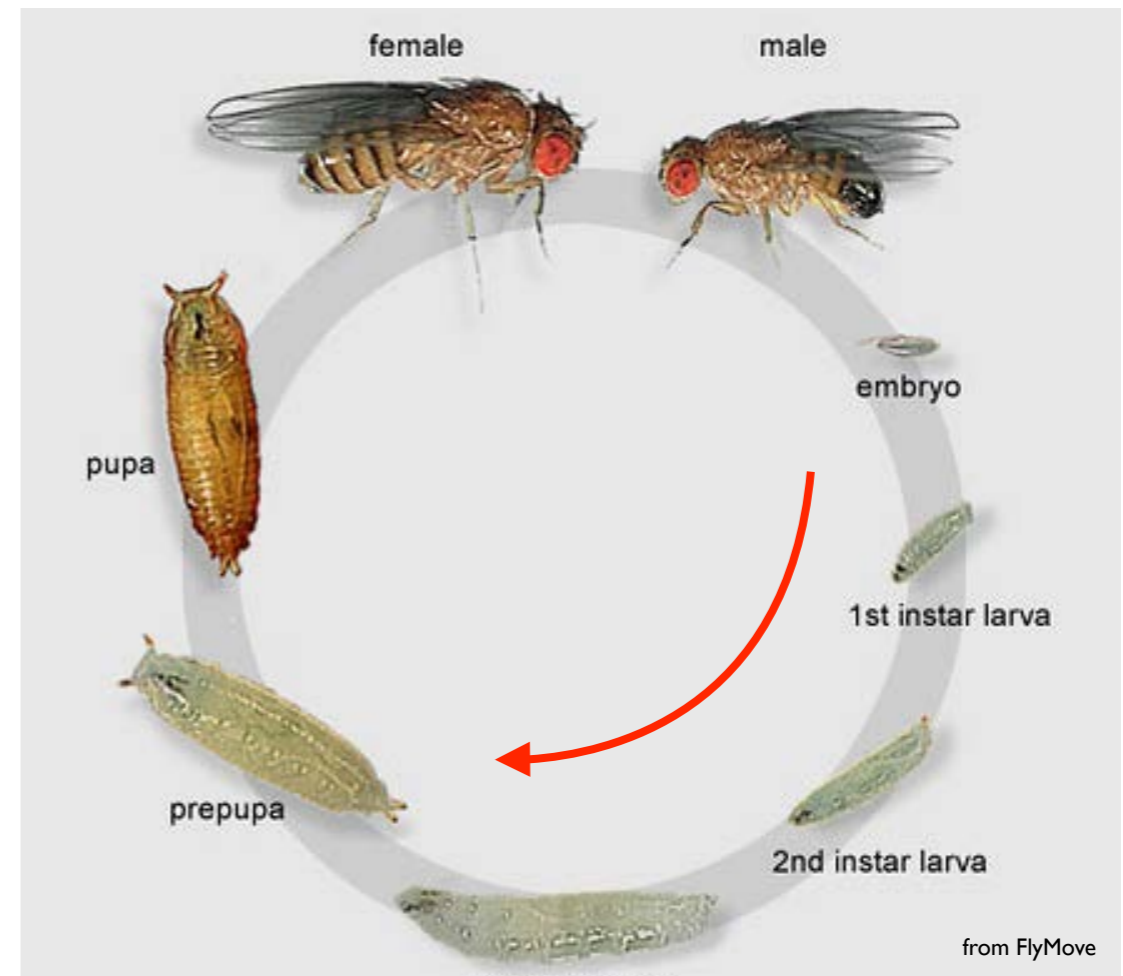


Ideal experimental model to probe the molecular underpinnings of Lactobacilli-mediated juvenile growth performance

Host side:

Upon undernutrition, microbiota in general and *L.plantarum* in particular promote juvenile growth...

...in a strain dependent manner



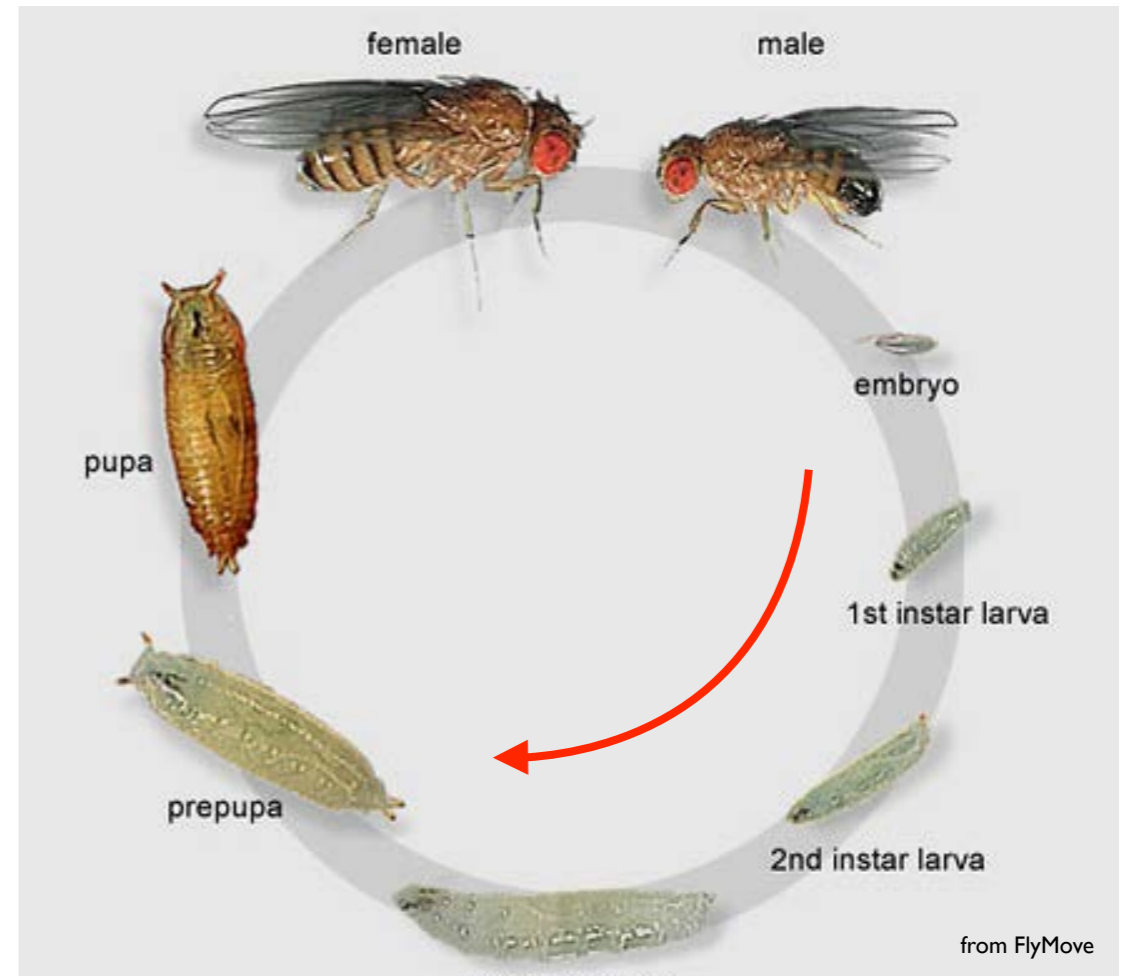
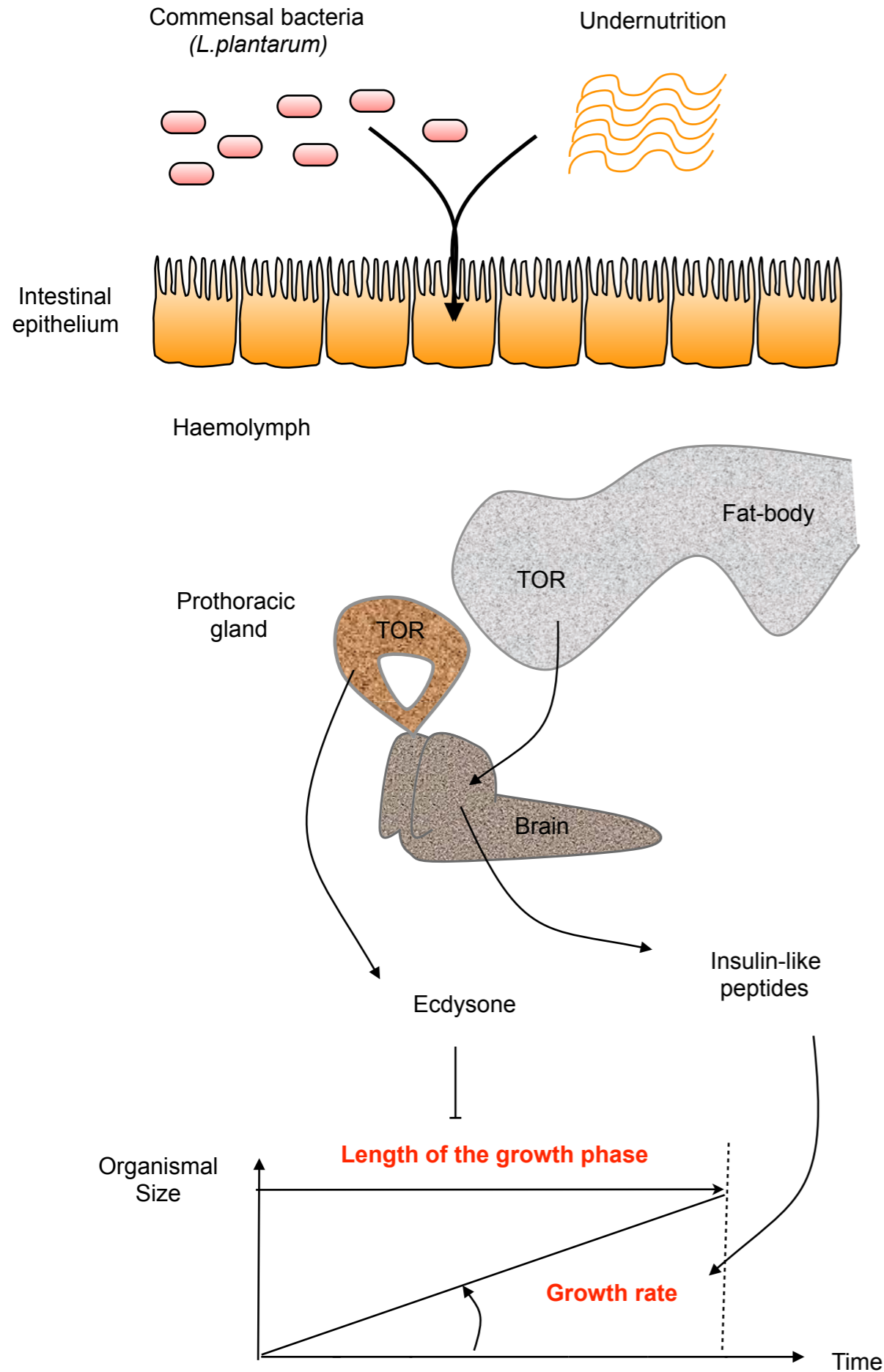
Storelli et al. (2011) Cell Metabolism 14, 403-414

Host side:

Upon undernutrition, microbiota in general and *L.plantarum* in particular promote juvenile growth...

...via enhanced maturation hormone and growth factors activity...

...in a strain dependent manner



Storelli et al. (2011) Cell Metabolism 14, 403-414

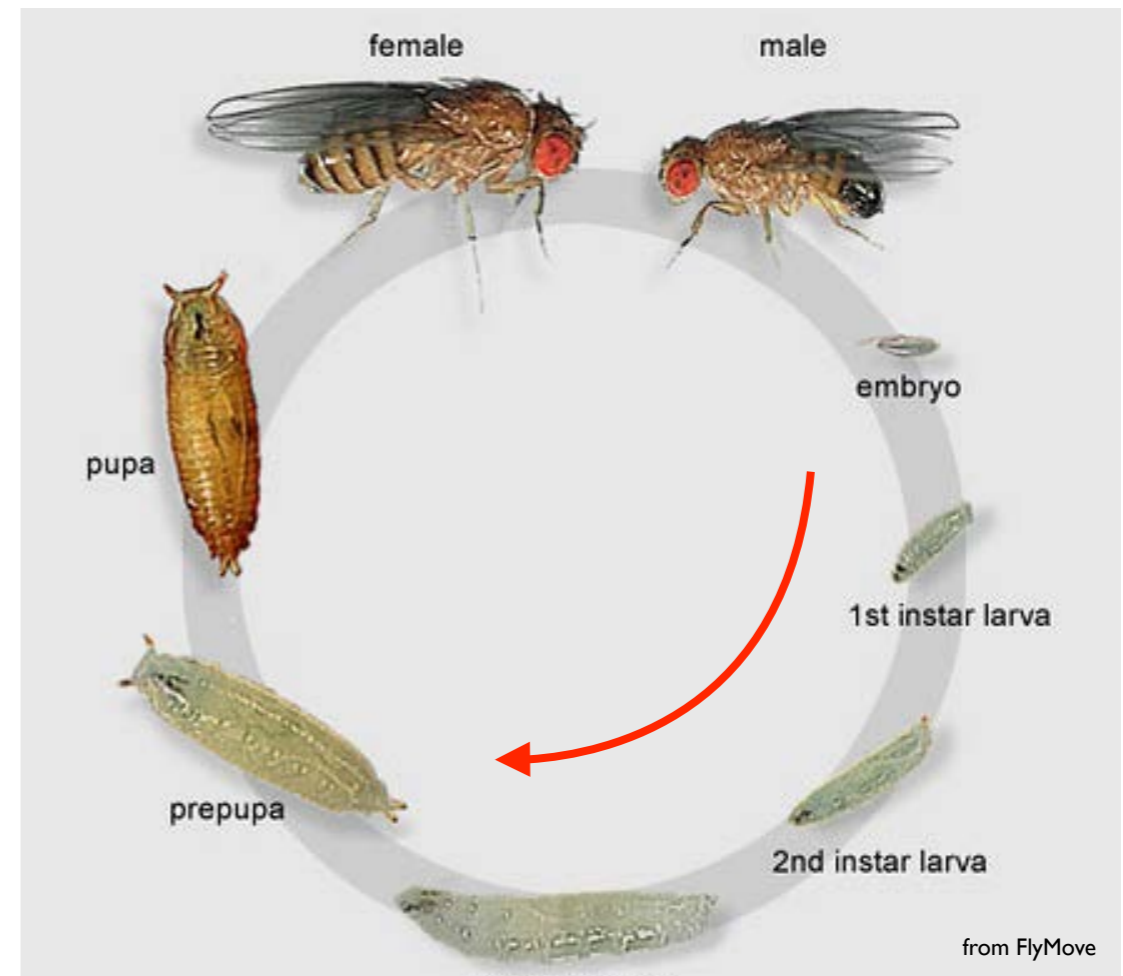
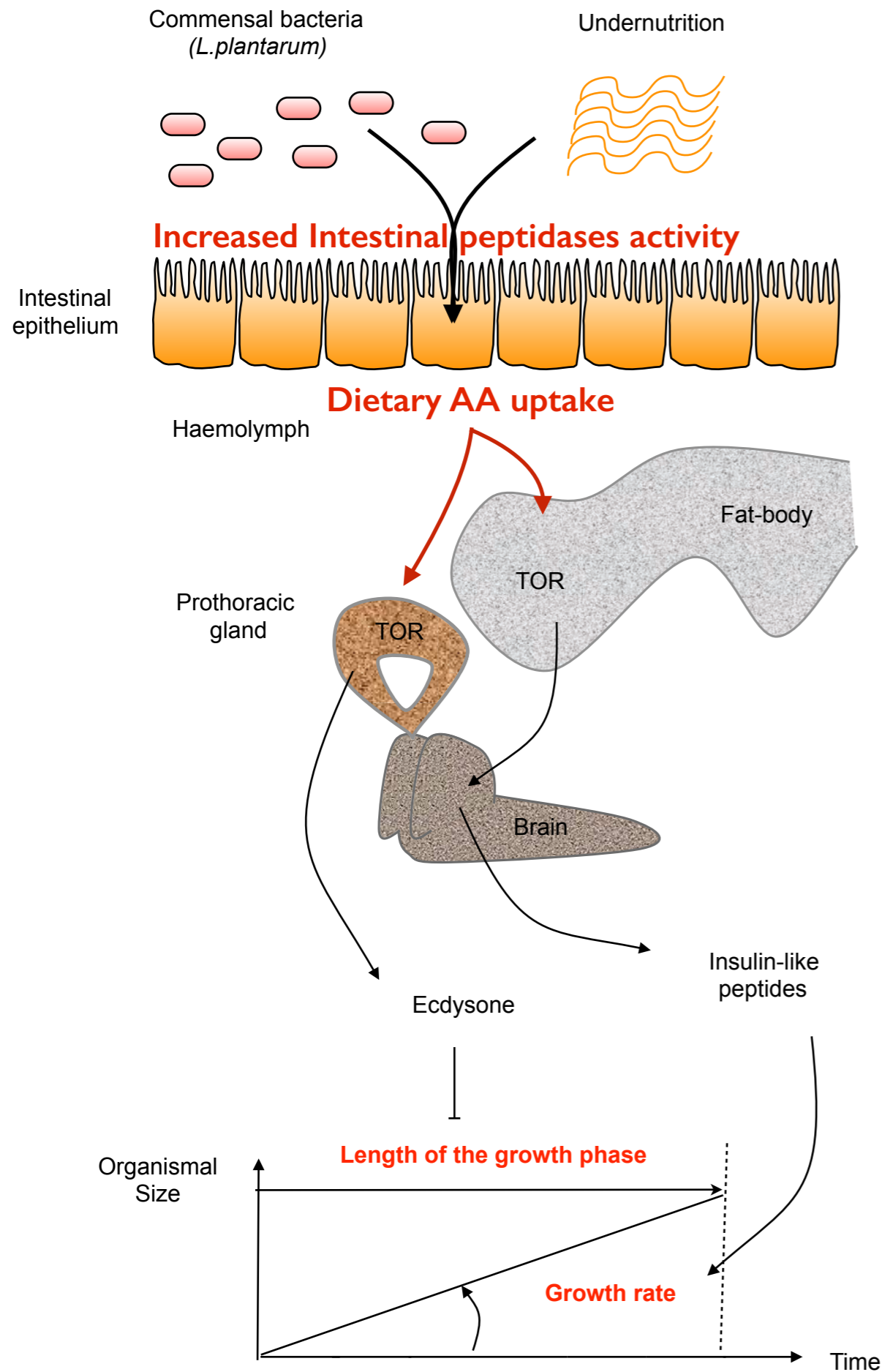
Host side:

Upon undernutrition, microbiota in general and *L.plantarum* in particular promote juvenile growth...

...via enhanced dietary AA uptake...

...via enhanced maturation hormone and growth factors activity...

...in a strain dependent manner



Storelli et al. (2011) Cell Metabolism 14, 403-414

Erkosar et al. (2014) PLoS ONE 9, e94729

Erkosar et al. (2015) Cell Host and Microbe 18, 445-55

Role of microbial environment on mammalian juvenile growth upon undernutrition?



Do the intestinal microbiota and/or selected Lactobacilli strains influence mouse juvenile growth upon chronic undernutrition

Collab:

Dr M.Schwarzer & Dr H.Kozakova
Laboratory of Gnotobiology
Institut of Microbiology
Science Academy of Czech Republic

Dr H.Vidal & Dr J.Rieusset
CarMeN Laboratory
INSERM/Univ. Claude Bernard Lyon



Gnotobiotic
Balb/c line

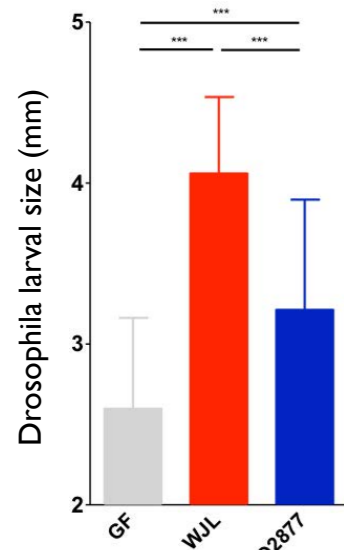
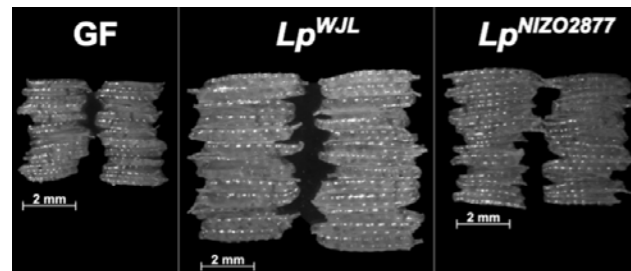
Do the intestinal microbiota and/or selected Lactobacilli strains influence mouse juvenile growth upon chronic undernutrition

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 Laboratory of Gnotobiology
 Institut of Microbiology
 Science Academy of Czech Republic

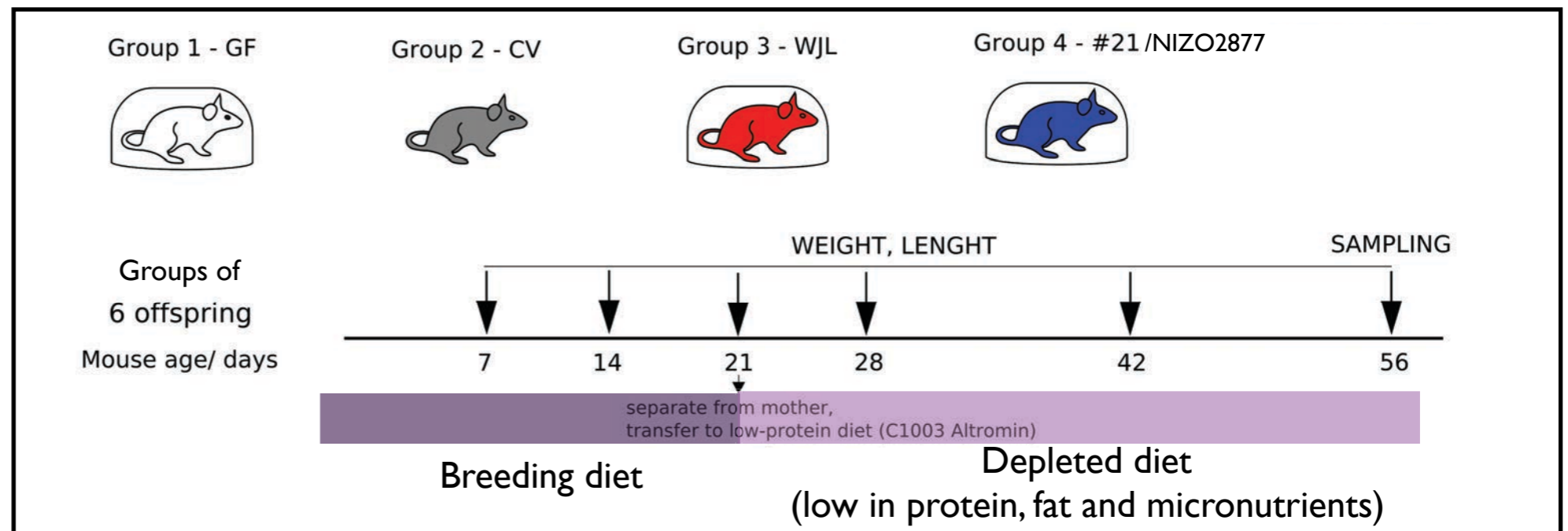
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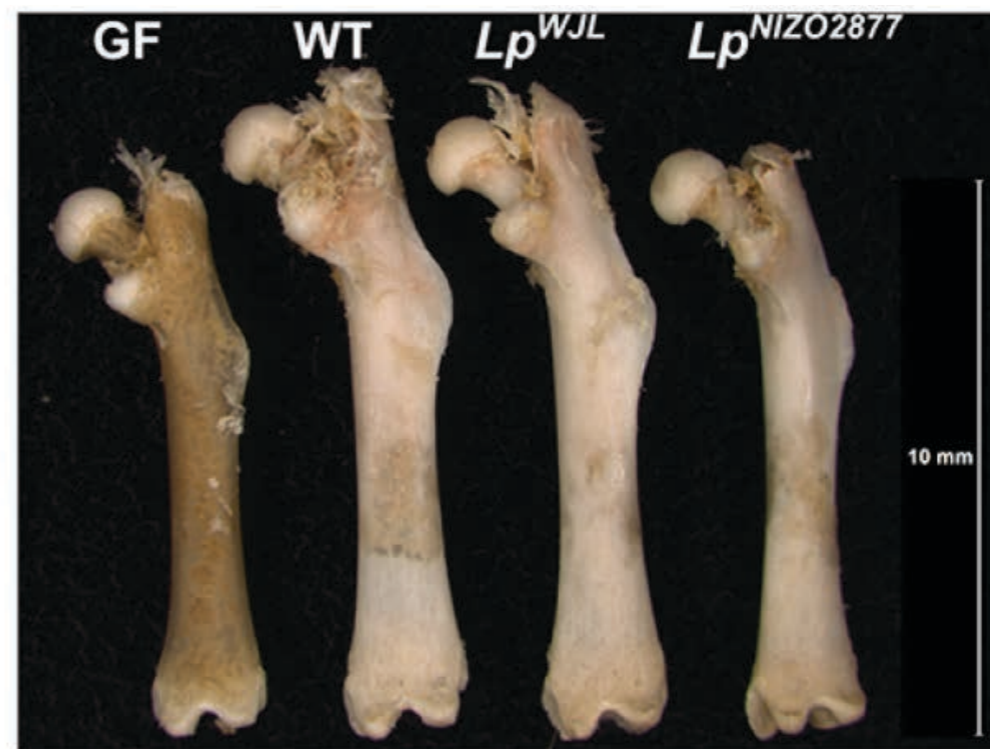
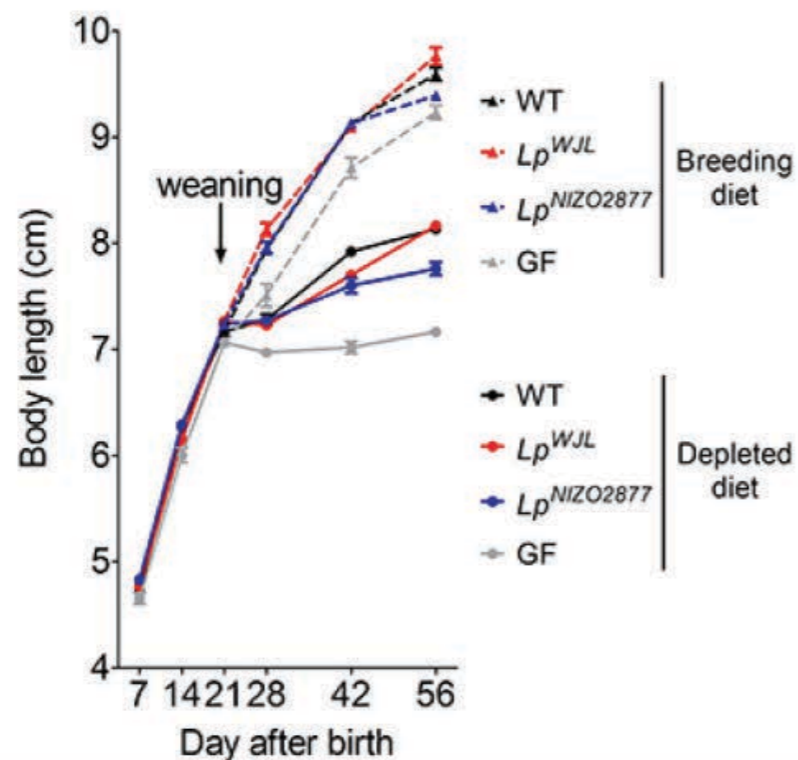
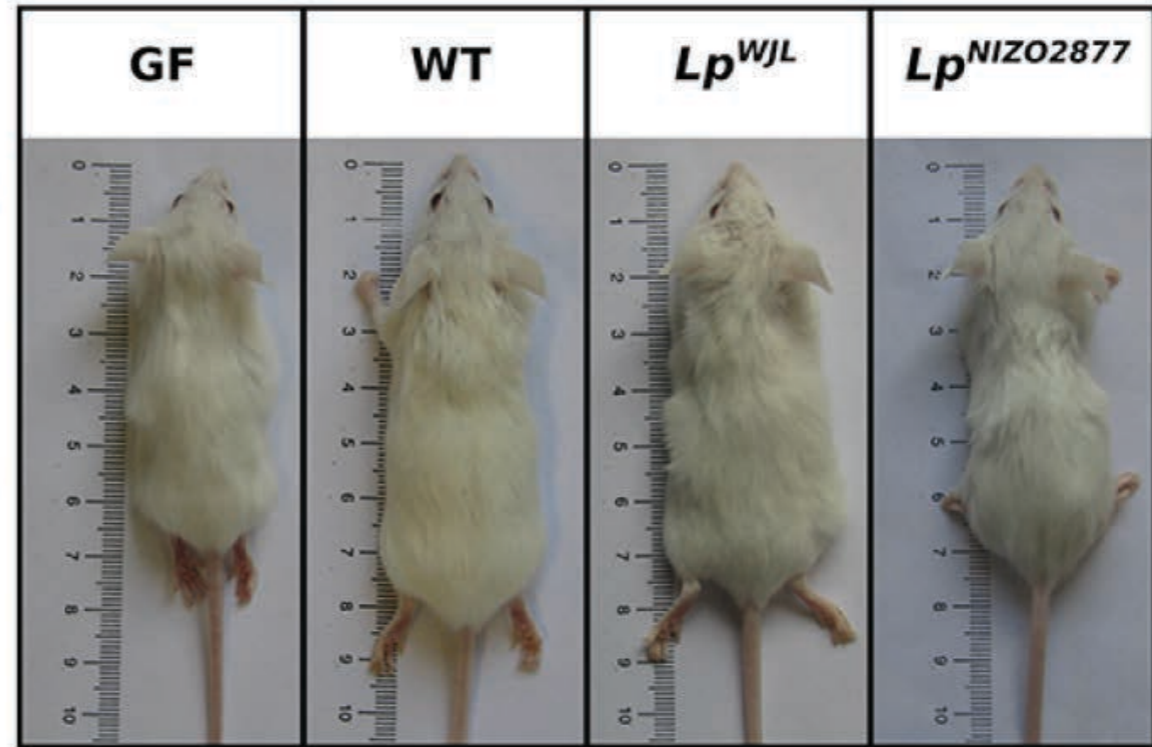
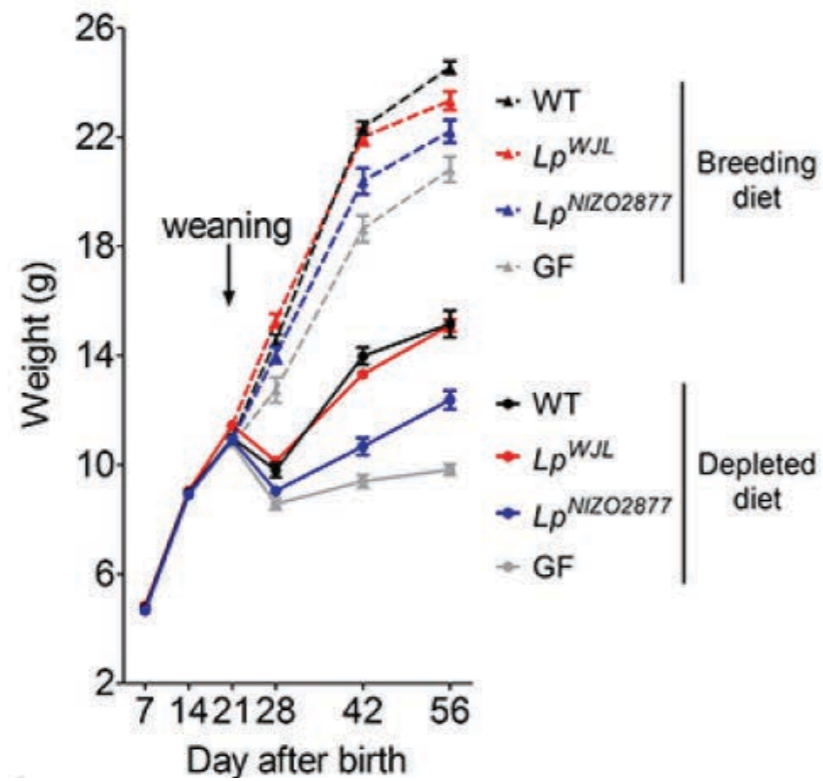
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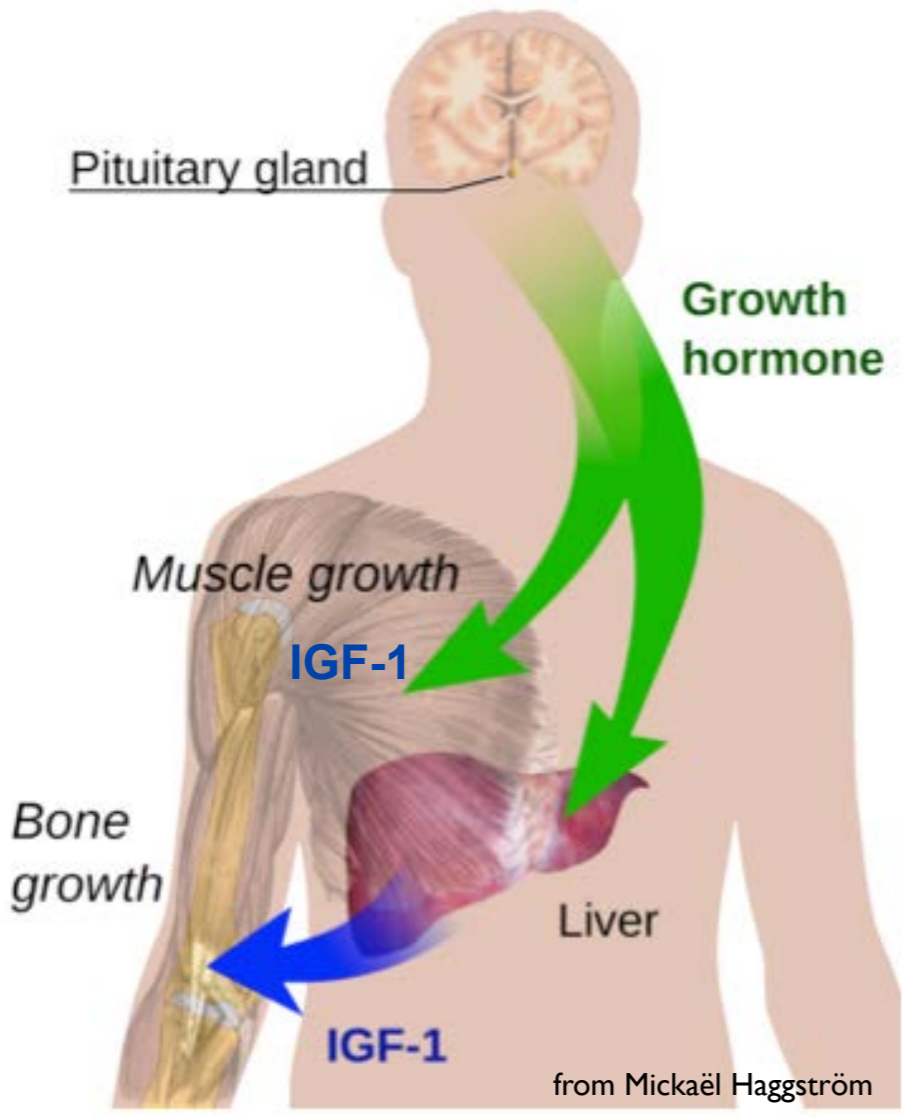
Selected Lactobacilli
growth promoting strains



Microbiota and selected Lactobacilli strains maintain mouse juvenile growth upon chronic undernutrition

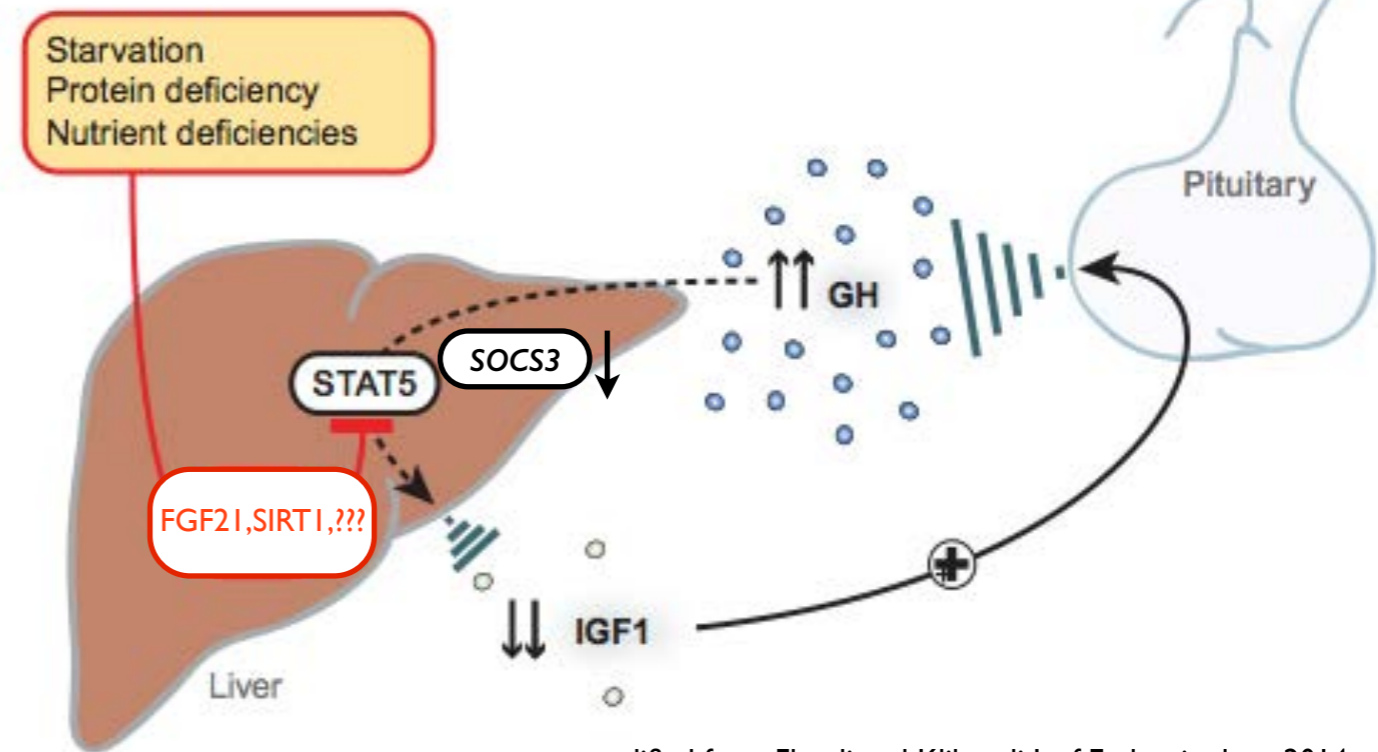
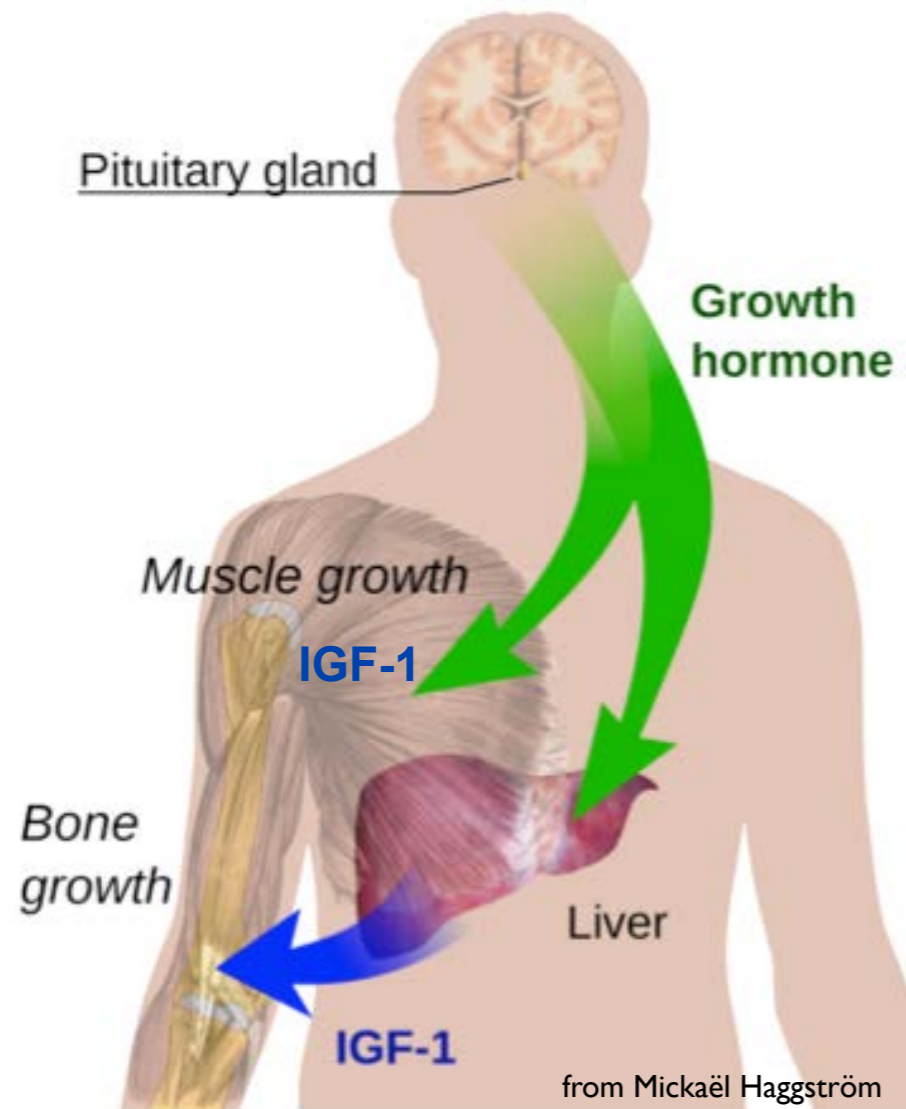


Somatotropic axis regulates post-natal growth...

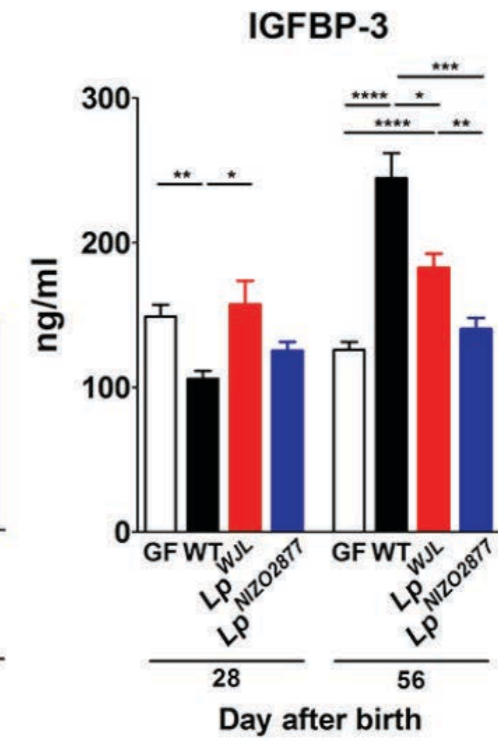
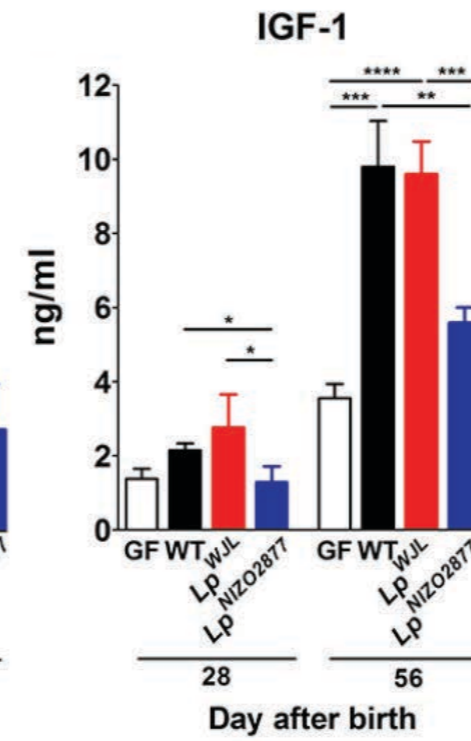
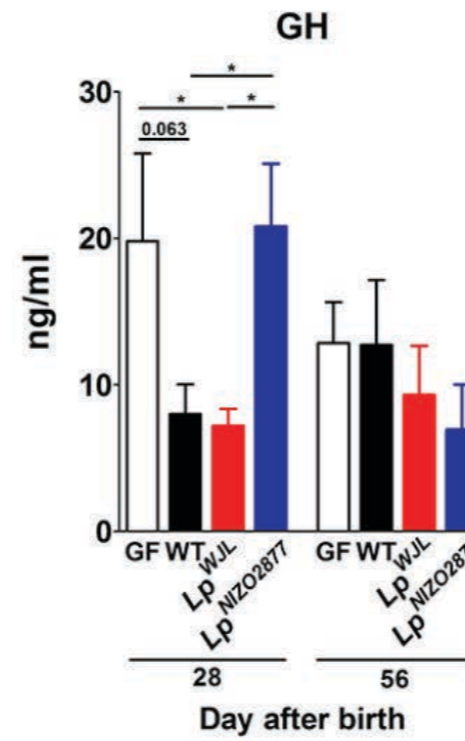
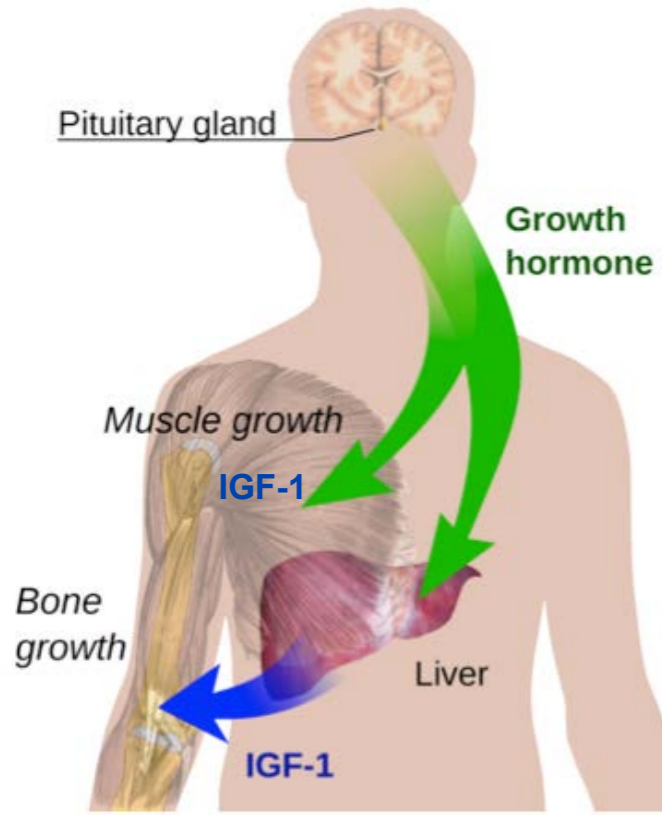


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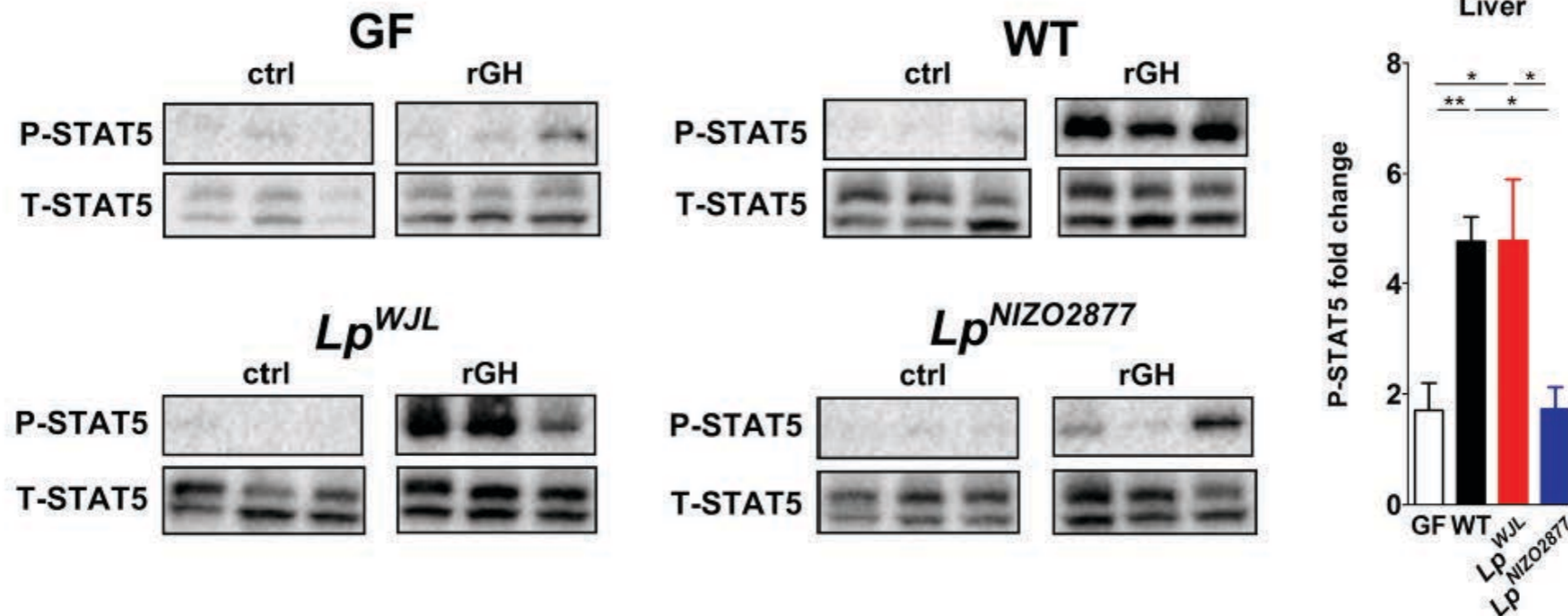
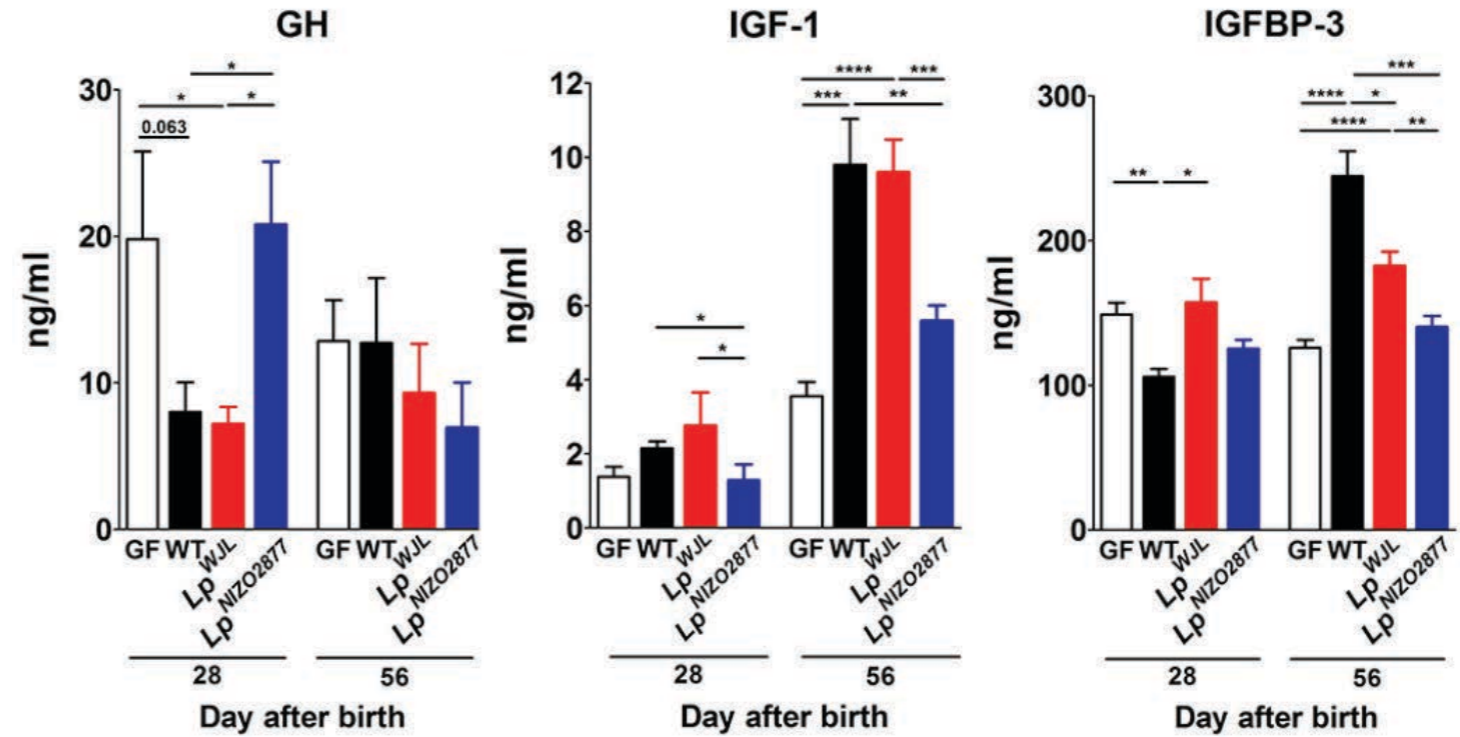
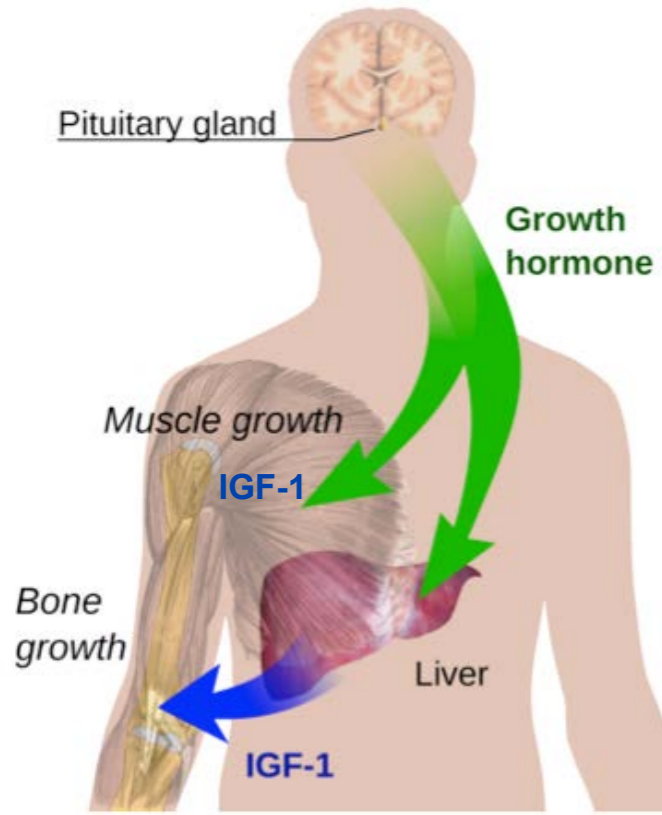
...its activity is altered upon undernutrition (state of GH-resistance)



Microbiota and selected Lactobacilli maintain tissue sensitivity to GH upon chronic undernutrition

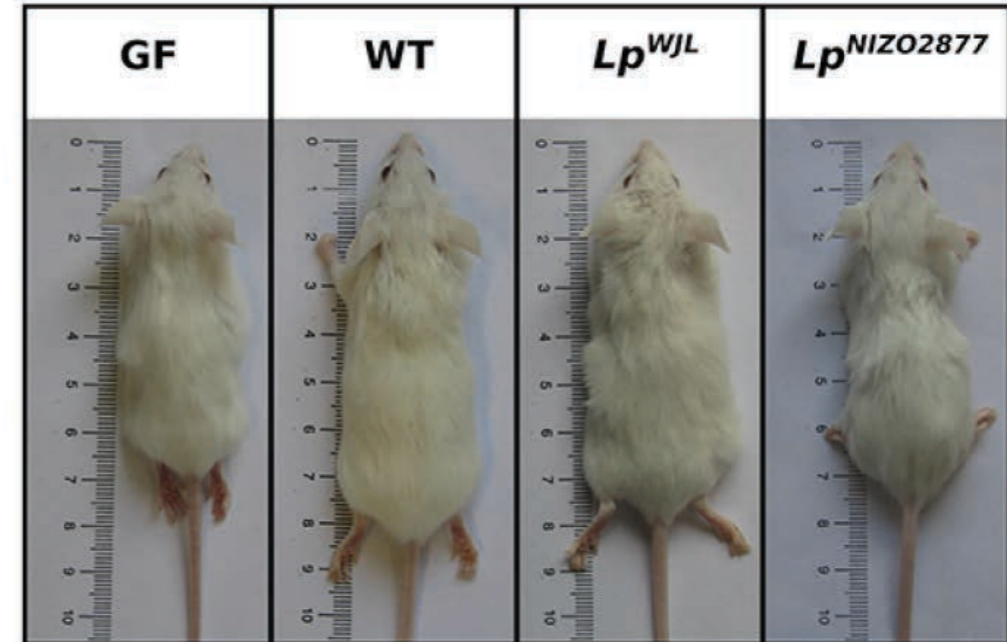
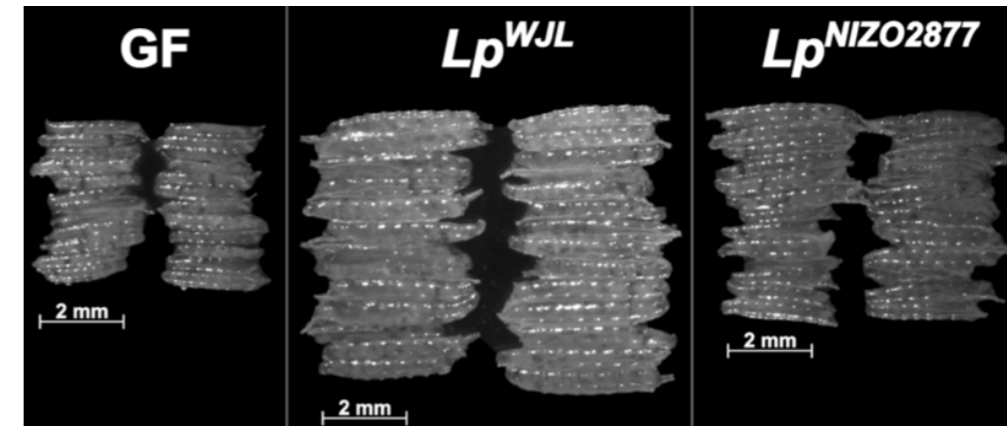


Microbiota and selected Lactobacilli maintain tissue sensitivity to GH upon chronic undernutrition



Take home messages

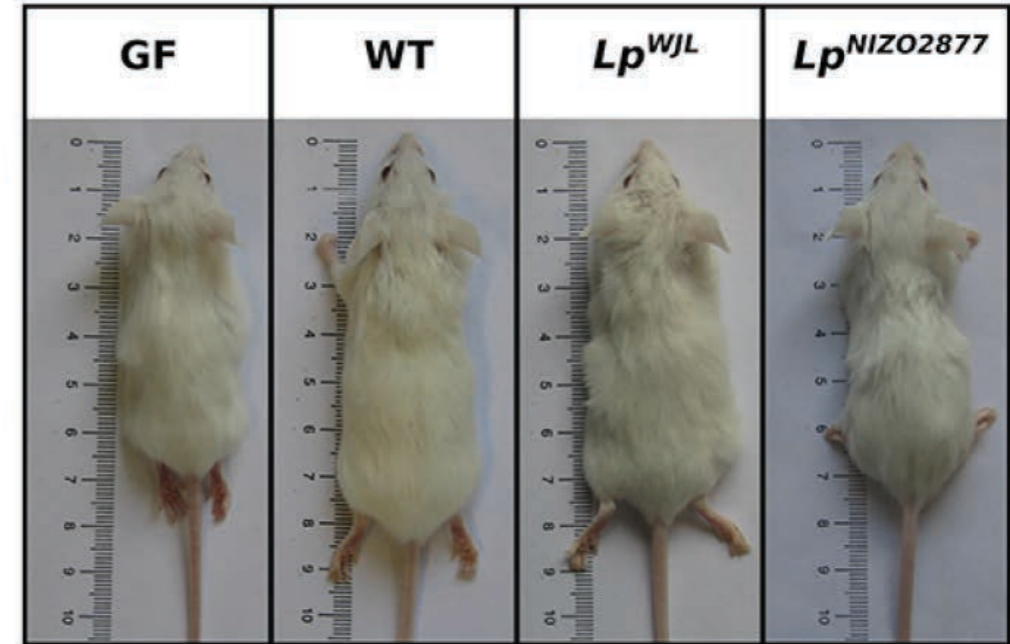
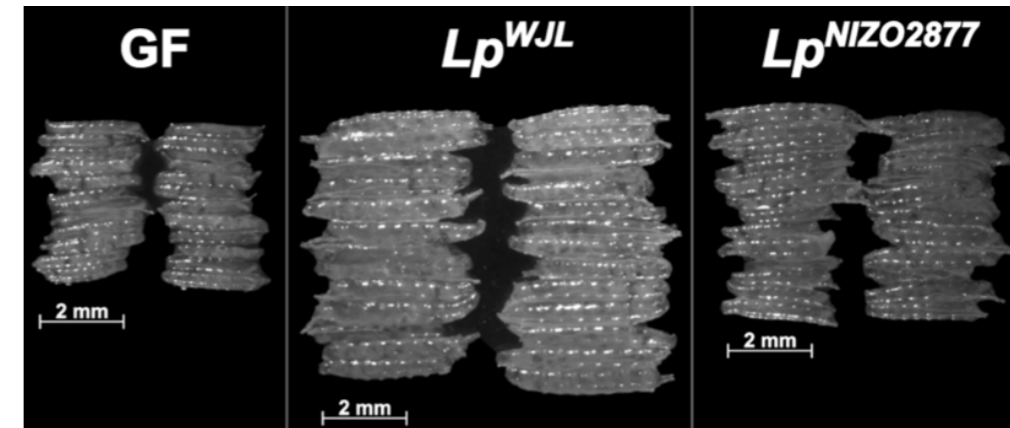
The microbiota acts as a buffer to the adverse effects of chronic undernutrition on linear growth



Take home messages

The microbiota acts as a buffer to the adverse effects of chronic undernutrition on linear growth

The microbiota maintains somatotrophic axis activity (improved GH-sensitivity)

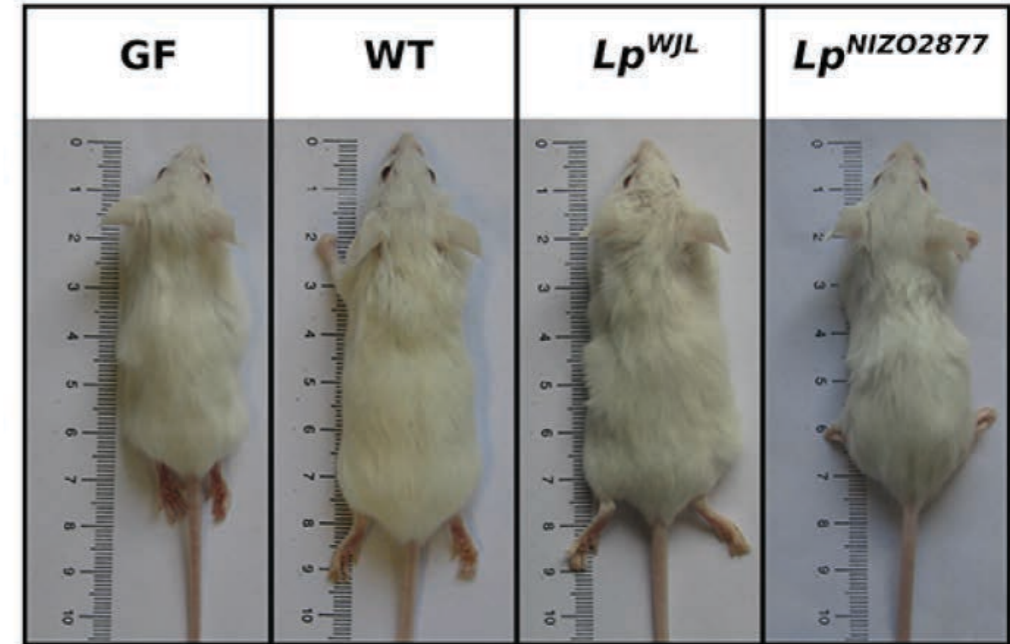
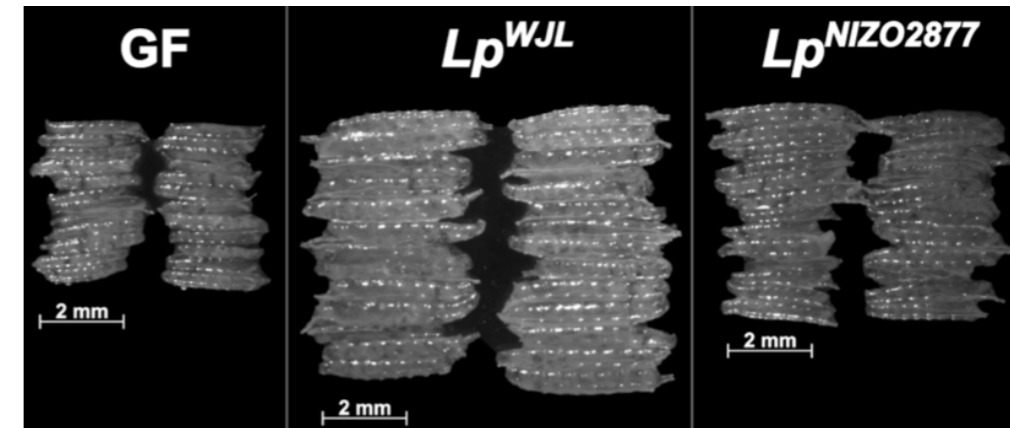


Take home messages

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Selected *Lactobacilli* strains recapitulate the microbiota effect in a strain dependent manner



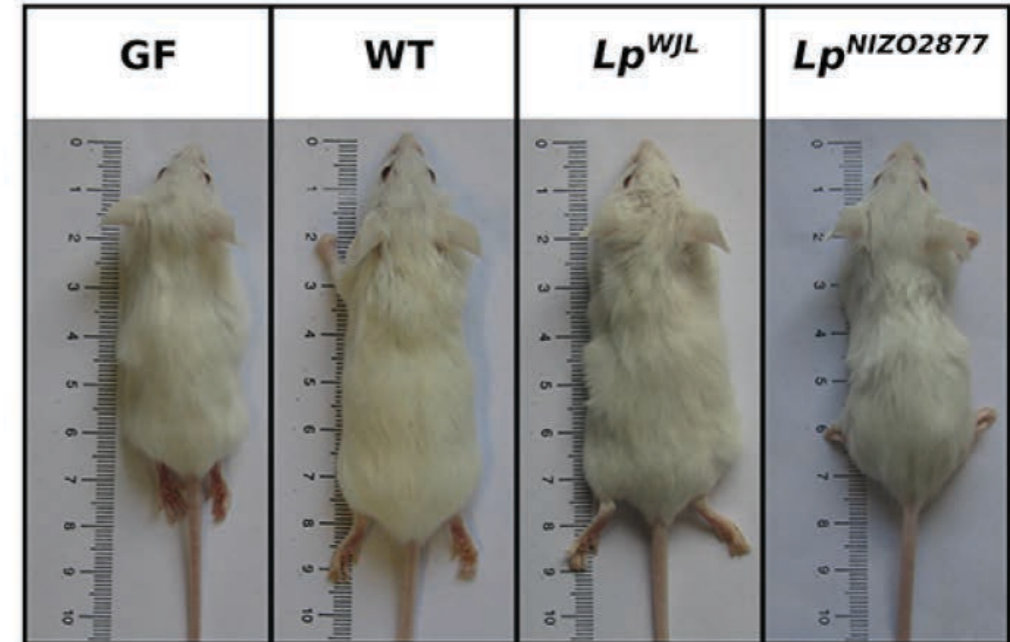
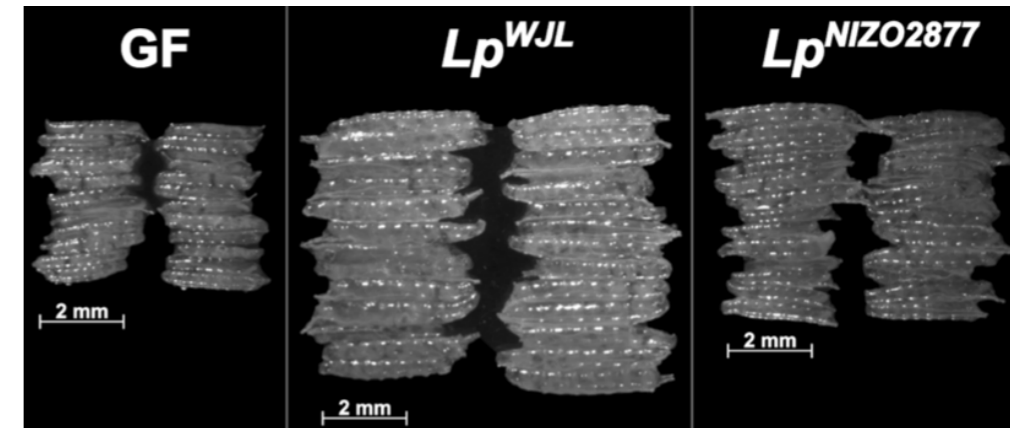
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Evolutionary conserved functionality of selected *Lactobacilli* strains to maintain juvenile growth upon chronic undernutrition



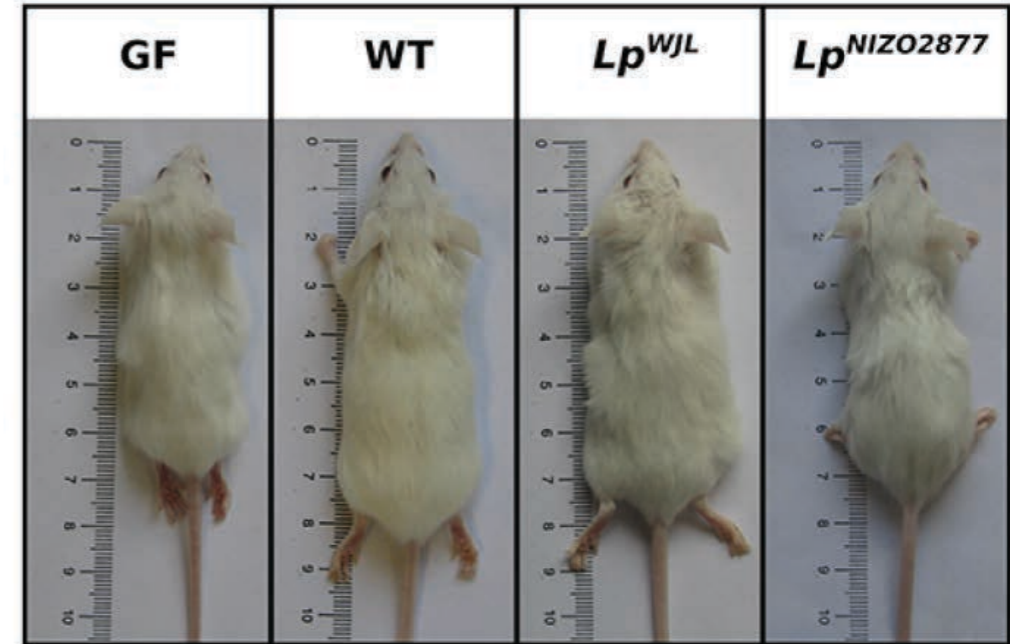
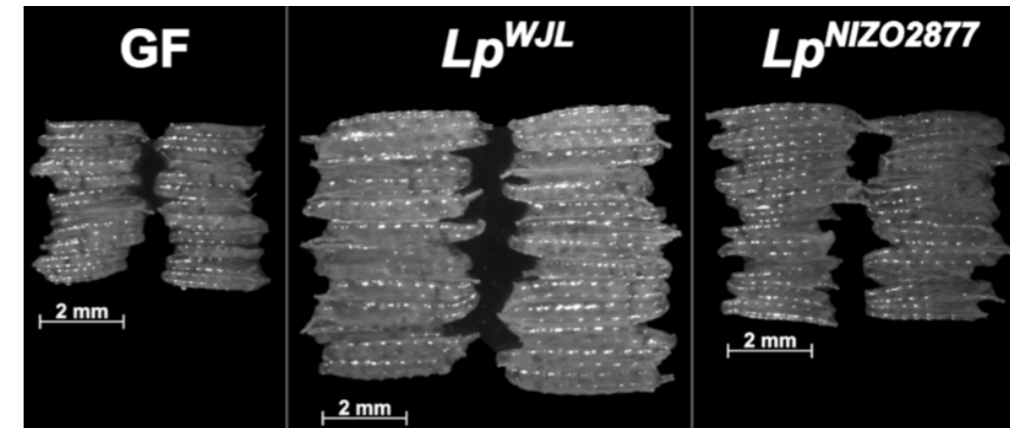
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Perspectives

Effect of Lp^{WJL} on CONV mice linear growth upon chronic undernutrition



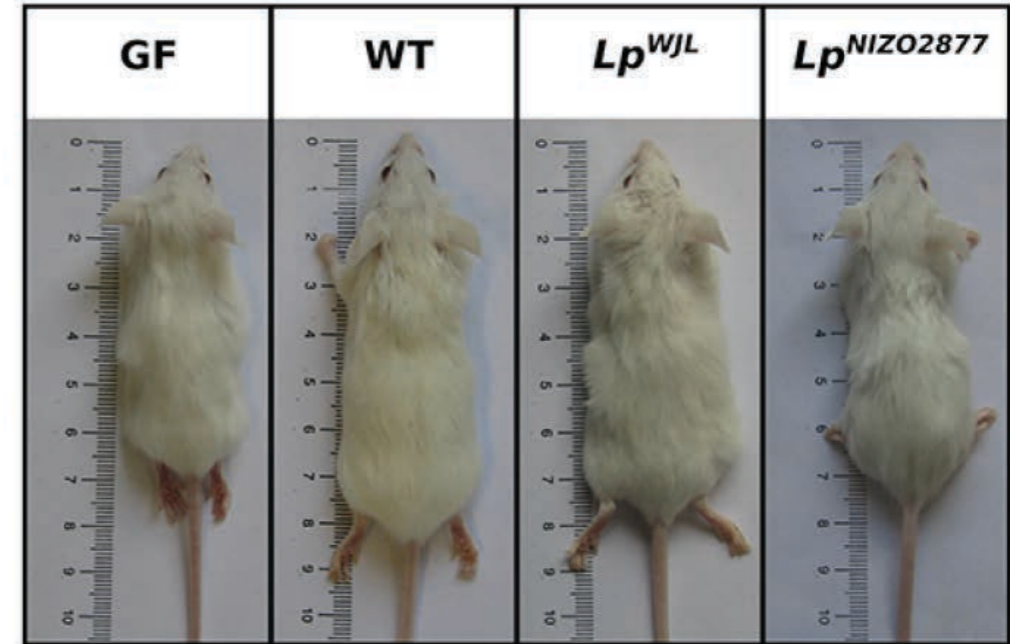
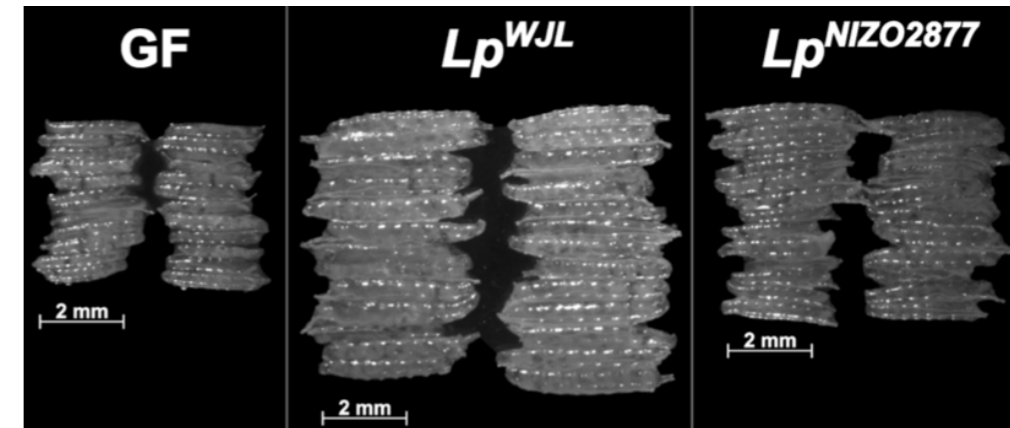
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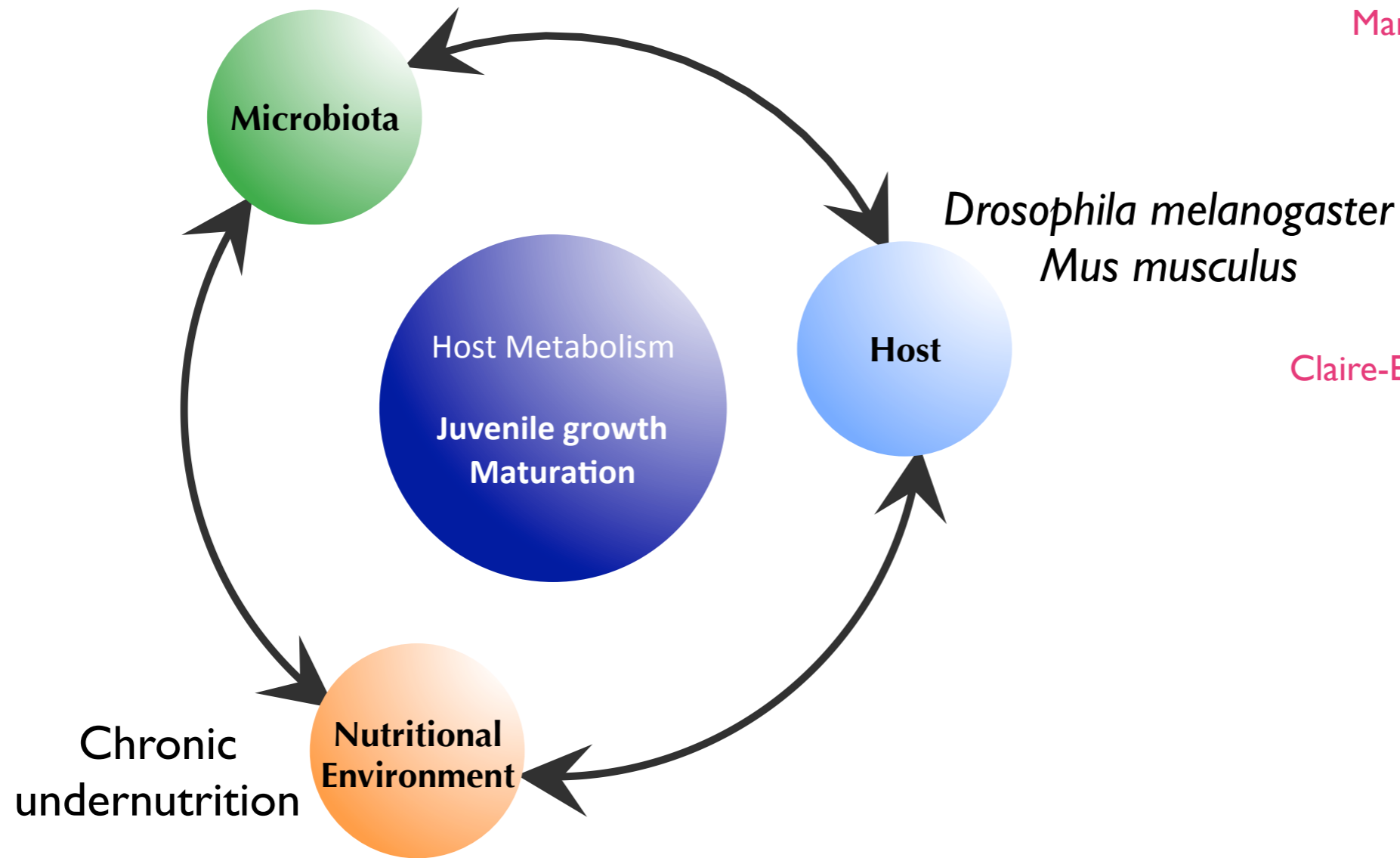
Perspectives

Effect of Lp^{WJL} on CONV mice linear growth upon chronic undernutrition

How Lp^{WJL} impinges on the somatotrophic axis activity



Lactobacillus plantarum



Lacto side

Renata Matos (post-doc)

Maria-Elena Martino (post-doc)

Hugo Gervais (AI CDD)

Fly side

Maura Strigini (post-doc)

Dali Ma (IR CDD)

Mélisandre Téfit (Ph'D)

Claire-Emmanuelle Indelicato (Ph'D)

Loan Bozonnet (AI CDD)

Mouse side

Martin Schwarzer (post-doc)

Kassem Makki (post-doc)

Anne Lambert (AI UCBLI)

Past members

Berra Erkosar (post-doc)

Gilles Storelli (Ph'D)

Mélanie Mitchell (IE CDD)

Noémie Bozonnet (IE CDD)

