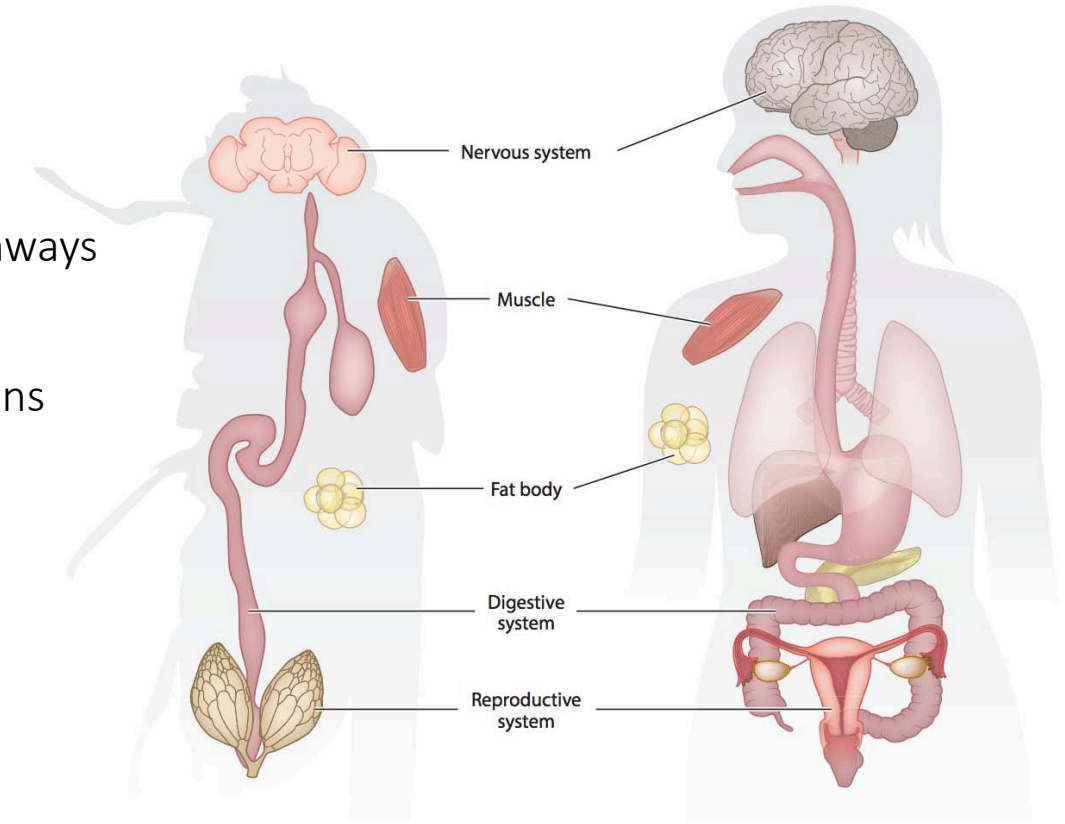
Drosophila as a model for nutritional physiology



Pierre Léopold – Institut Curie, Paris

Drosophila has organs

- conserved metabolic pathways
- conserved metabolic organs
- conserved hormones
- large population samples



- organ-specific gene silencing
- organ explant co-culture
- identification of neural circuitries

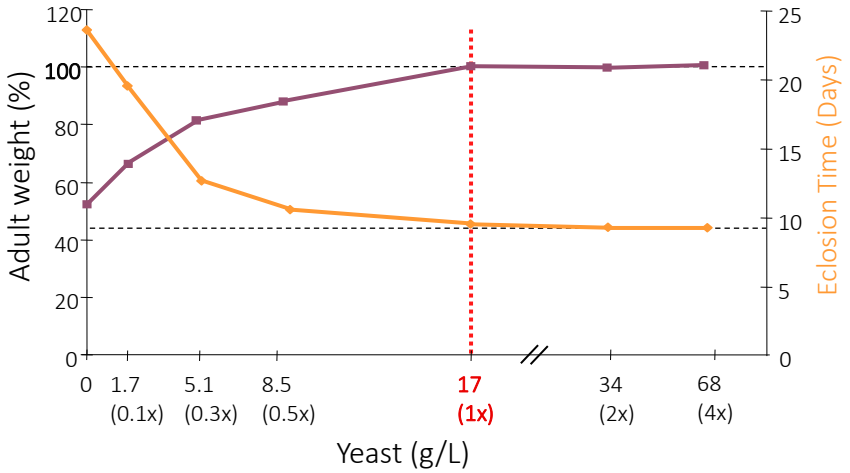
from Droujinine and Perrimon, Ann. Rev.Genet. 2016

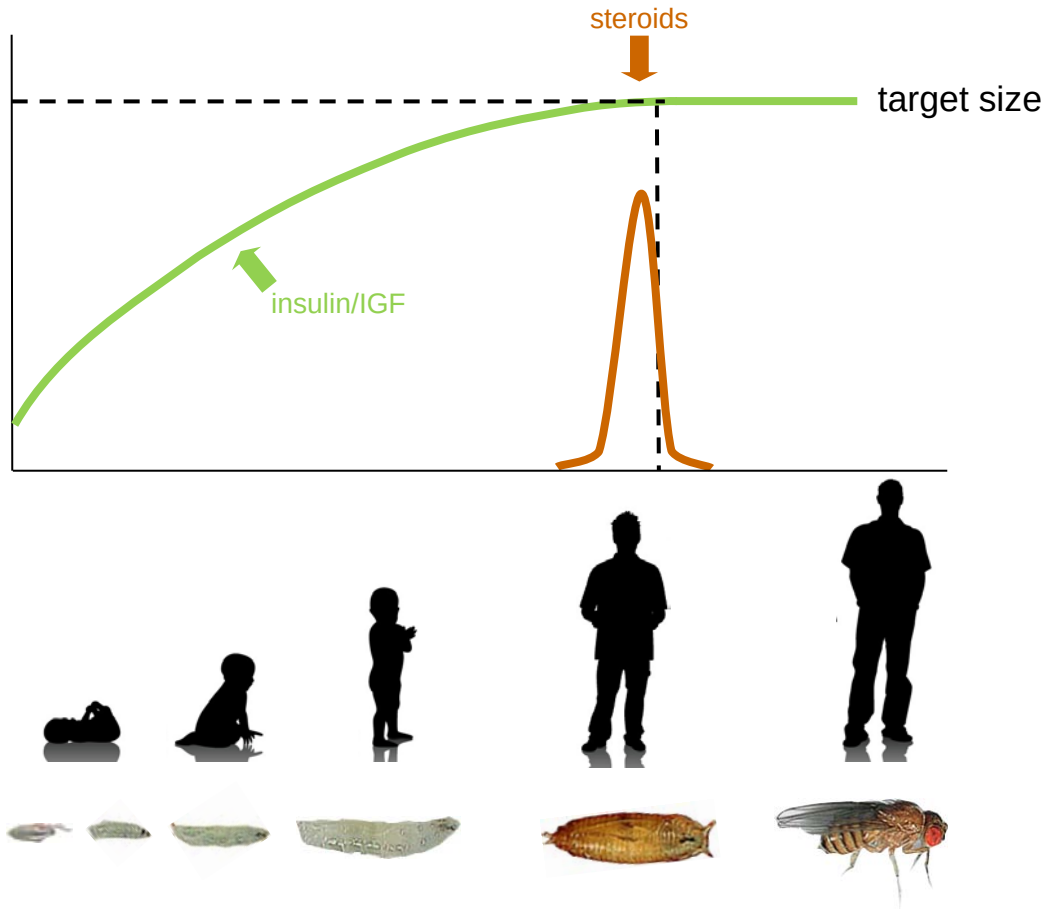
nutritional control of growth



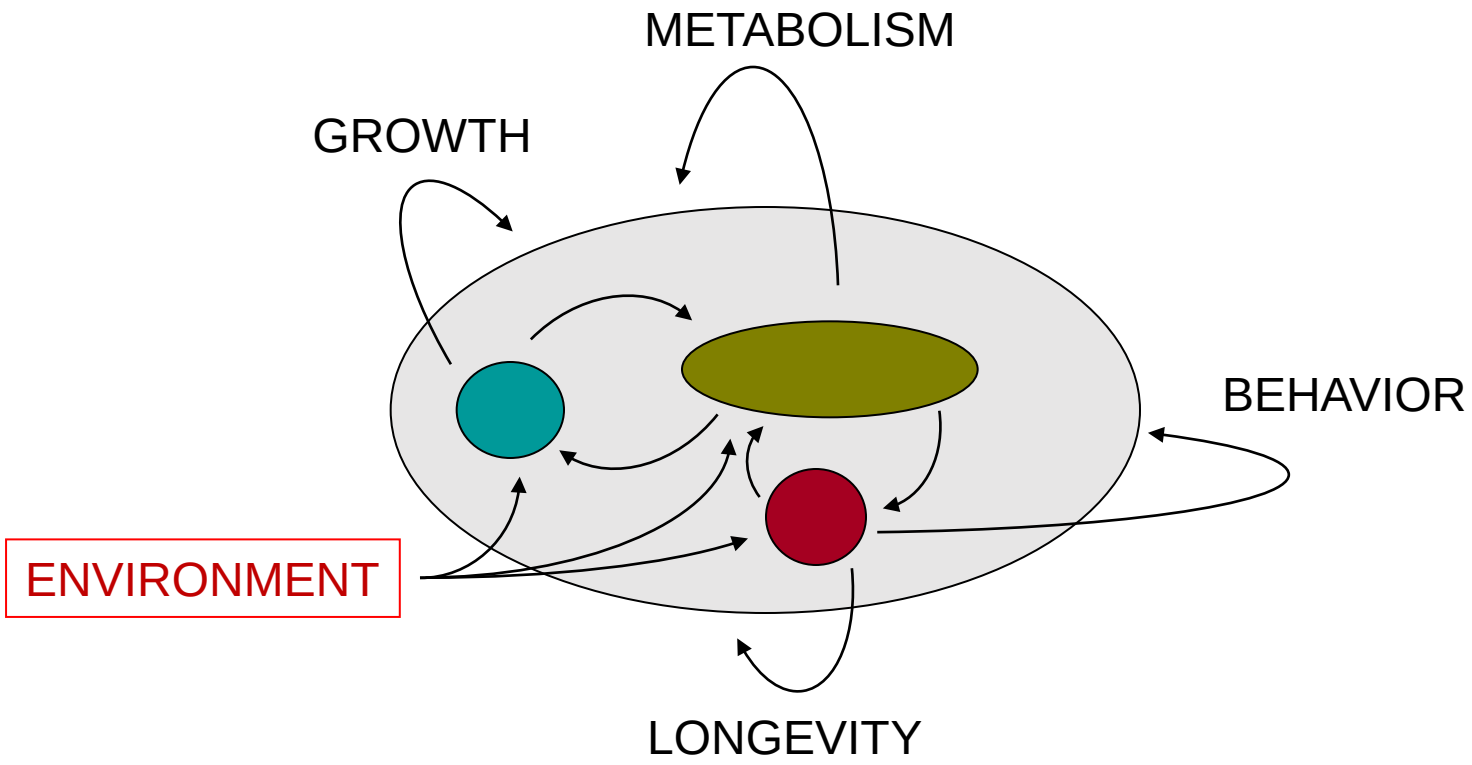
1.7g/L

17g/L

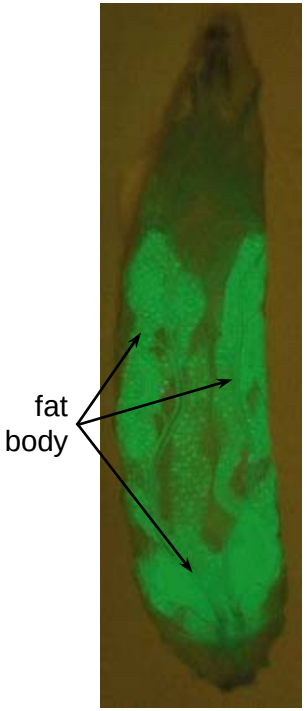


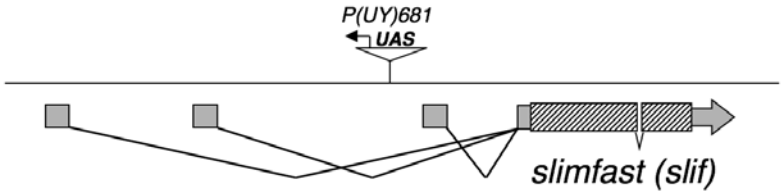

steroids
target size
insulin/IGF

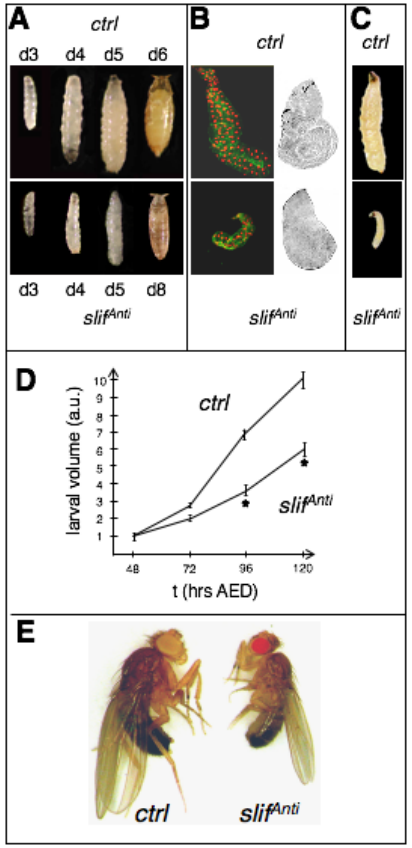
homeostasis and inter-organ communications



the larval fat body controls systemic growth

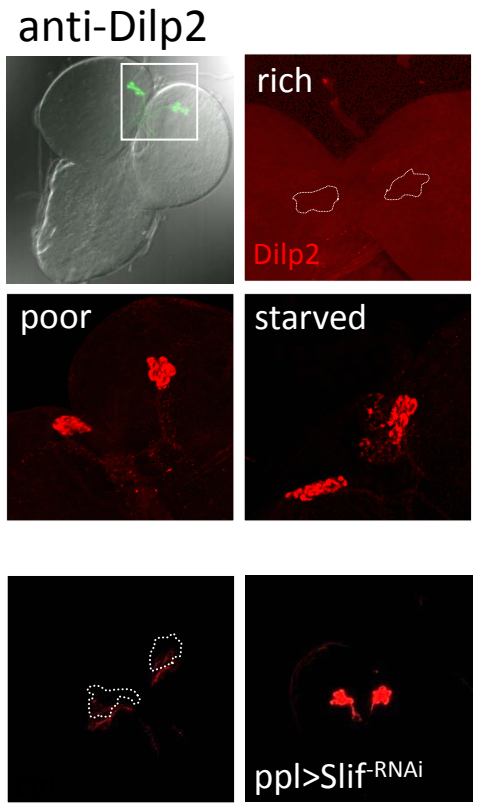


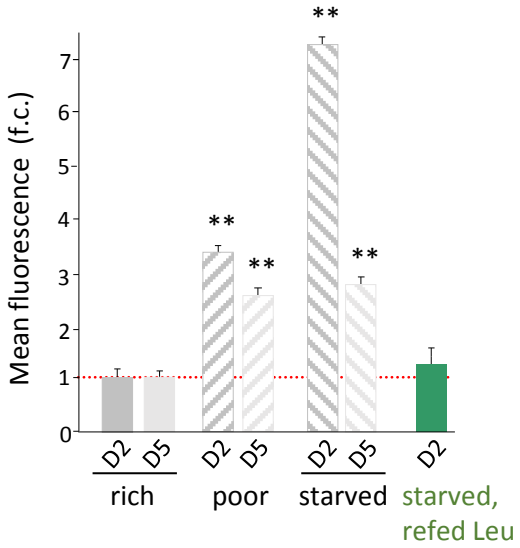




Colombani et al. Cell 2003
Britton & Edgar Development 1998
Martin et al. Mech. Dev. 2000

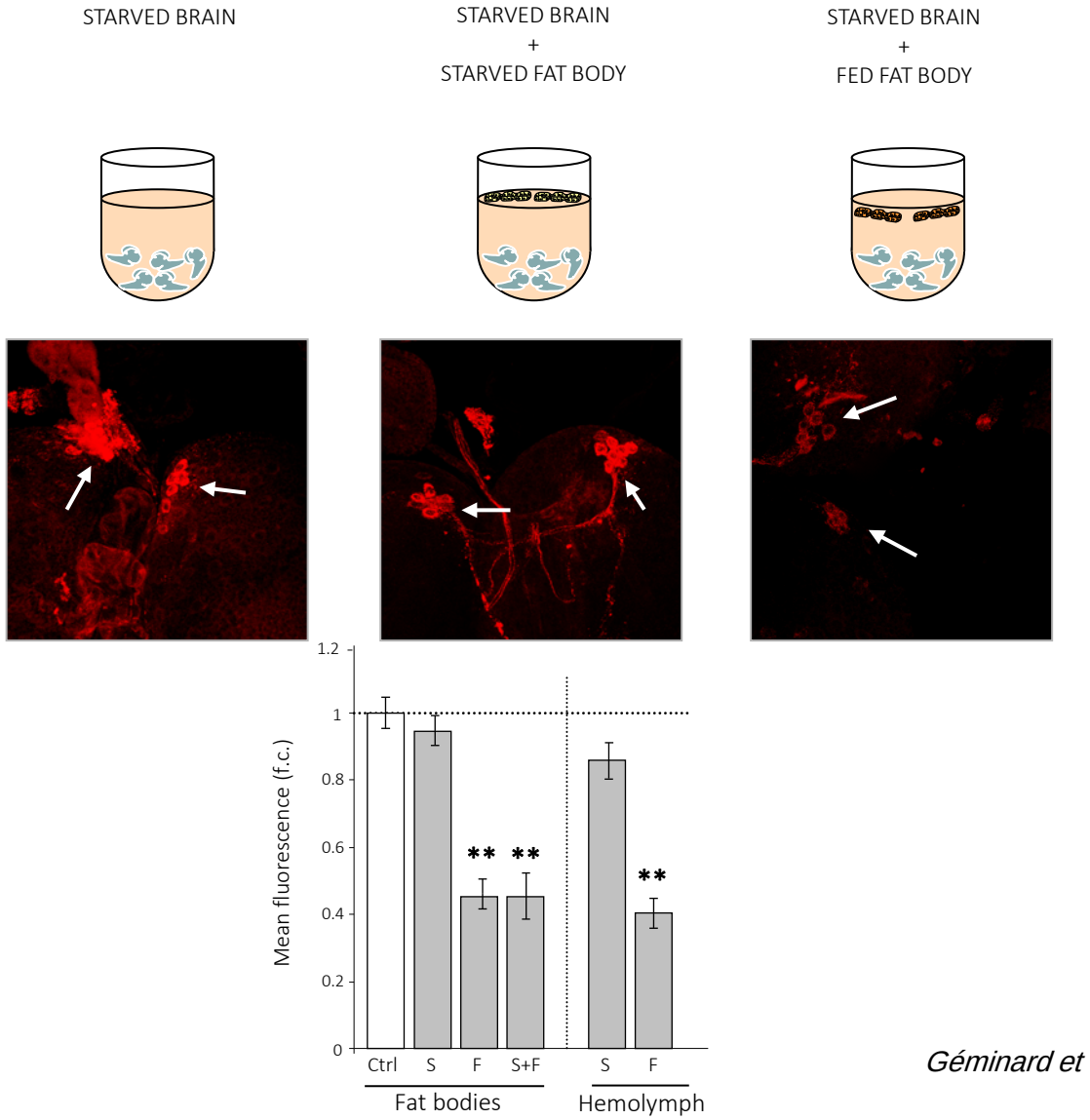
nutrition controls insulin secretion via the fat body



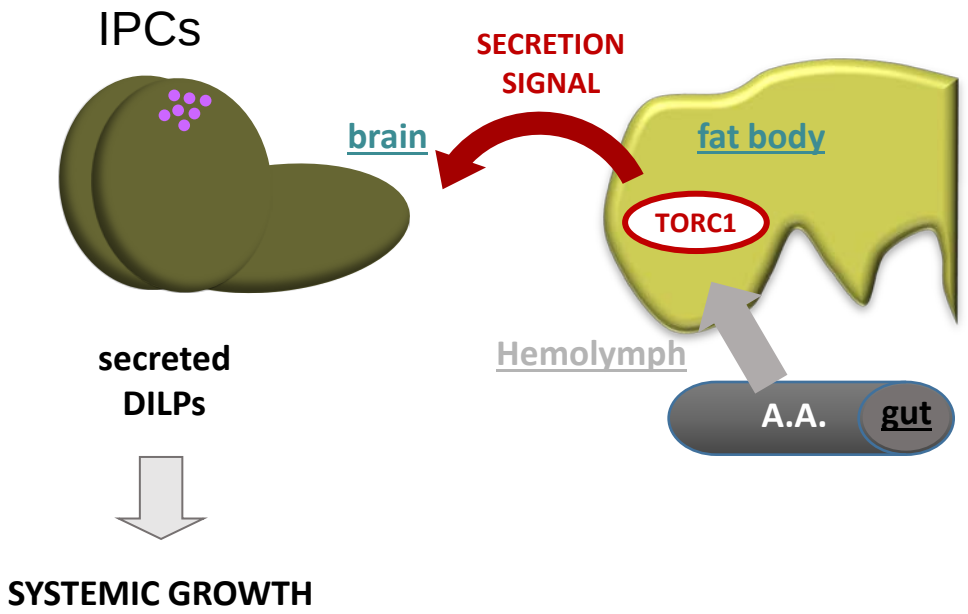


Géminard et al. Cell Metab. 2009

remote control of insulin secretion

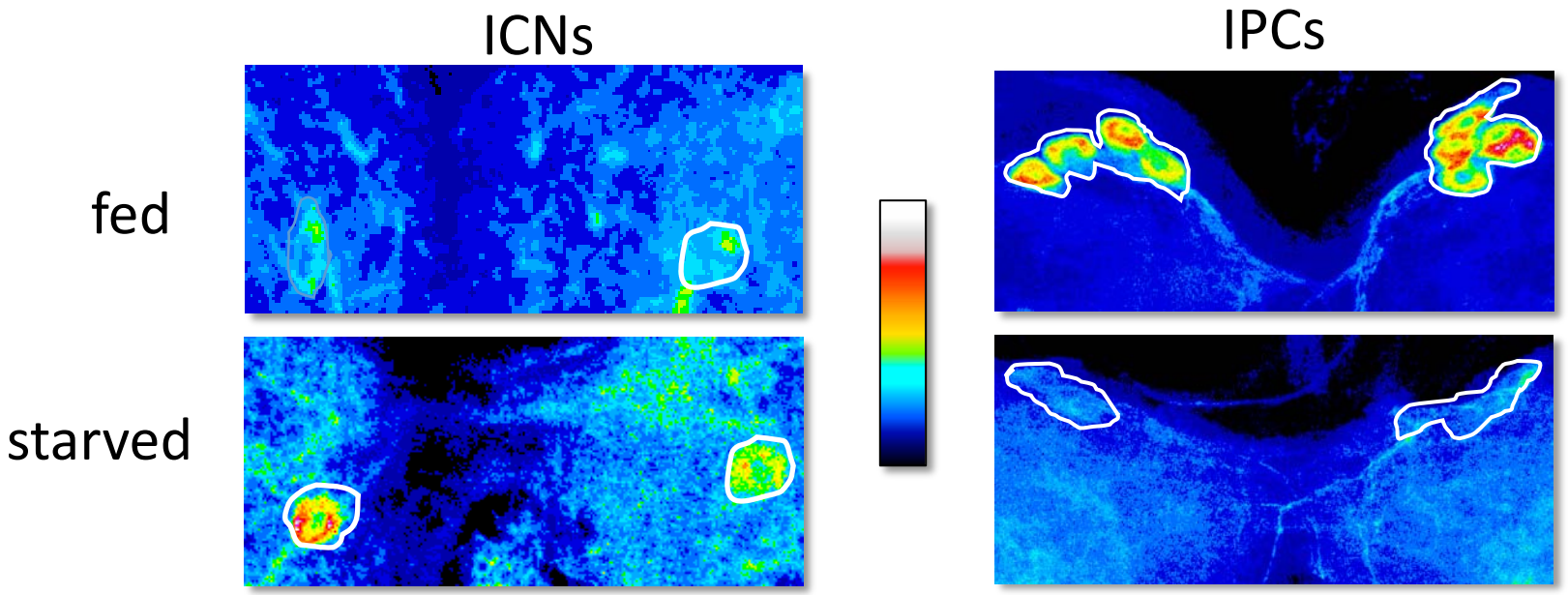


Géminard et al. Cell Metab. 2009

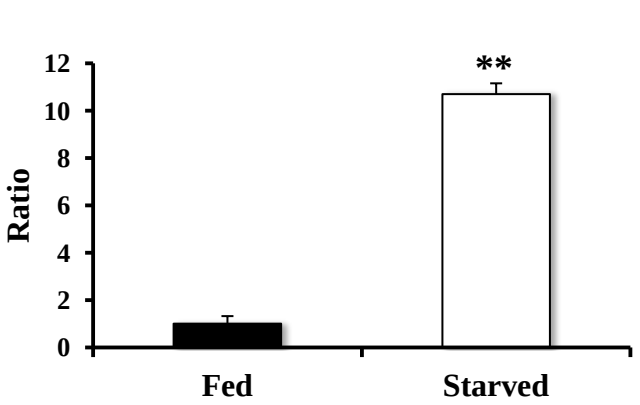


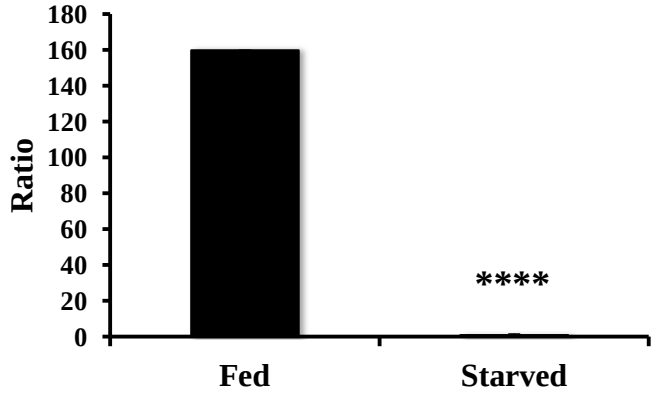
Géminard et al. Cell Metab. 2009

a new pair of IPC-Contacting Neurons activated by starvation

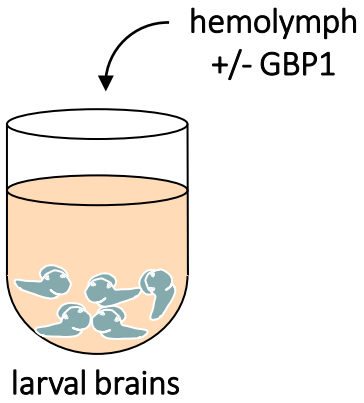


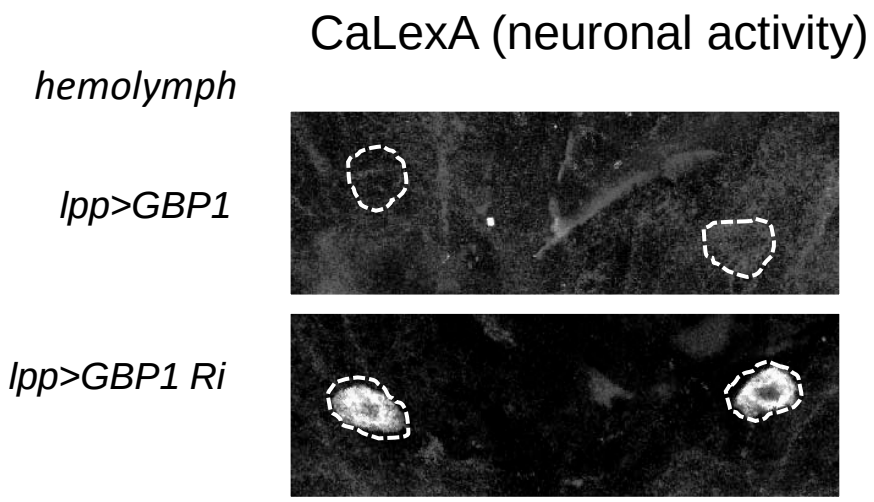
fru-Gal4, UAS-mLexA-VP16-NFAT, LexAop-CD2-GFP



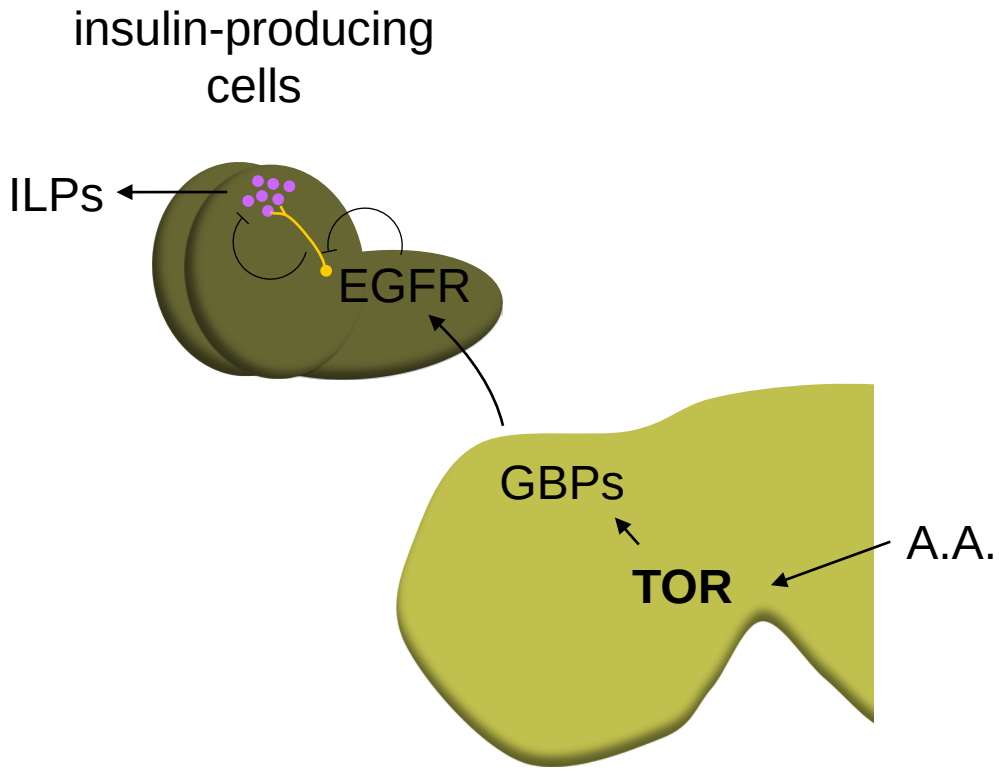


hemolymph GBP1 inhibits ICN activity



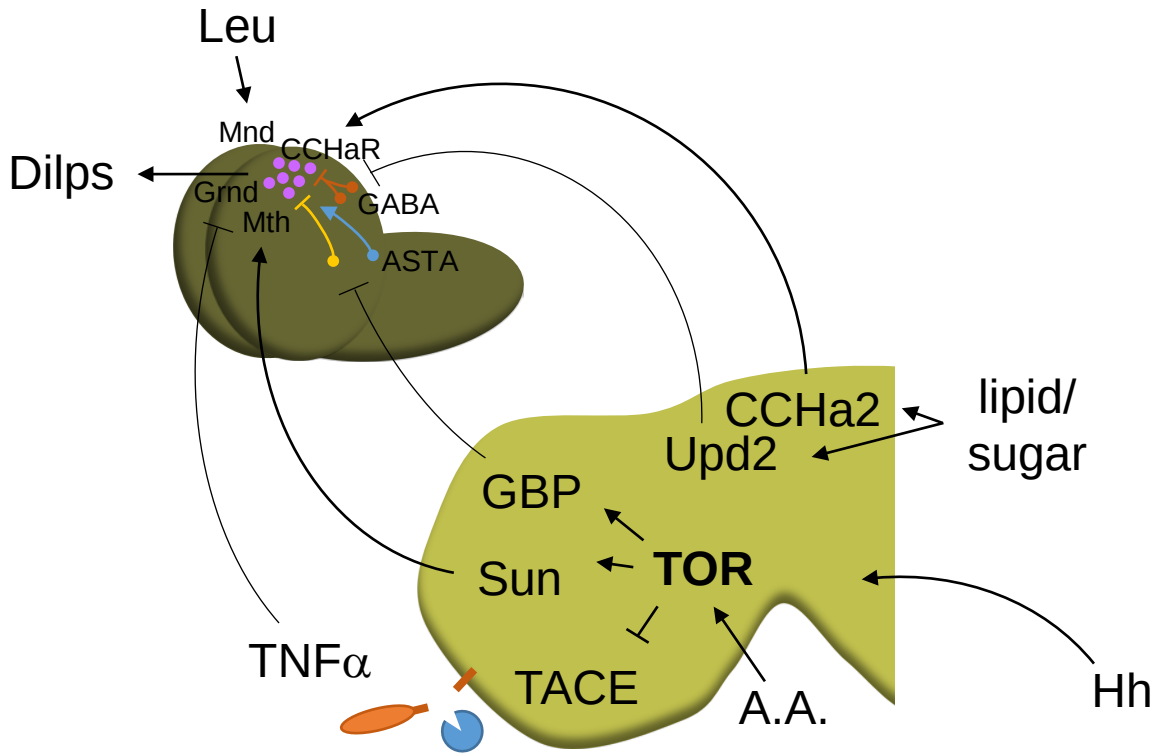


GBPs control insulin secretion through EGFR activation in ICNs



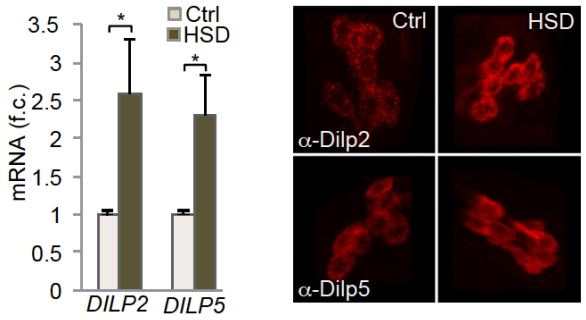
Meschi et al. DevCell 2018

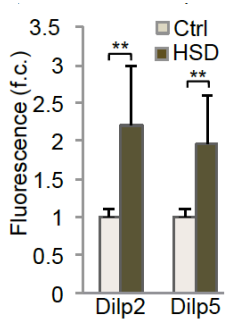
orchestration of the nutrient response through IPC function

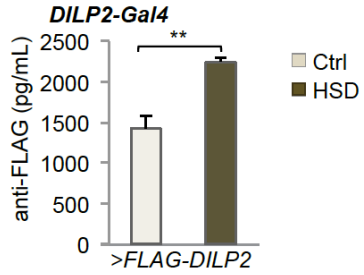


Rajan & Perrimon, Cell 2012
Rodenfels et al. G&D 2014
Sano et al. PLOS Genet. 2015
Hentze et al. Sci.Rep. 2015
Koyama & Mirth, PLOS Biol. 2016
Manières et al. Cell Report 2016
Agrawal et al. Cell Metab 2016
Delanoue et al. Science 2016
Meschi et al. DevCell 2018

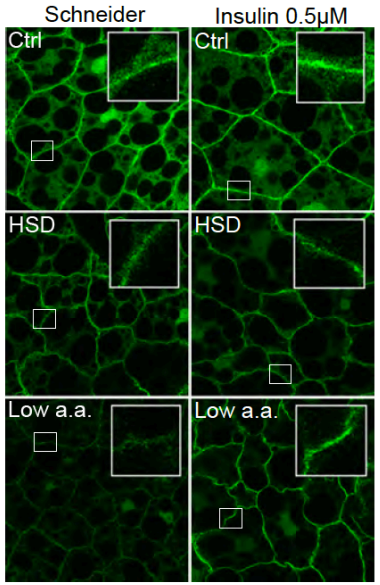
high sugar-induced insulin resistance

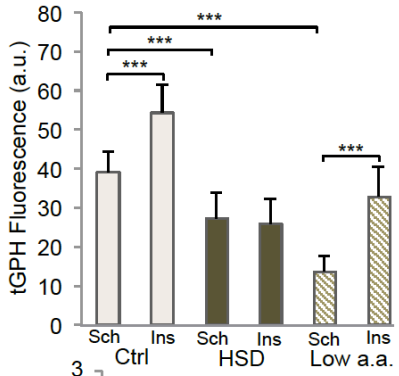


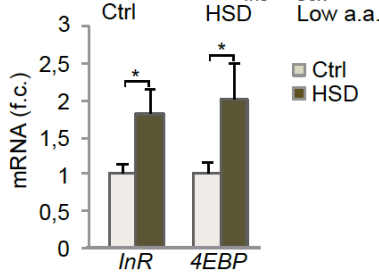




Fat body

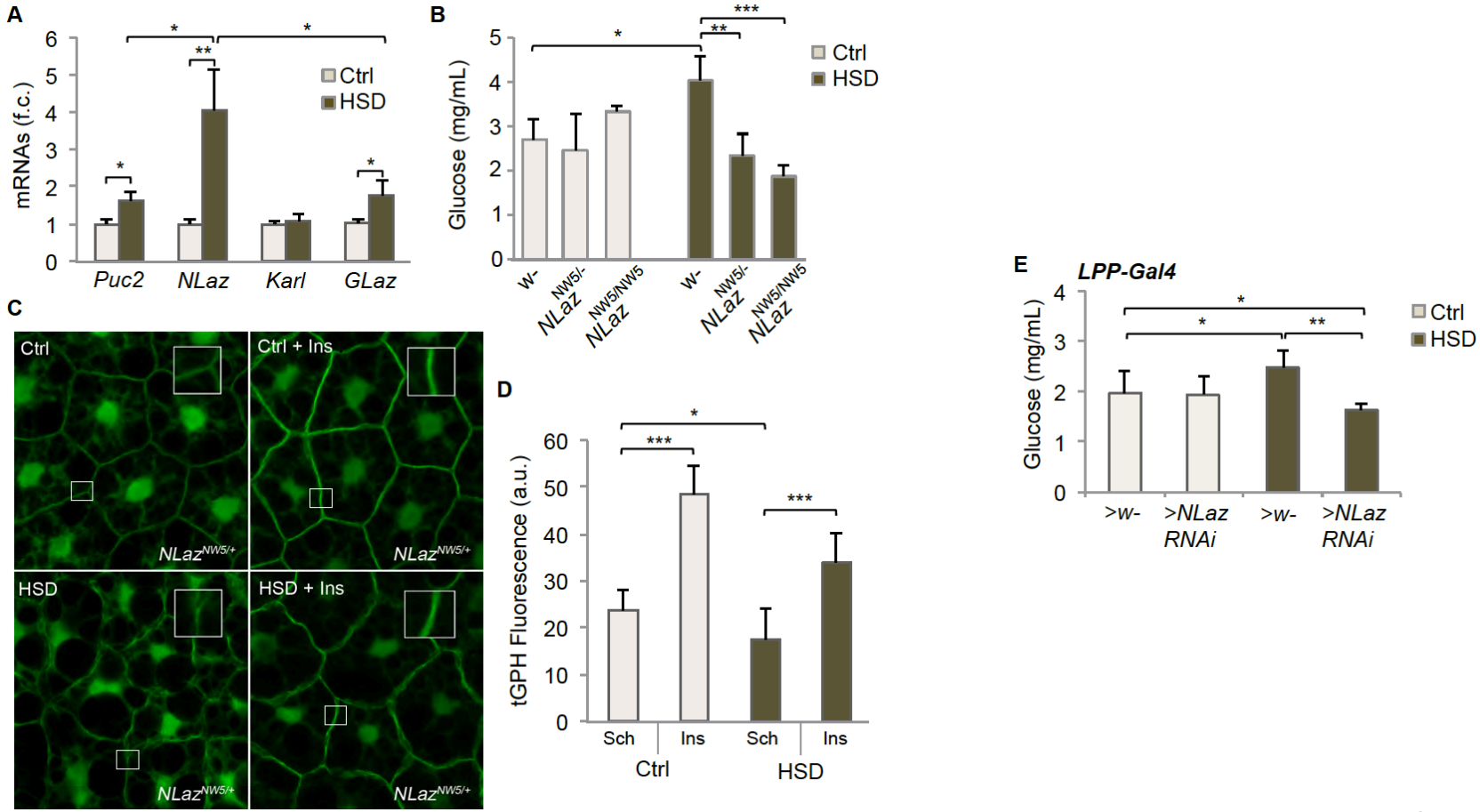






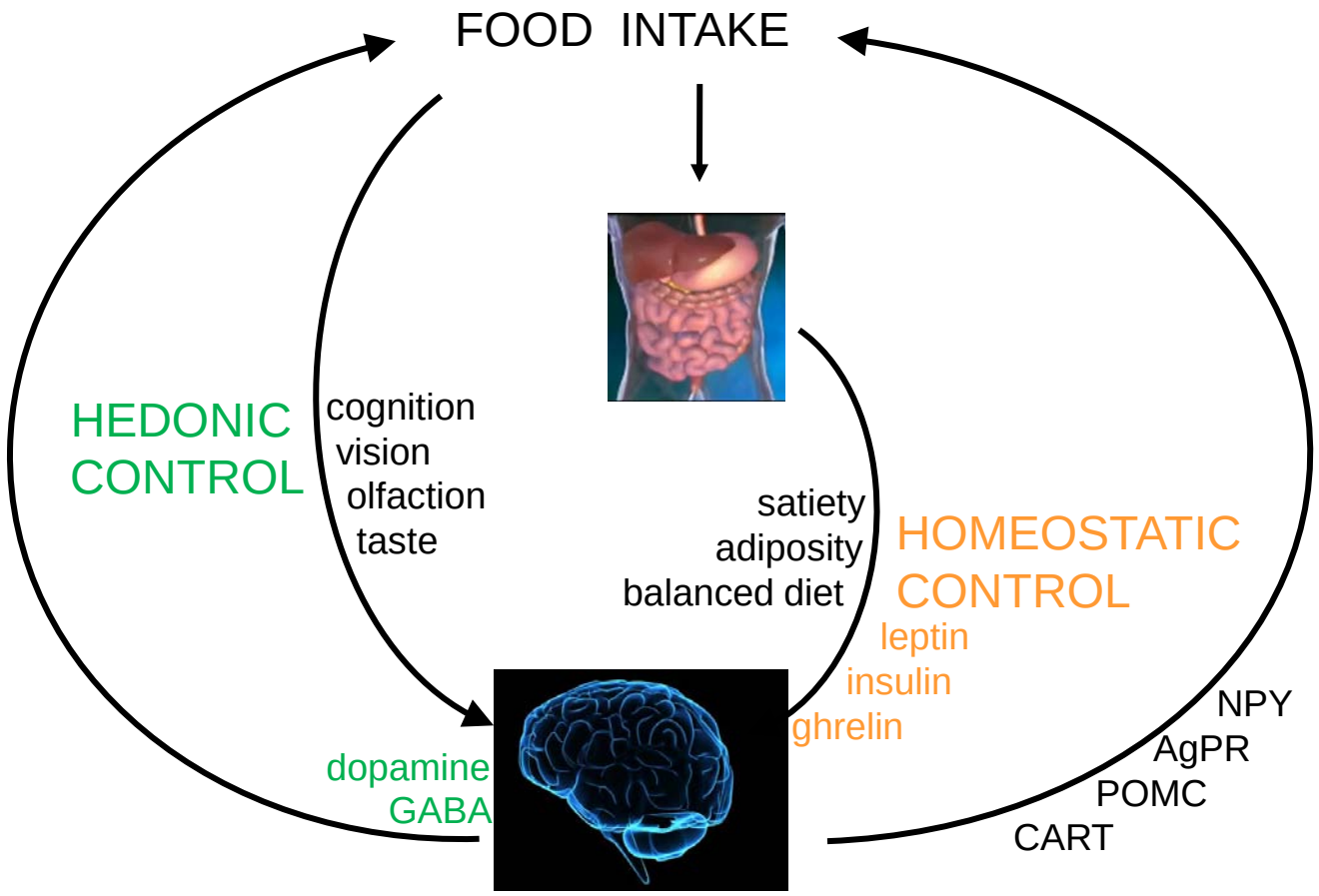
Pasco & Léopold, PLoSOne 2012

the fly lipocalin NLaz is required for high sugar-induced insulin resistance

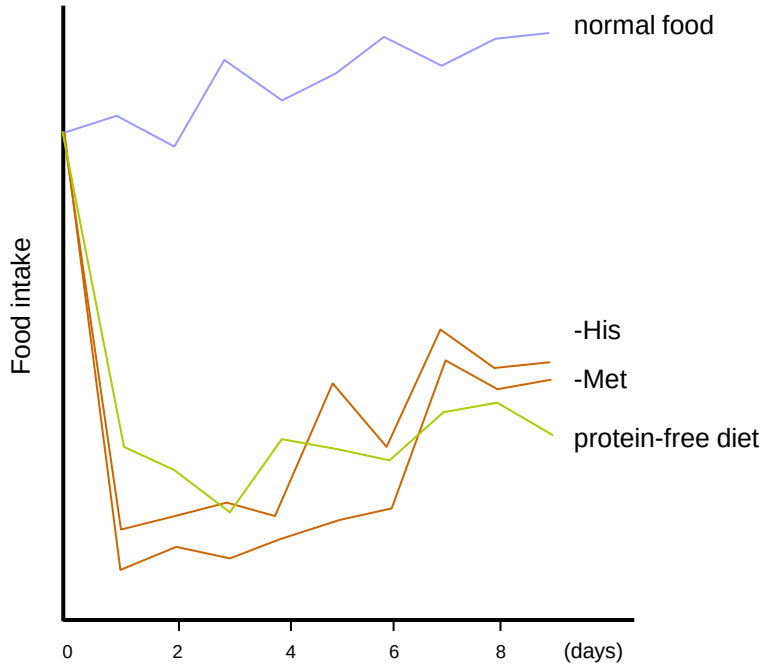


Pasco & Léopold, PLoSOne 2012

amino acid sensing in the brain

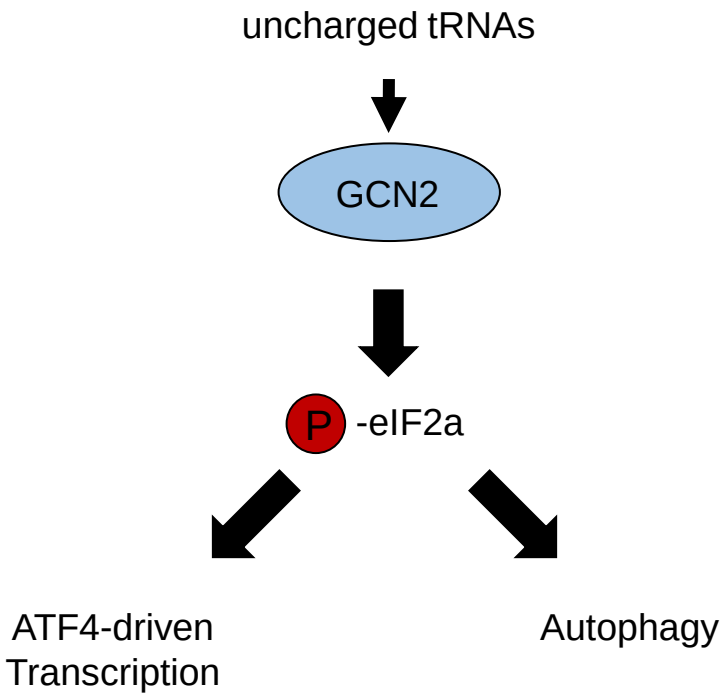


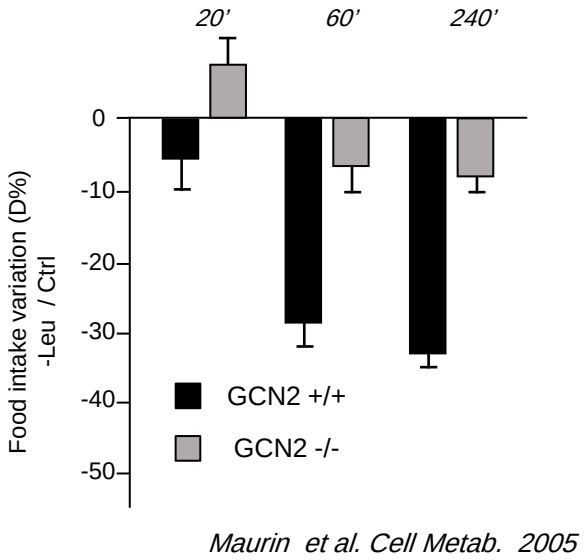
aversion towards a deficiency for essential amino acids



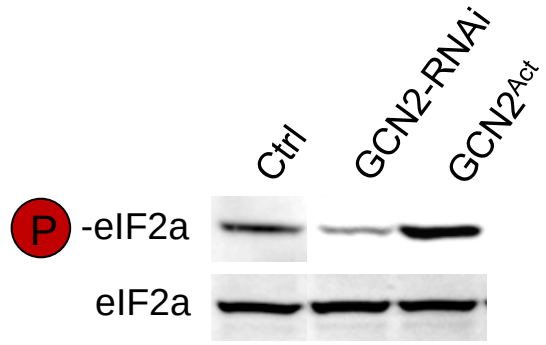
Peng et al. 1975

GCN2 controls food intake in the brain (mouse)

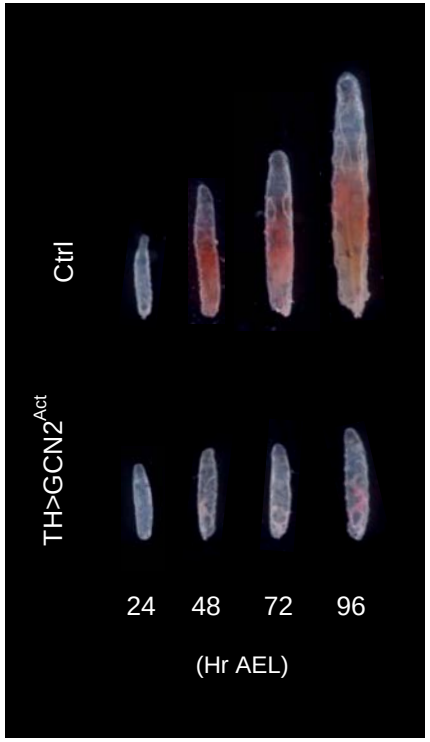


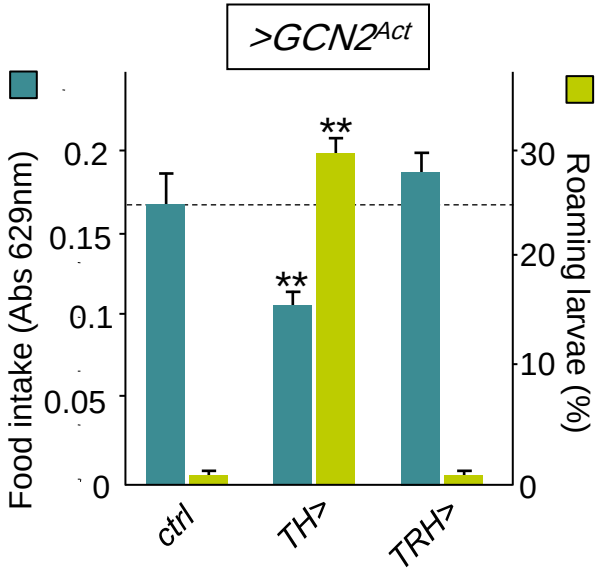


Maurin et al. Cell Metab. 2005



GCN2 controls food intake in the brain (Drosophila)

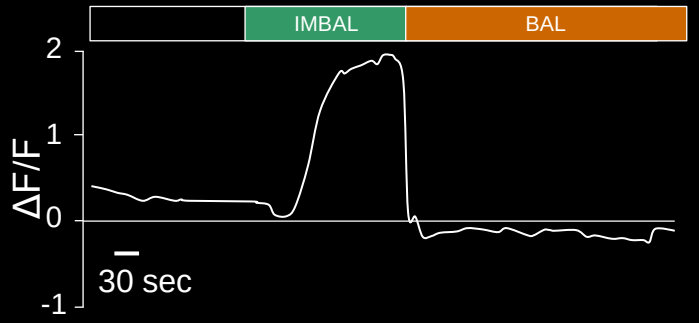


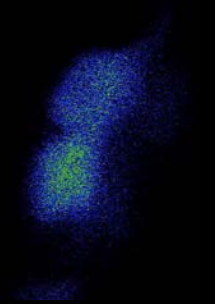


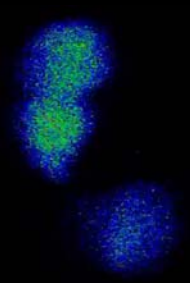
imbalanced a.a. diet activates DA neurons in vitro

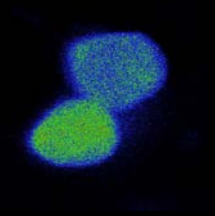




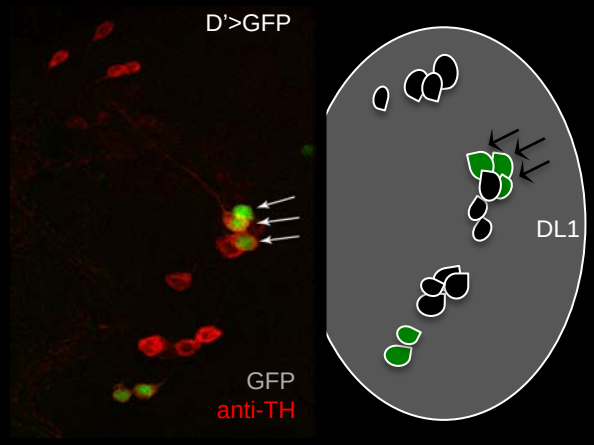


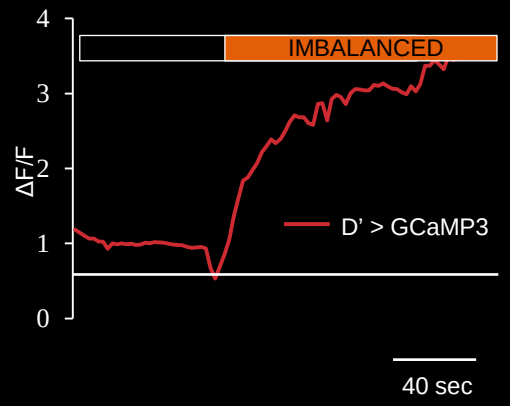


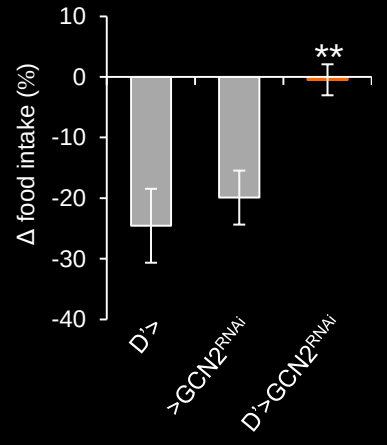




imbalanced a.a. diet activates 3 DA neurons controlling diet aversion

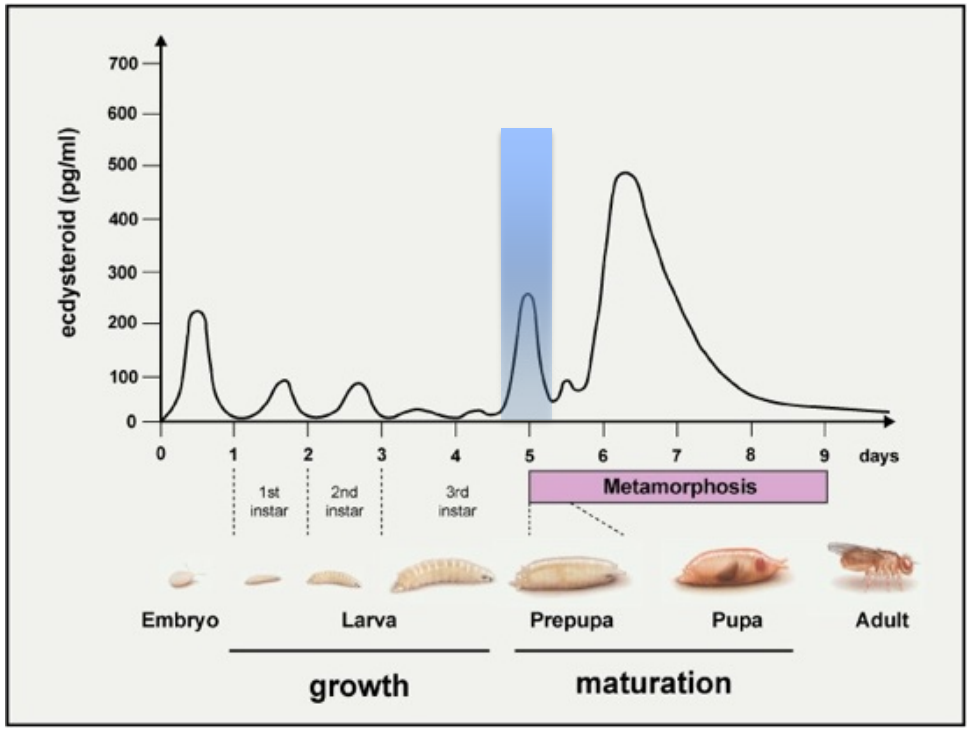


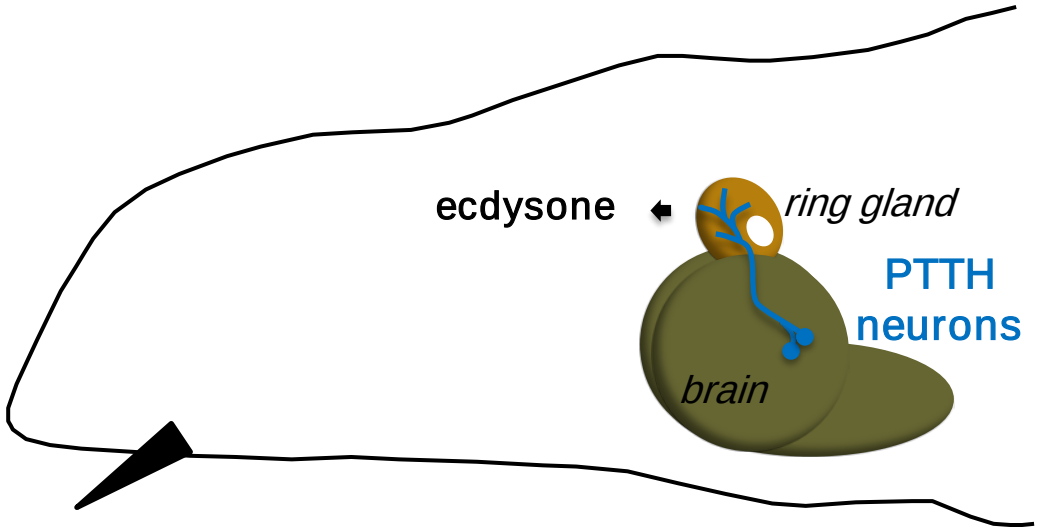




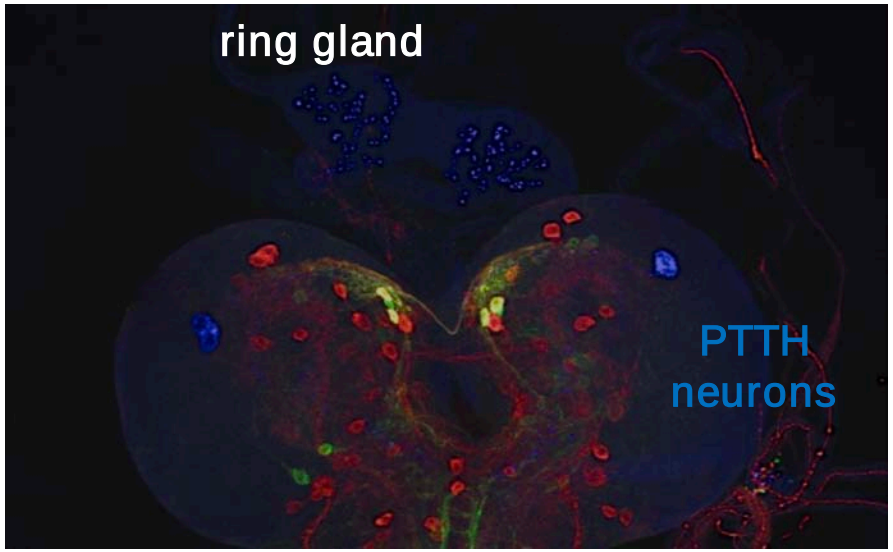
Bjordal et al., Cell 2014

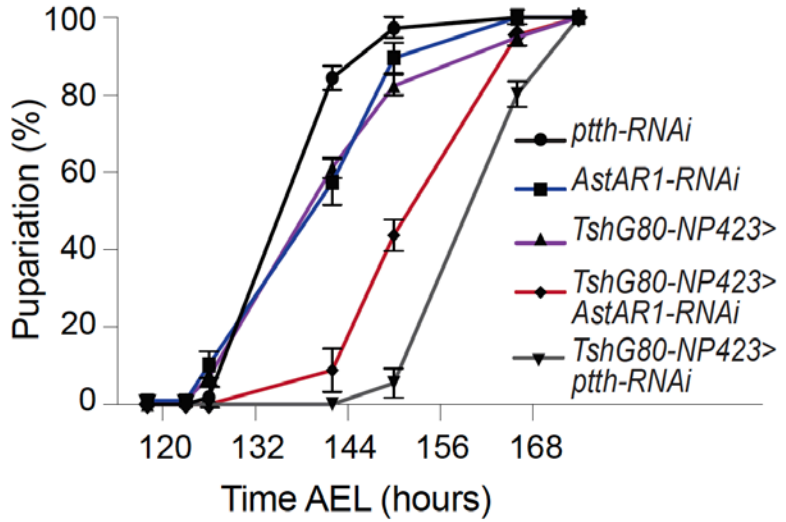
hormonal control of developmental transitions

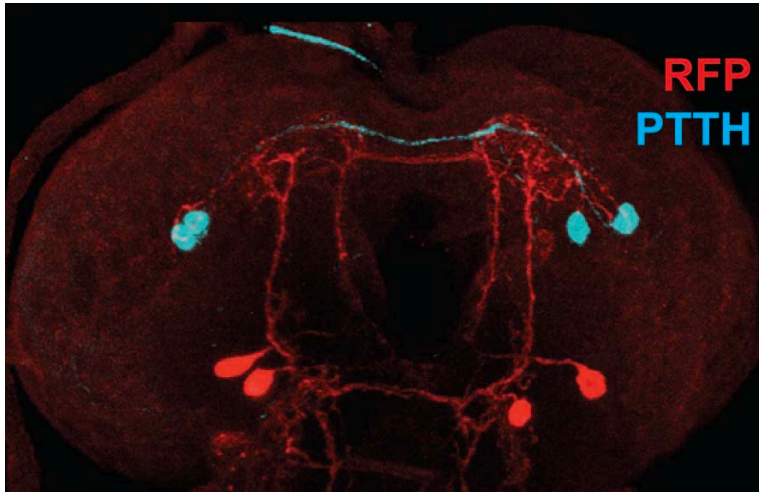


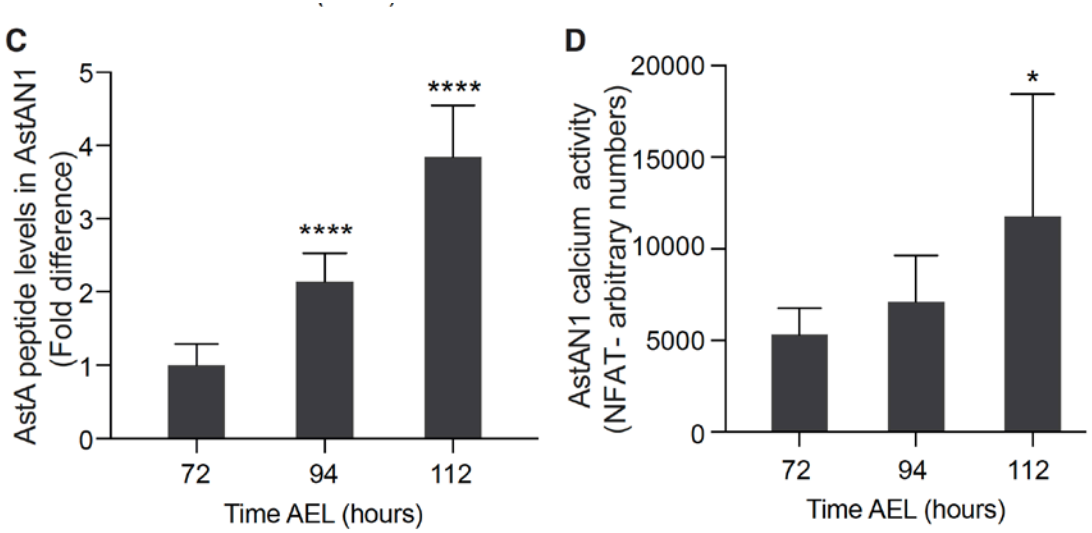


hormonal control of developmental transitions

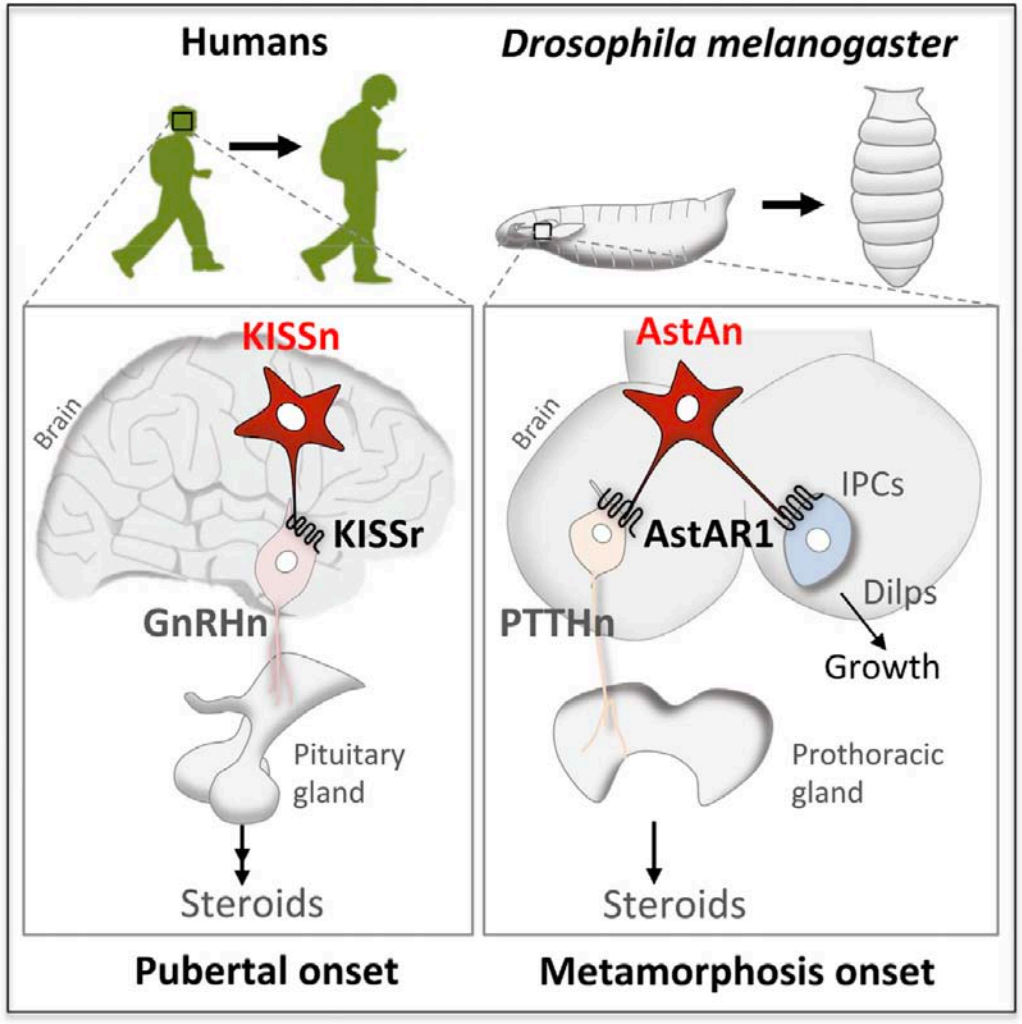





RFP
PTTH

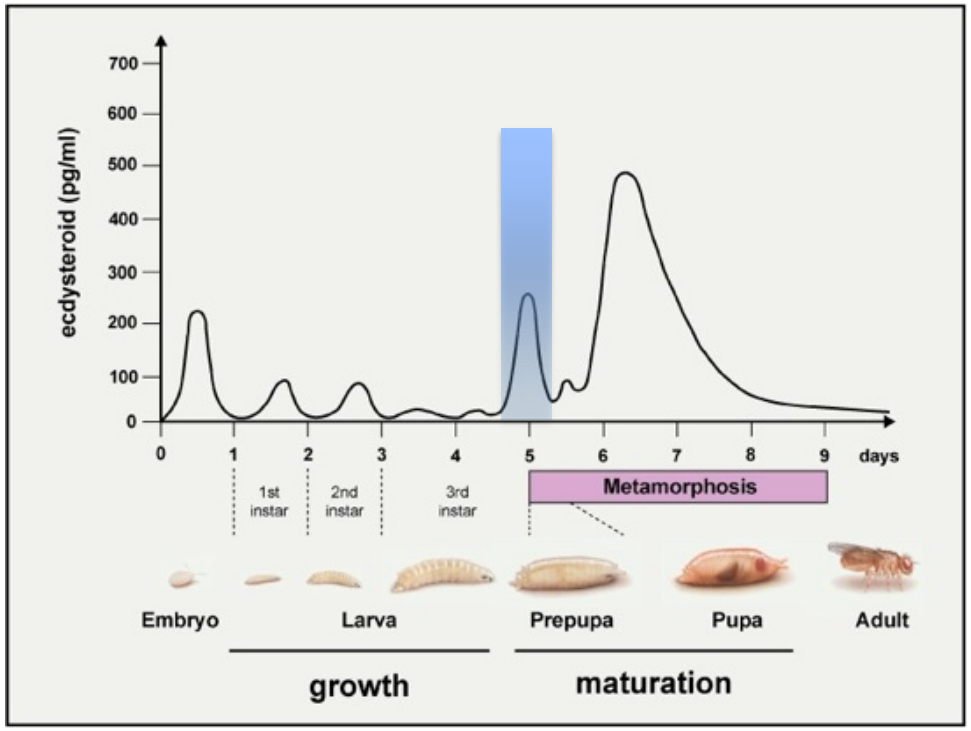

C
AstA peptide levels in AstAN1
(Fold difference)
5
4
3
2
1
0
****
****
72
94
112
Time AEL (hours)
D
AstAN1 calcium activity
(NFAT- arbitrary numbers)
20000
15000
10000
5000
0
*
72
94
112
Time AEL (hours)

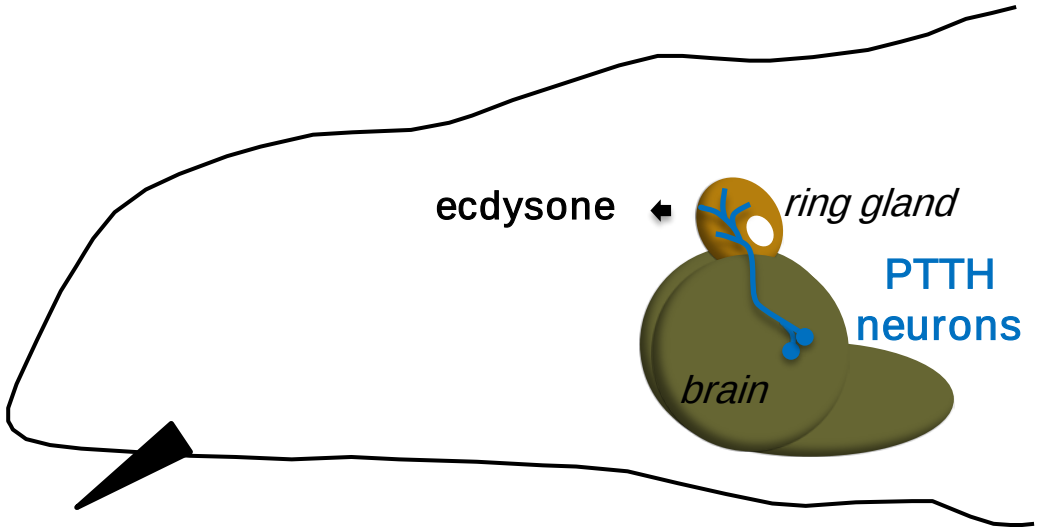
an evolutionary conserved mechanism timing juvenile-to-adult transition



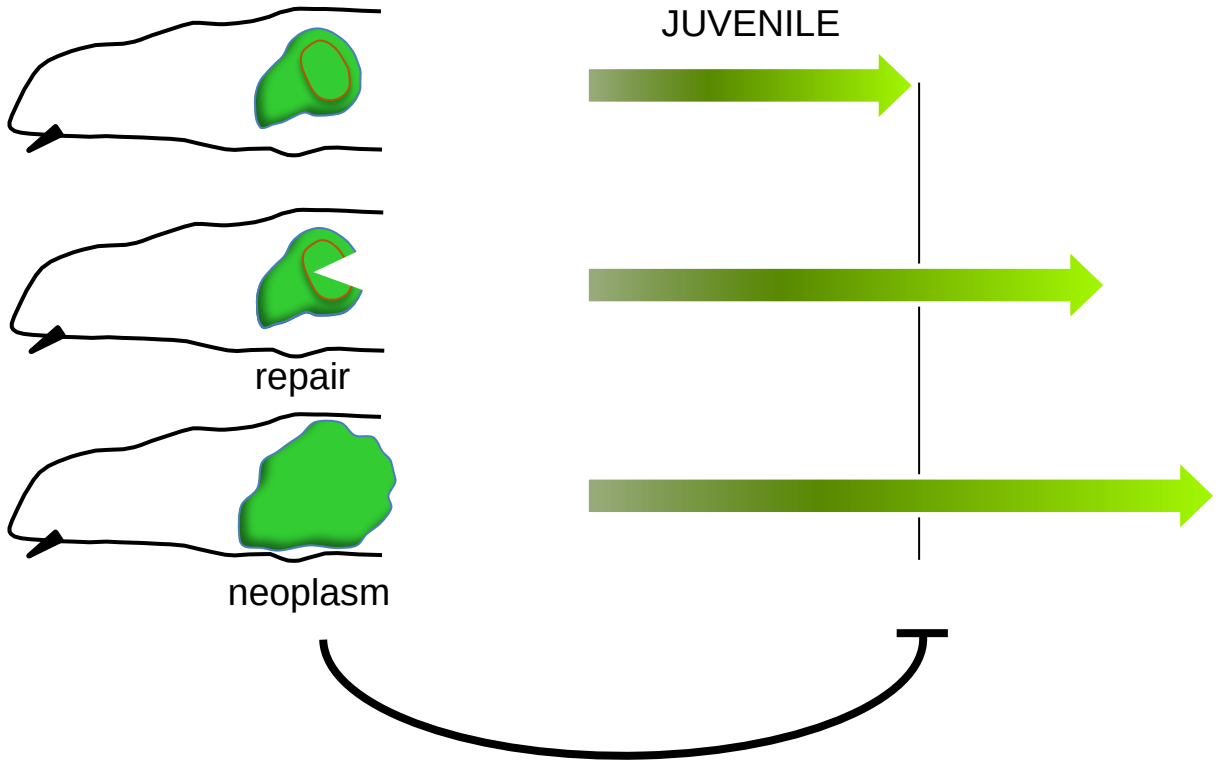
Deveci et al., Curr. Biol. 2019

control of developmental transitions





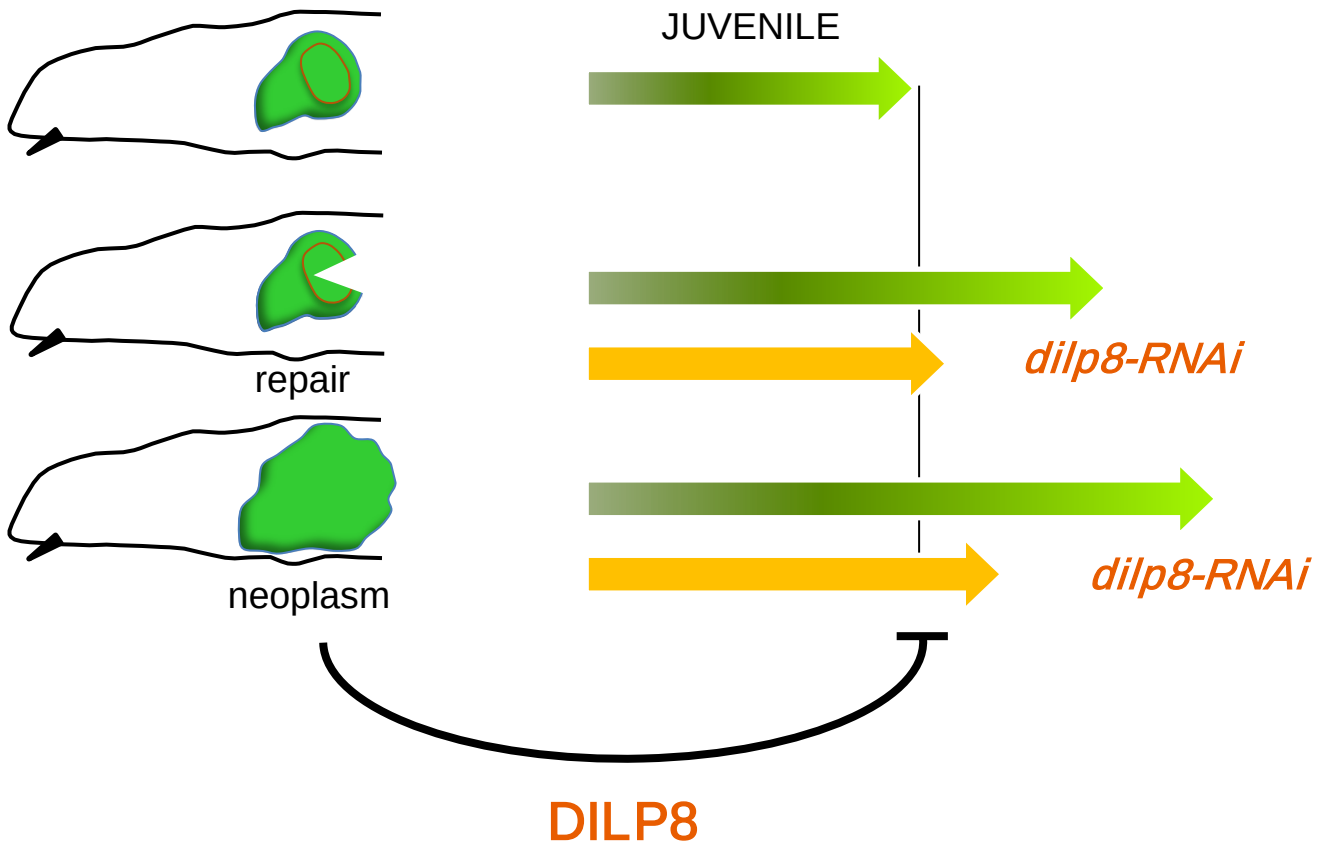
organ growth controls the timing of maturation



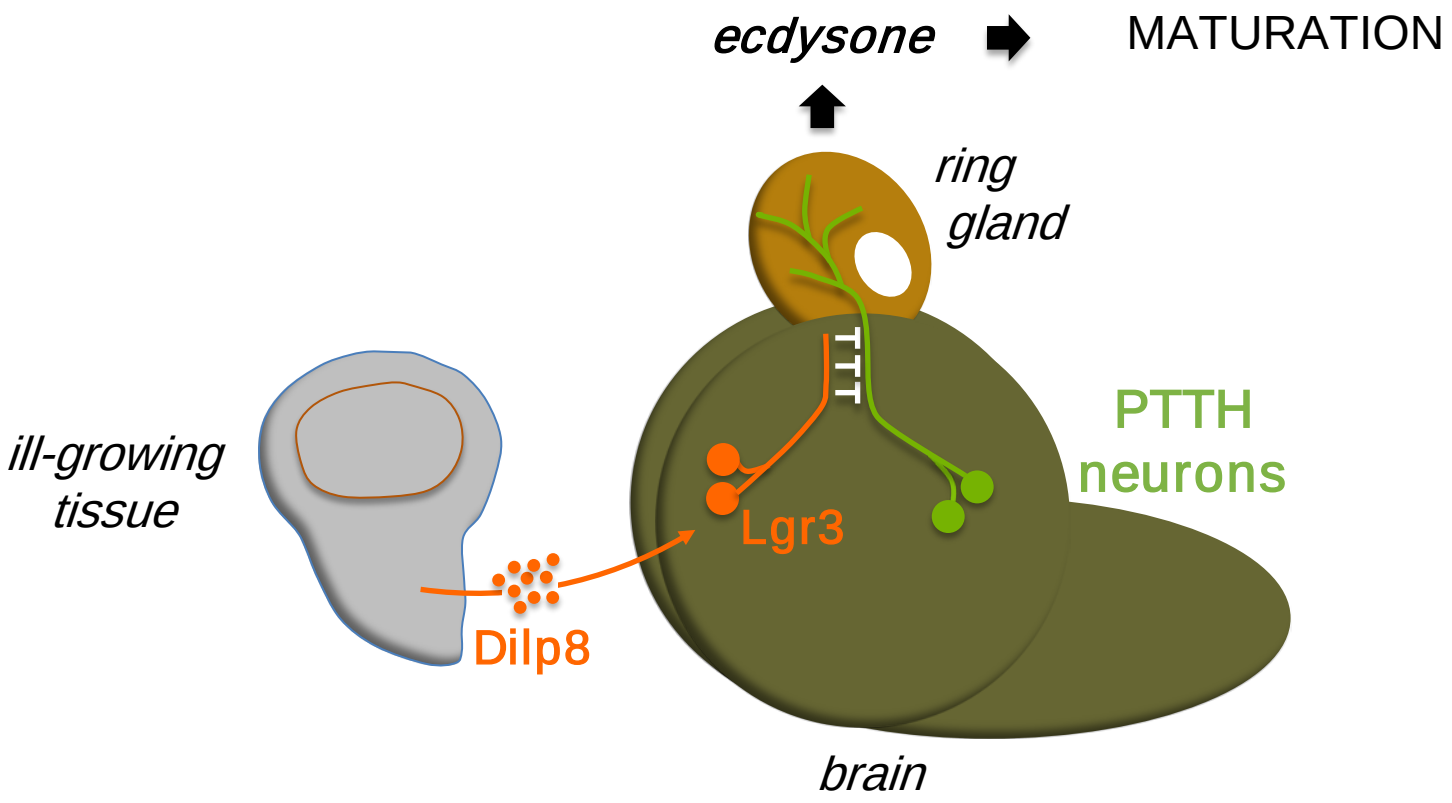
A. Shearn, 1974
P. Simpson, 1976, 1980
P. Bryant, 1980

→ developmental checkpoint

screening for the control of maturation timing



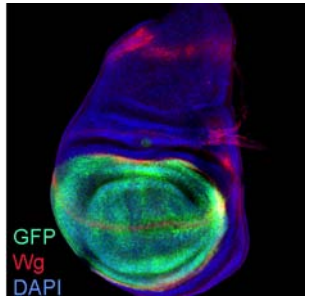
Colombani et al. 2012



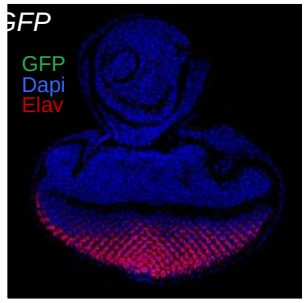
Colombani et al. Science 2012
Colombani et al. Current Biol. 2015
Boone et al. Nat. Commun. 2016

coordination of organ growth

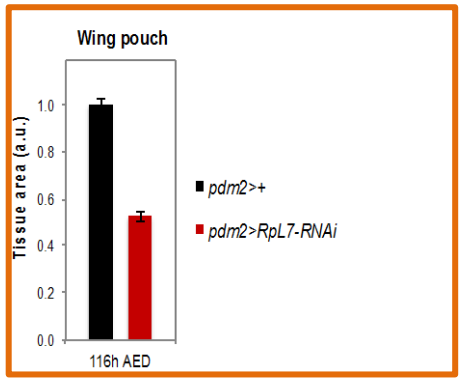
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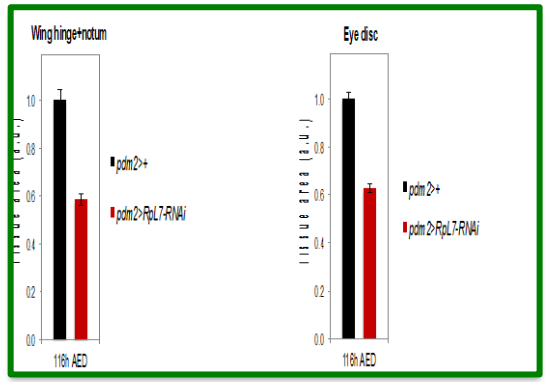
wing disc



eye disc



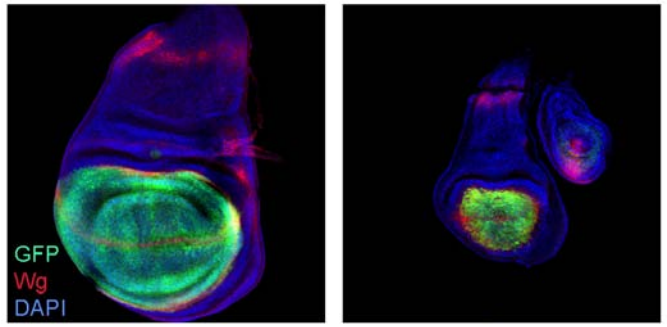
autonomous



non-autonomous

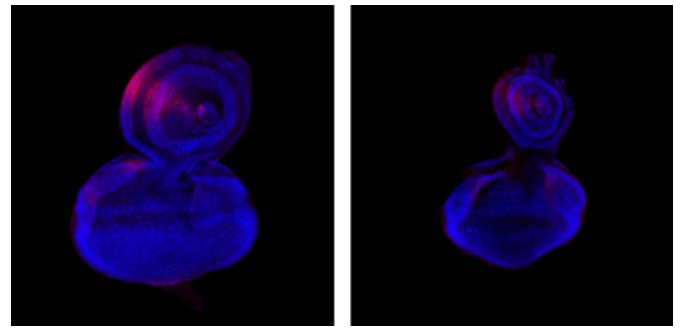






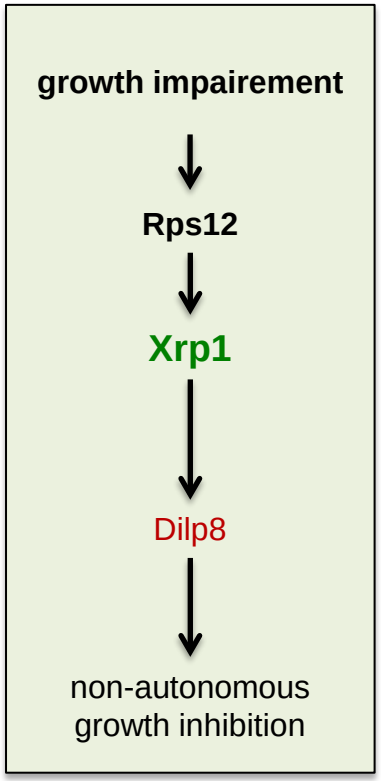
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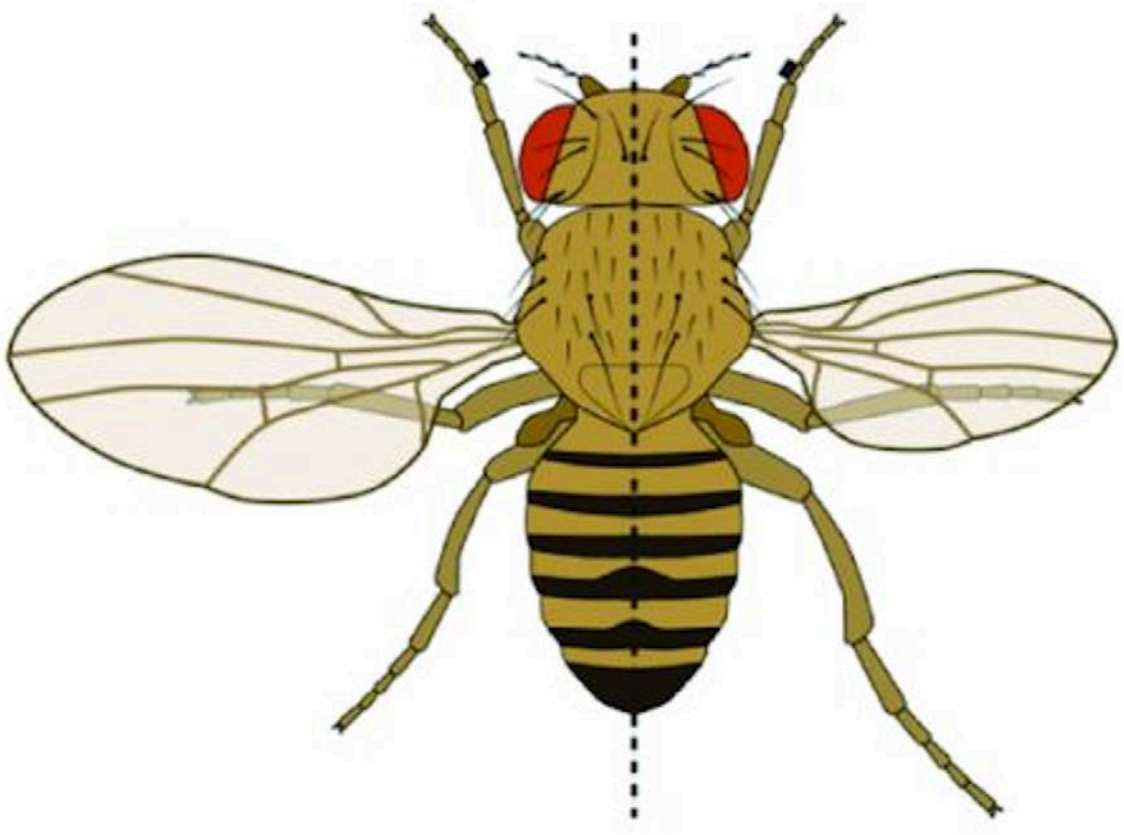
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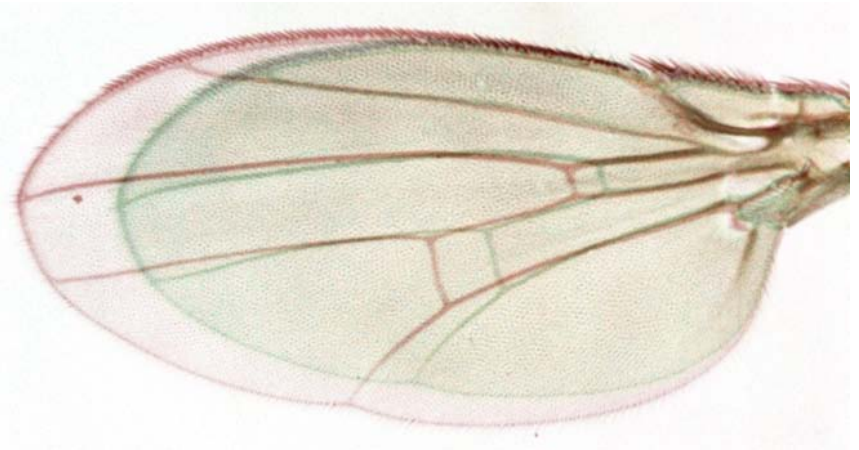


Boulan et al. Dev. Cell. 2019

dilp8/lgr3 controls developmental stability



dilp8$^{KO/ExA}$



Fluctuating Asymmetry index: $\Sigma(Ai)^2/n$

Garelli et al., Science 2012
Boone et al. Curr. Biol. 2015
Garelli et al. Nat. Comm. 2015
Vallejo et al. Science 2015



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