Relation génotype-phénotype et évo-dévo: le cas du tétra cavernicole aveugle

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Paris-Saclay Institute of Neuroscience

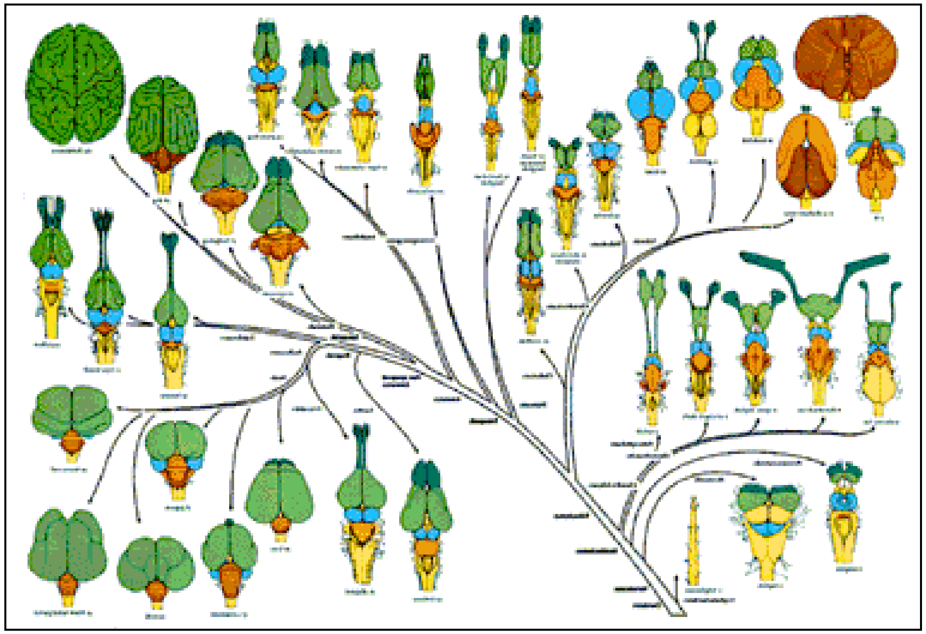
Gif sur Yvette

3 avril 2018

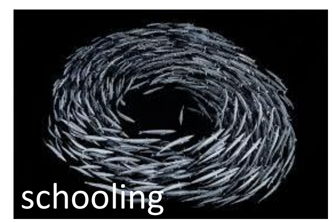
LabEx BASC

Biodiversité, Agroécosystèmes, Société, Climat

Developmental evolution of brain and behaviour



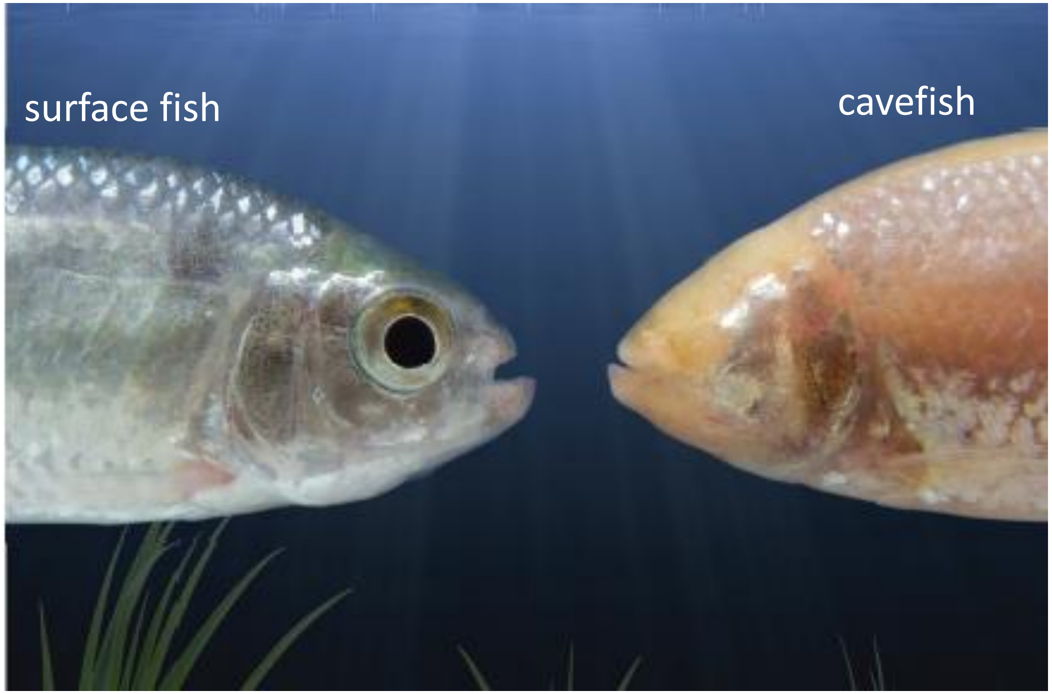
From Nieuwenhuys et al. 1998.
The Central Nervous System of Vertebrates



Model system

Astyanax mexicanus

One species, several populations or morphs



- Cavefish have undergone both gains and losses at the morphological, physiological, and behavioral levels

Blind cavefish: a natural mutant

Cavefish phenotype

Regressive morphological traits :
Eye loss by degeneration, pigmentation loss

Constructive morphological traits:
More tastebuds, more head neuromasts
larger jaws, more teeth…

Behavioral differences :
High locomotion activity , reduced sleep
Special feeding posture
Vibration Attraction Behavior
Non aggressive
No schooling

Blind cavefish: a natural mutant

Regressive morphological traits :
Eye loss by degeneration, pigmentation loss

Constructive morphological traits:

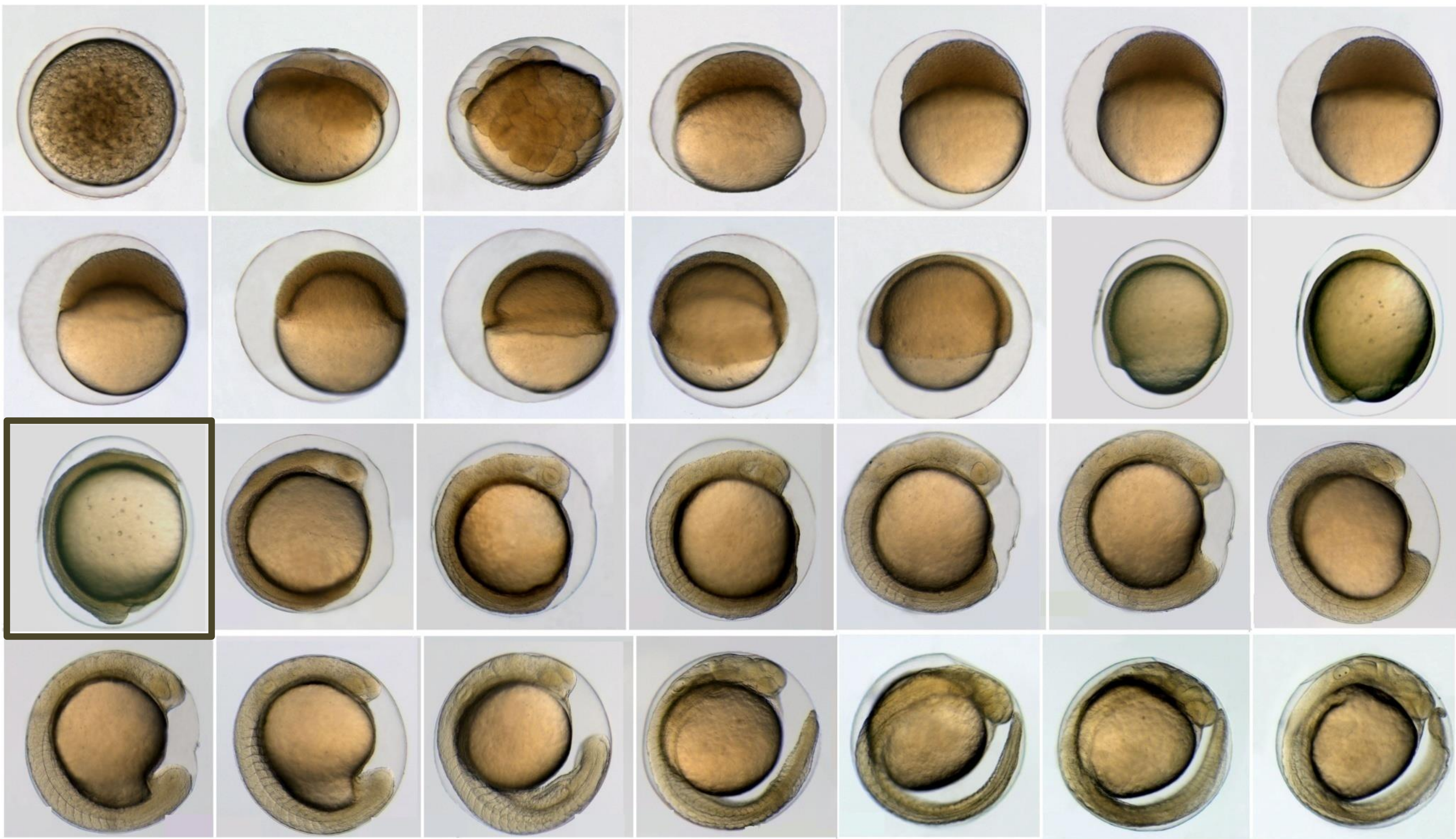
nasts

Developmental bases of these phenotypic changes??

leep

Non aggressive
No schooling

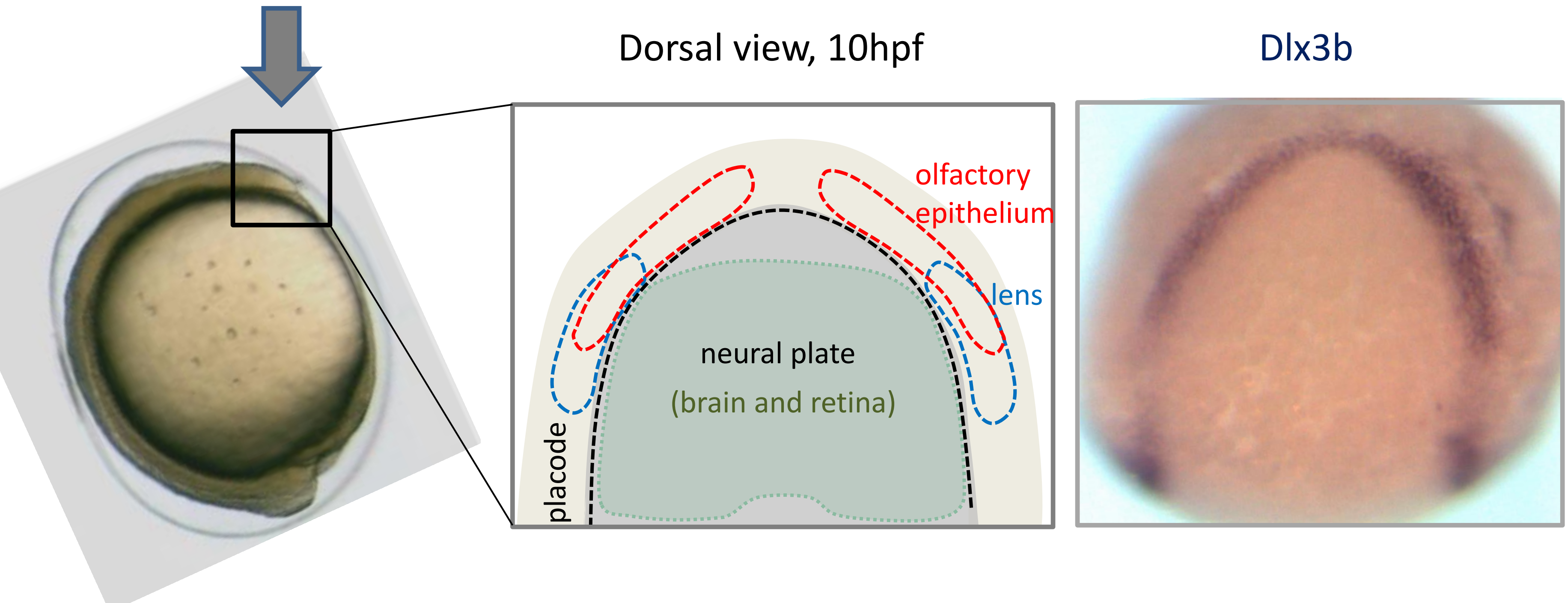
Embryogenesis



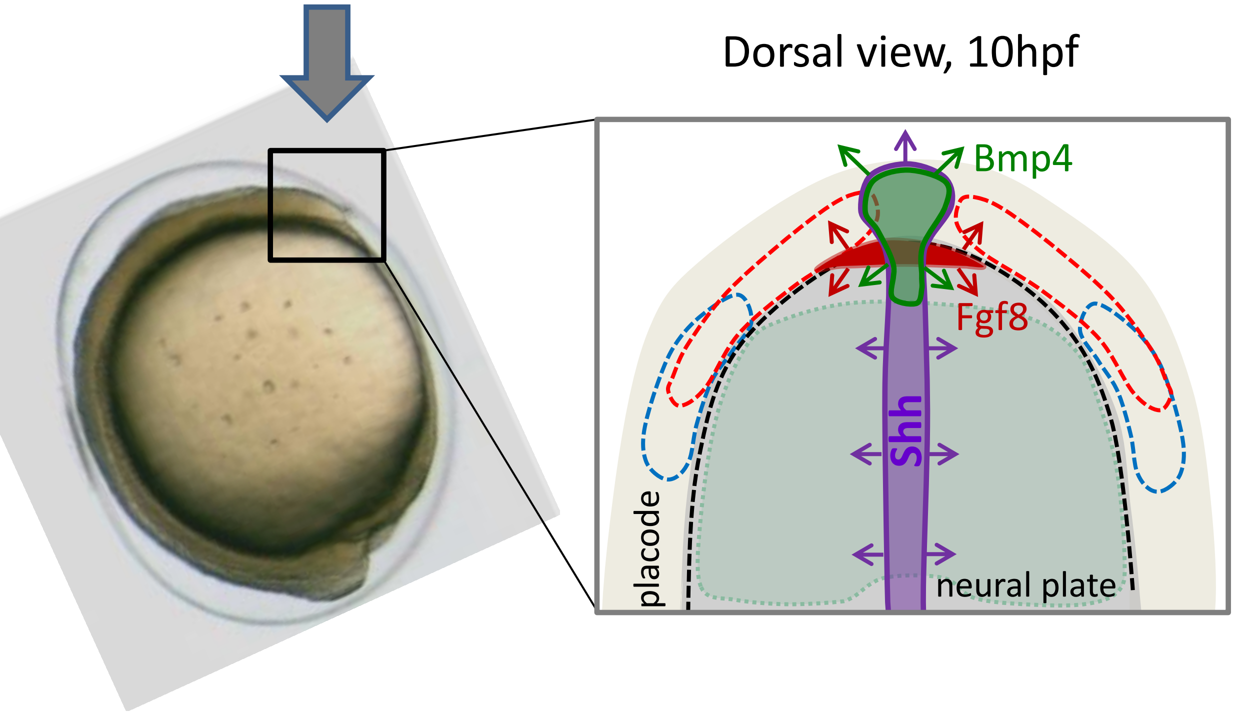
A. mexicanus developmental staging table

Hinaux et al, Zebrafish 2011

Neural plate and placodes

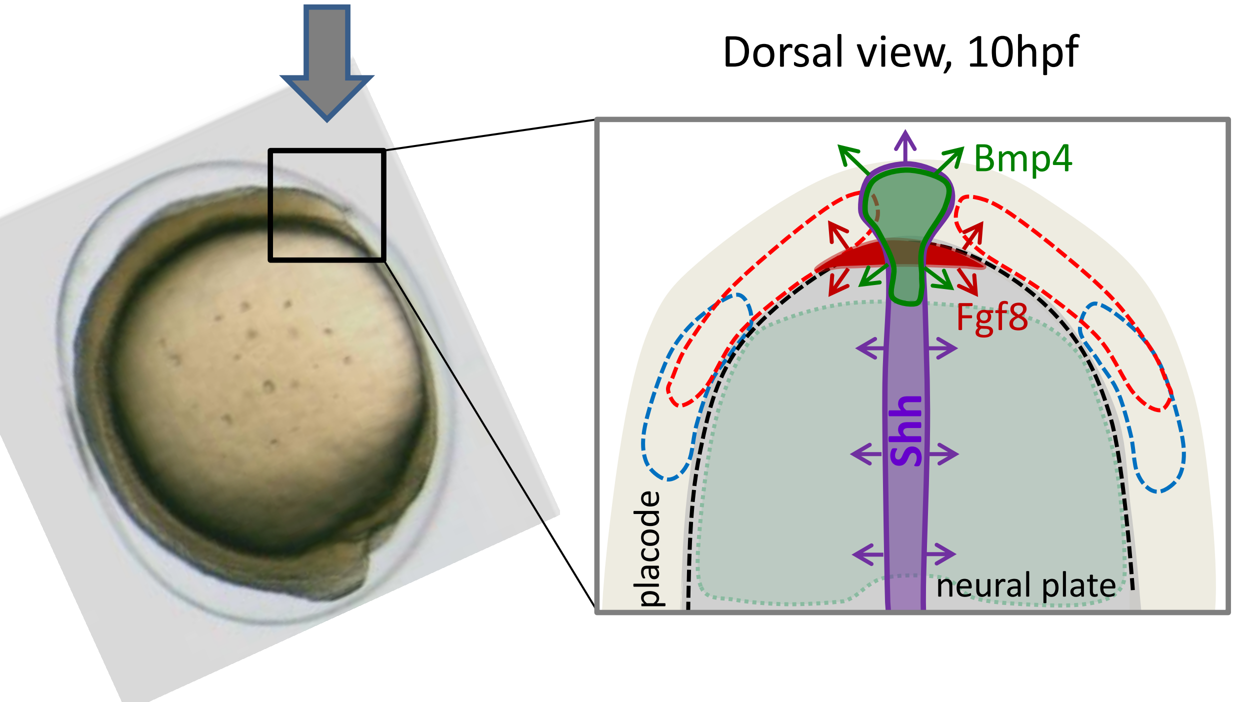


Signaling centers orchestrate head development

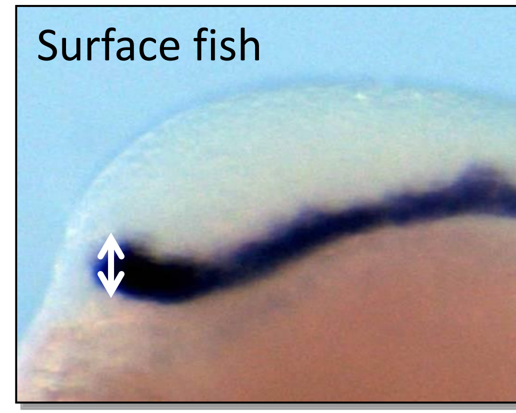


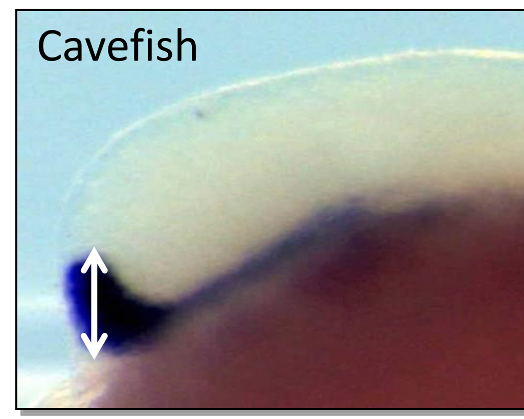
Signaling centers orchestrate head development

Dorsal view, 10hpf



Sonic Hedgehog (Shh)



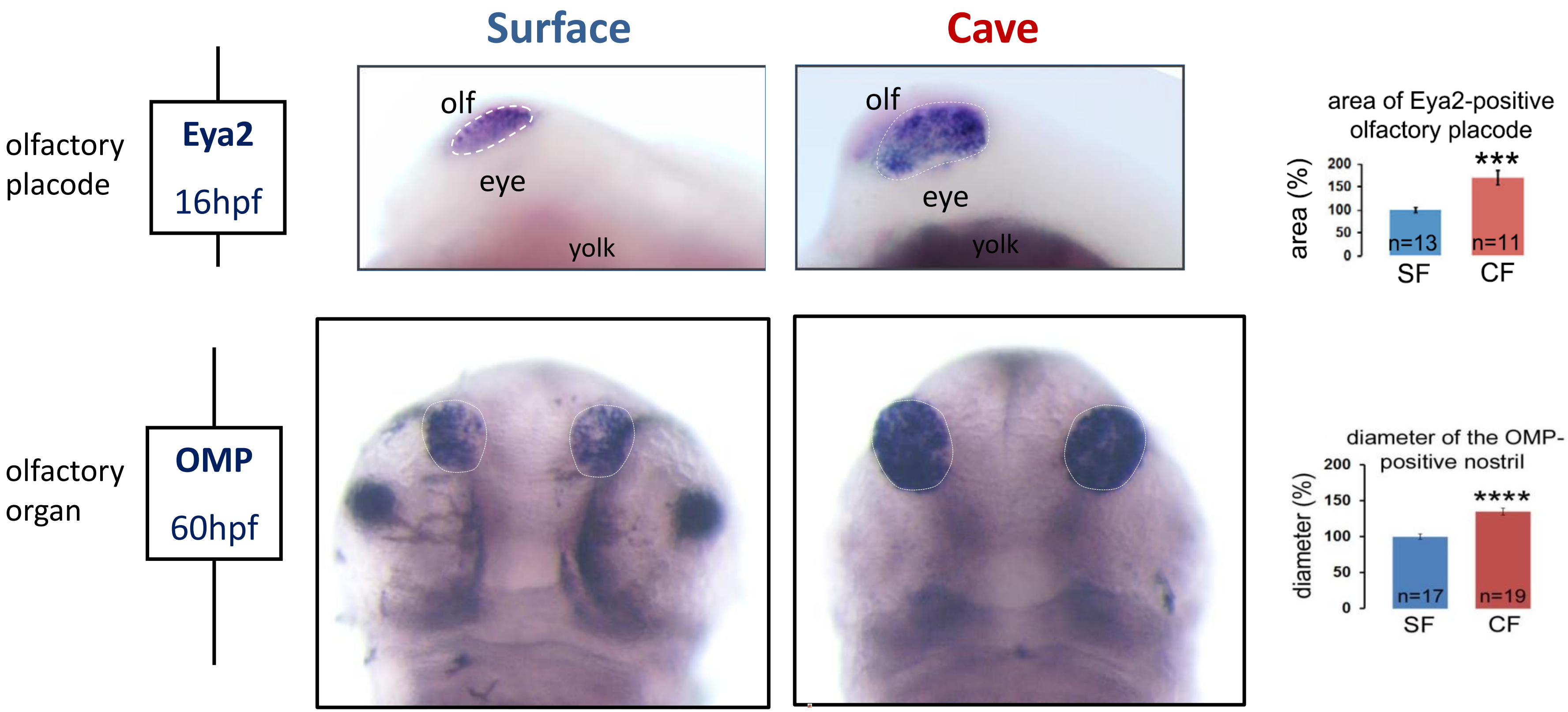


Lateral views

- Signaling centers are modified in cavefish

  Yamamoto et al., Nature 2004
  Pottin et al., Development 2011
  Hinaux et al., Development 2016

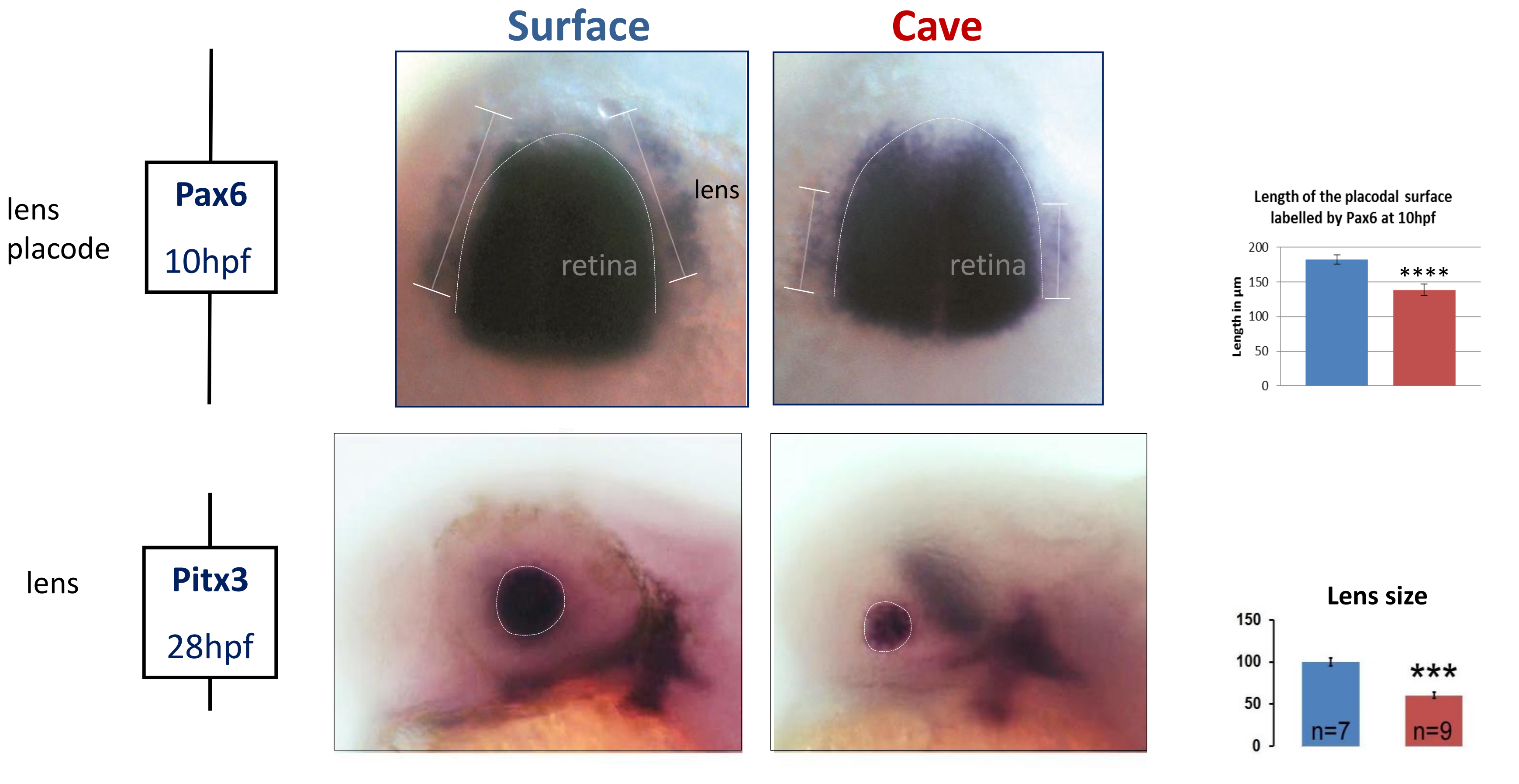
Placode patterning: olfactory placode



- The olfactory placode is enlarged in cavefish

Hélène Hinaux

Placode patterning: lens placode



- The cavefish lens placode is reduced, its olfactory placode is enlarged
- Major size differences, from very early on

Hélène Hinaux

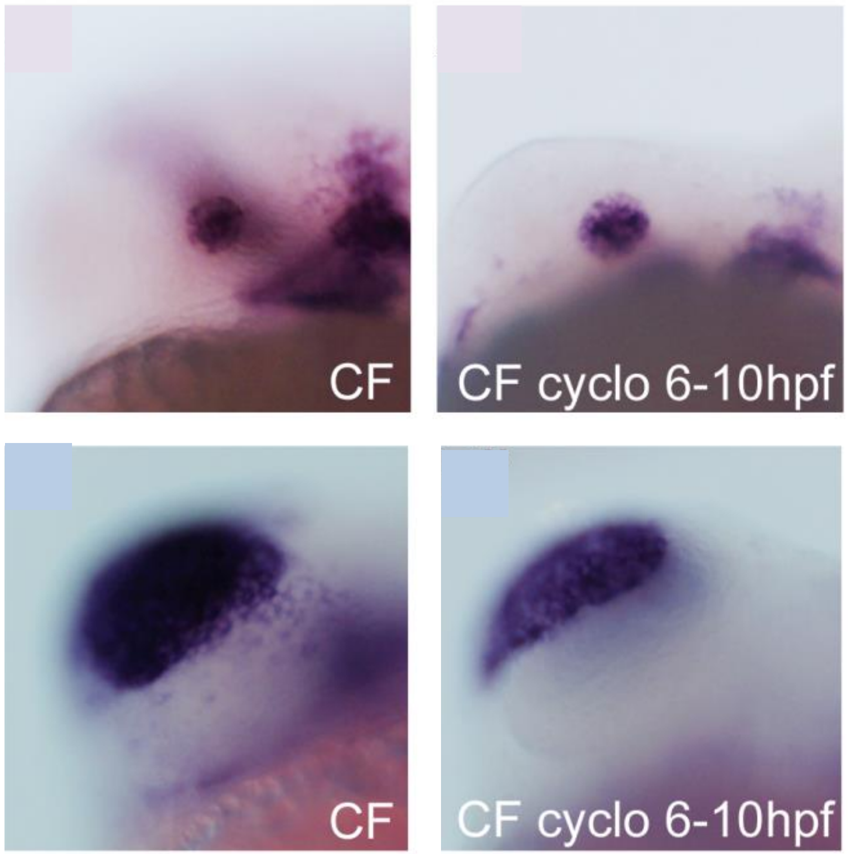
Manipulating Shh signaling in cavefish

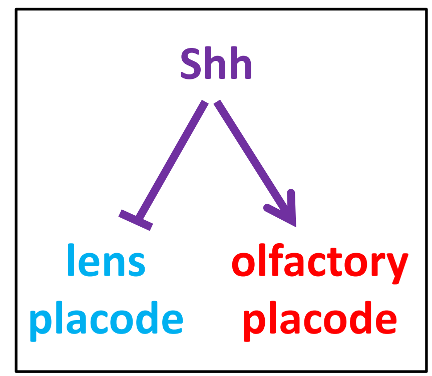
Control cavefish

Cavefish + Cyclopamine ⊣ Shh

Lens (Pitx3)

Olf. (Eya2)



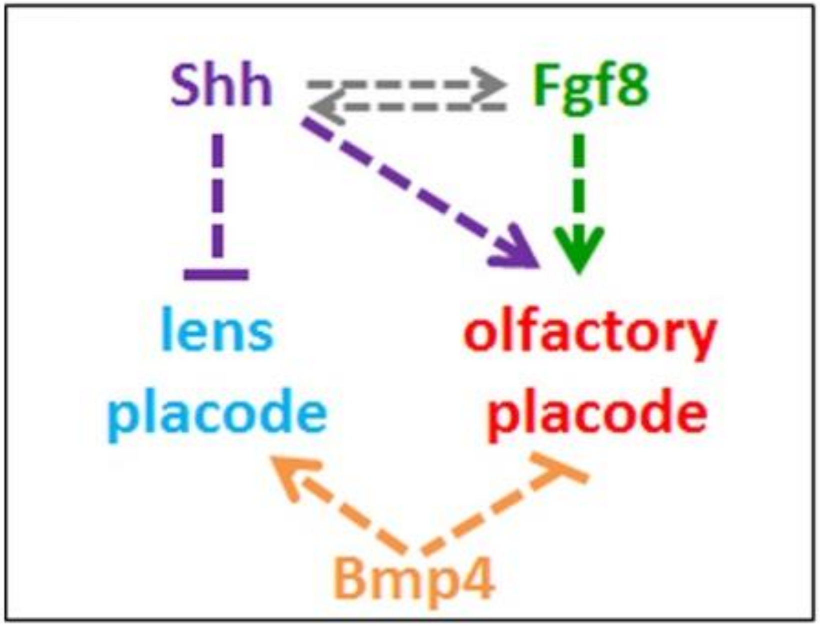


- Hedgehog signaling has opposing effects on the two sensory fates
- Example of morphogenetic effect

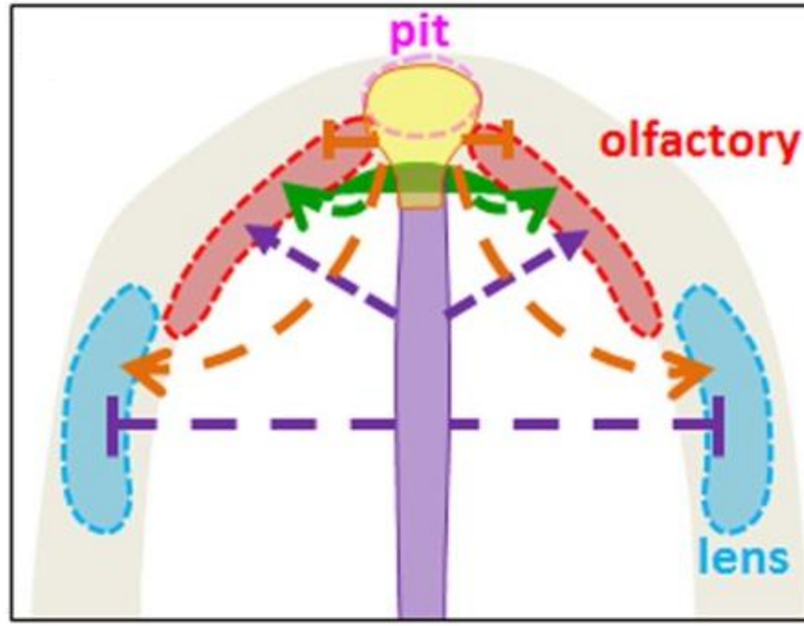
Hélène Hinaux

Signaling centers and cavefish placodes

Regulatory network



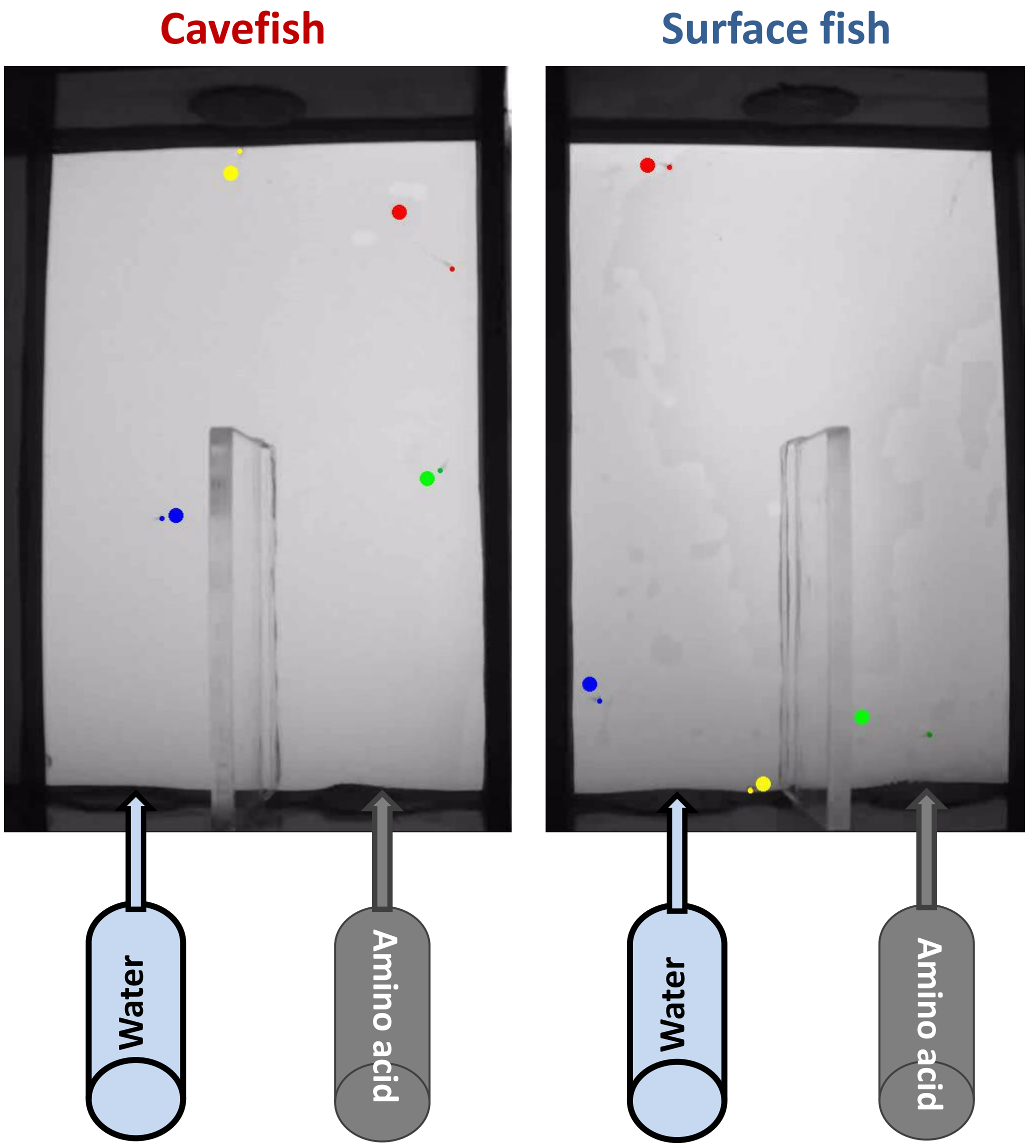
Embryonic context



Hinaux et al., Development 2016

- Trade-off between two sensory organs
- Example of developmental evolution of organ size, with potential adaptive value

Comparing olfactory capacities in surface and cavefish



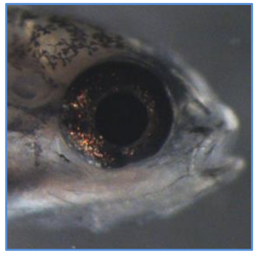
(Alanine 10^{-6}M)

Measuring response to
food-related odors
(amino acids)

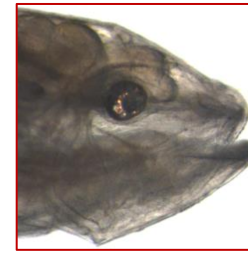
Yannick Elipot
Yoni Bibliowicz
Maryline Blin

Do cavefish smell better?

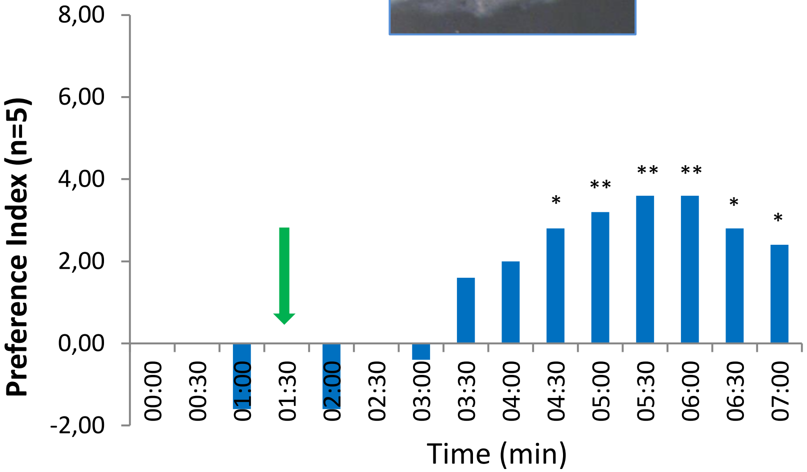
Surface Fish
One month

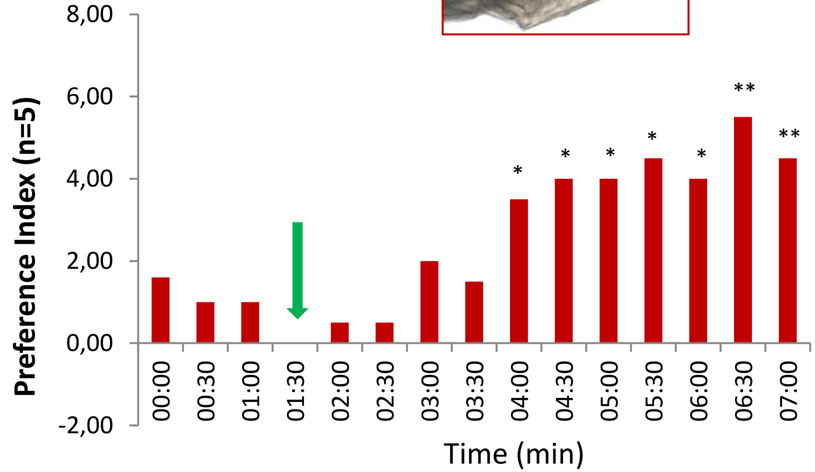


Cavefish
One month



Serine
10^{-5} M

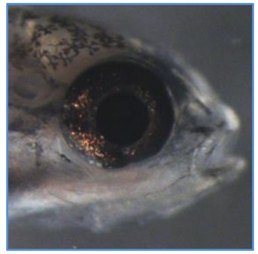




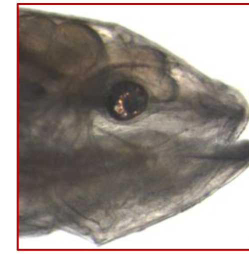
Yannick Elipot, Yoni Bibliowicz

Do cavefish smell better?

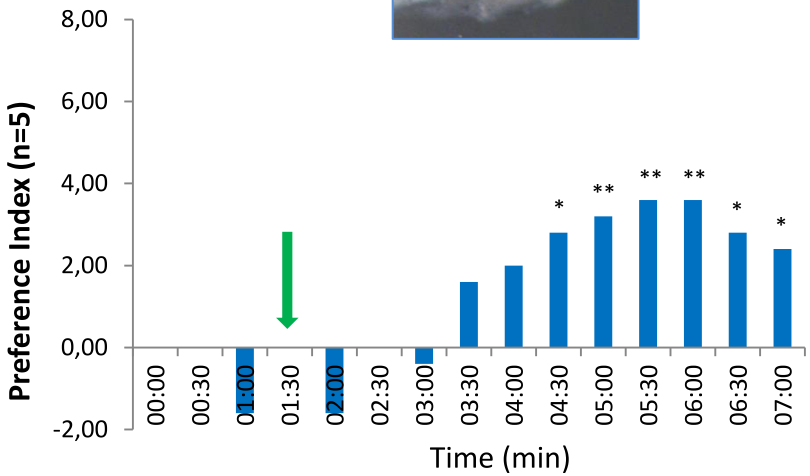
Surface Fish
One month

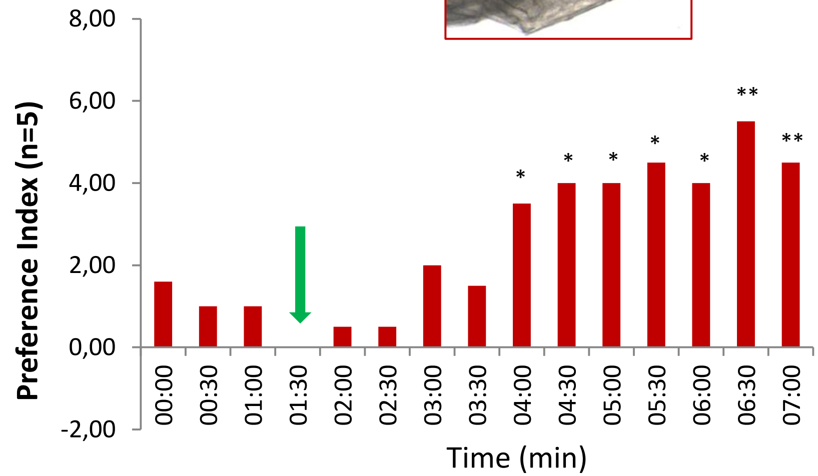


Cavefish
One month

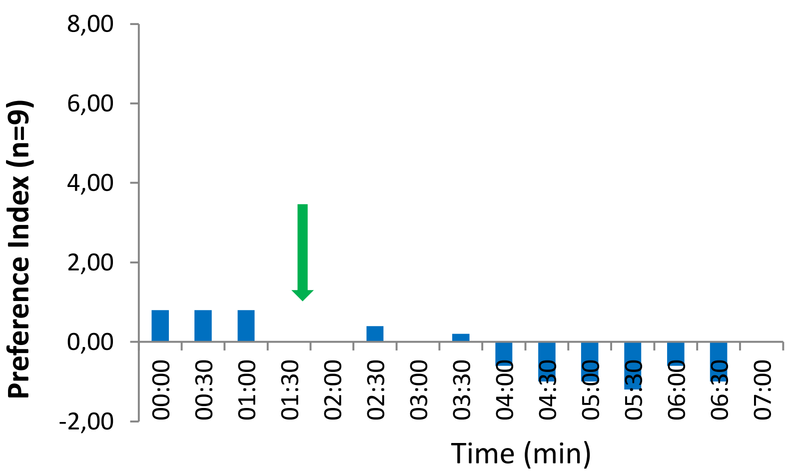


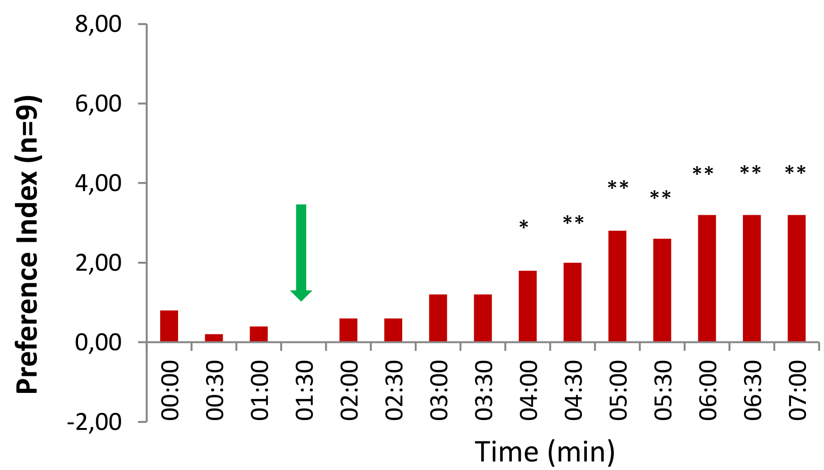
Serine
10^{-5} M





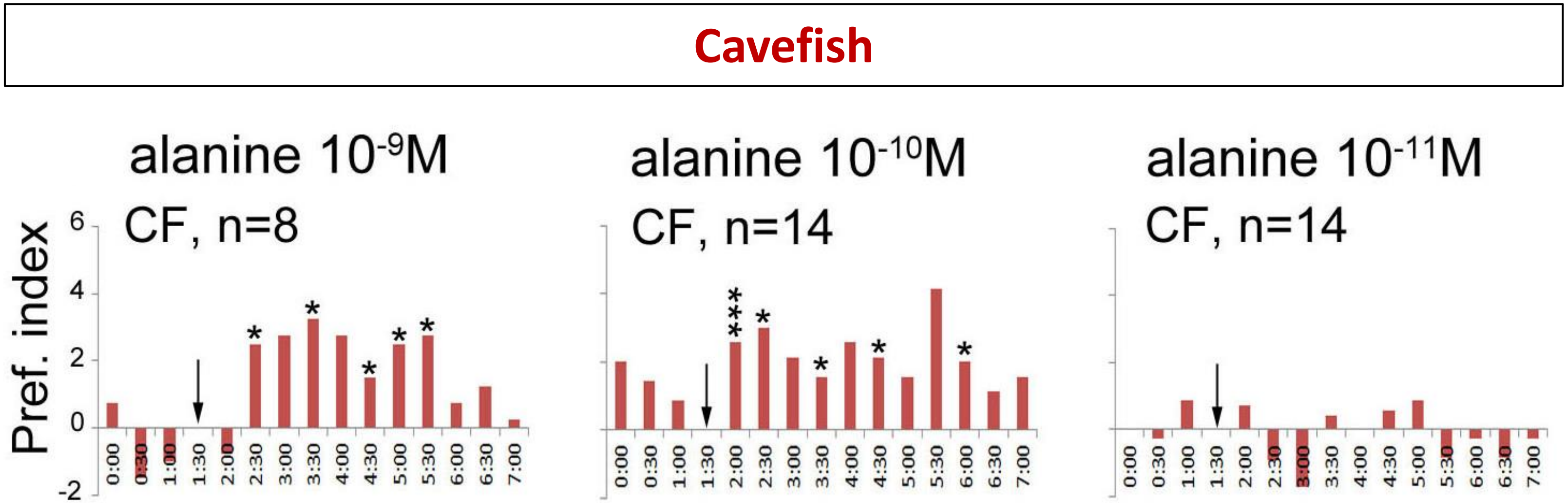
Serine
10^{-6} M

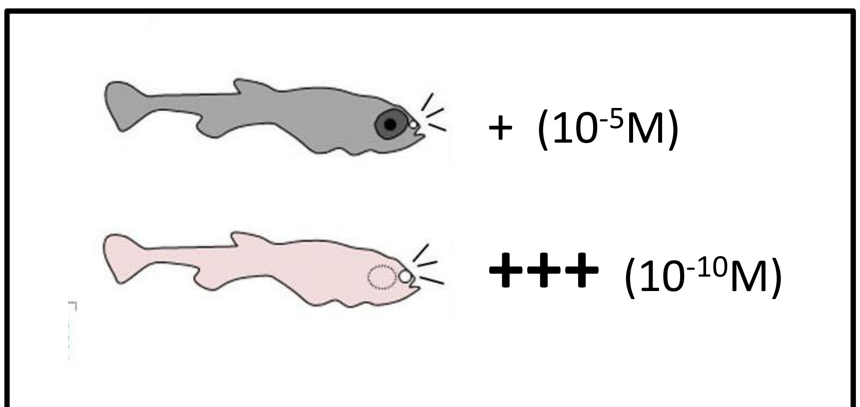




Yannick Elipot, Yoni Bibliowicz

How much do cavefish smell better?

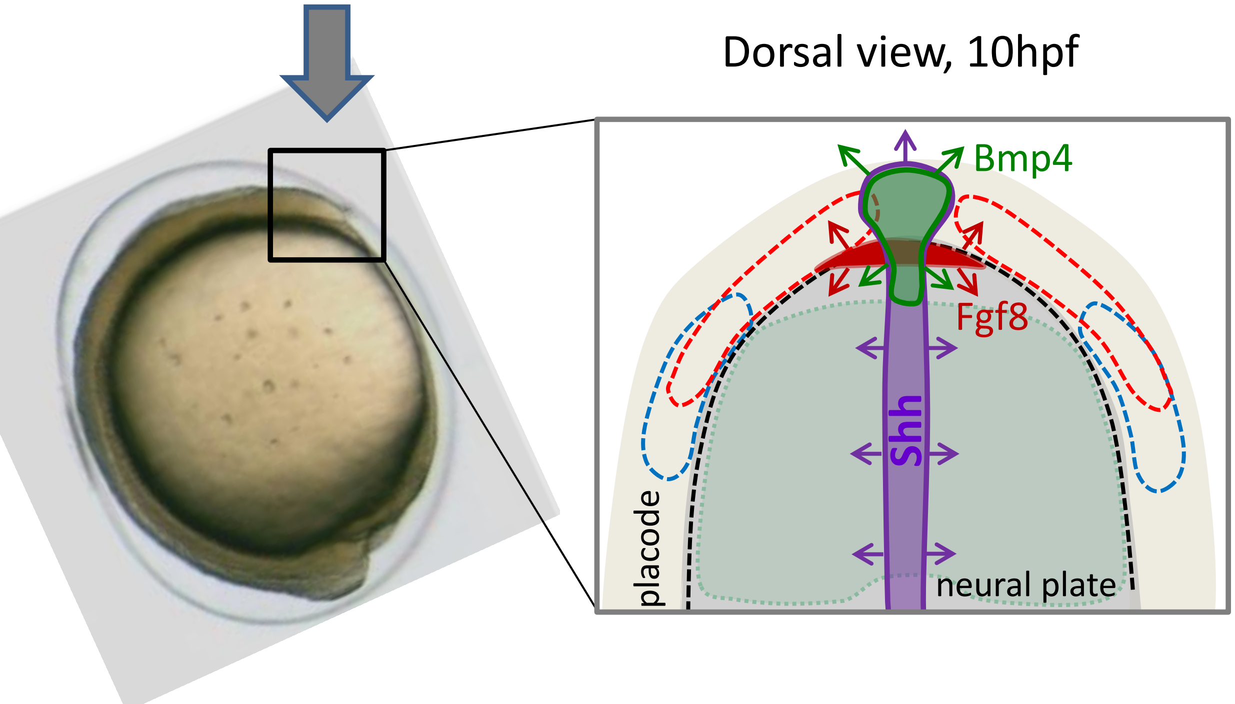




- Outstanding olfactory sensory specialisation

Yannick Elipot

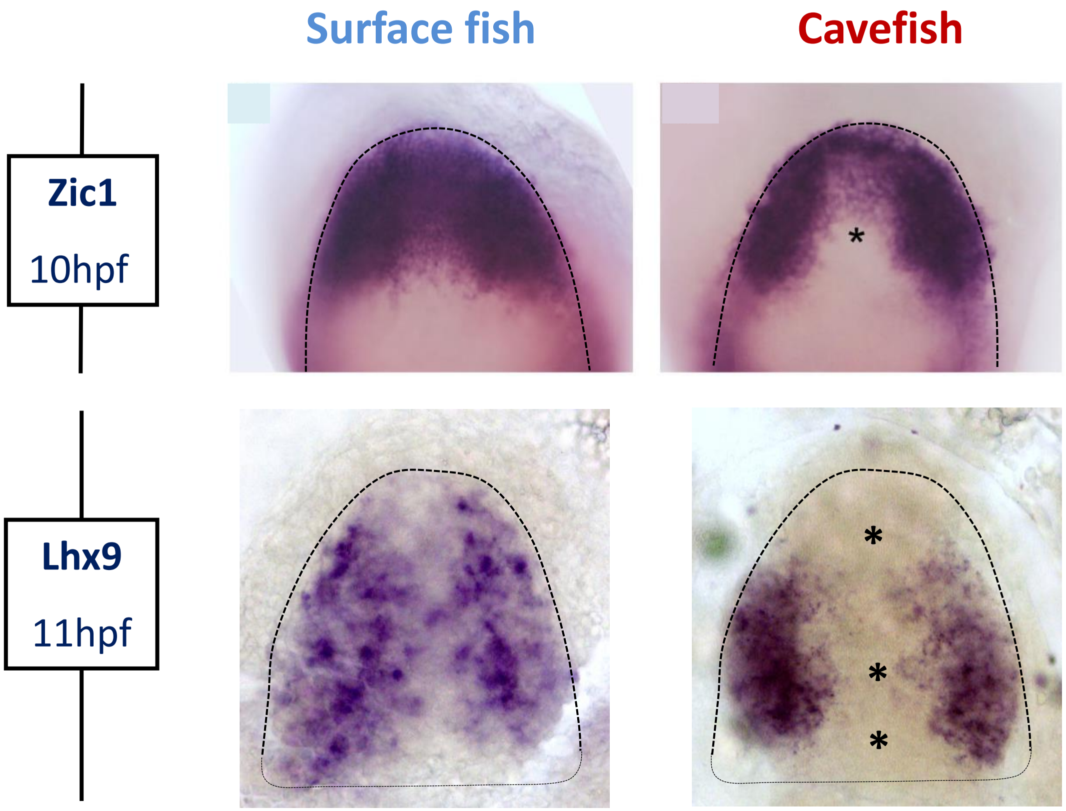
Signaling centers orchestrate head development

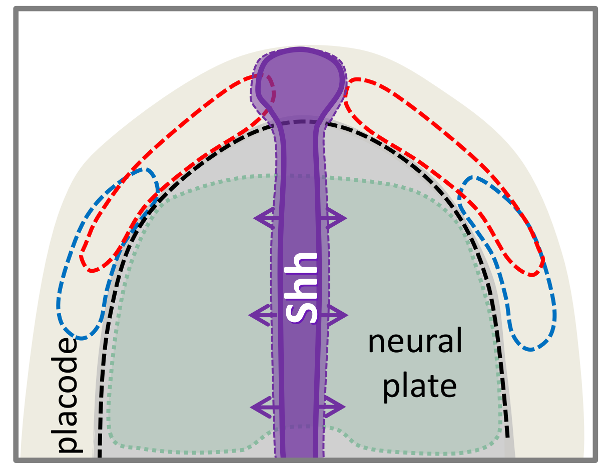


- Signaling centers are modified in cavefish

Yamamoto et al., Nature 2004
Pottin et al., Development 2011
Hinaux et al., Development 2016

Neural plate patterning



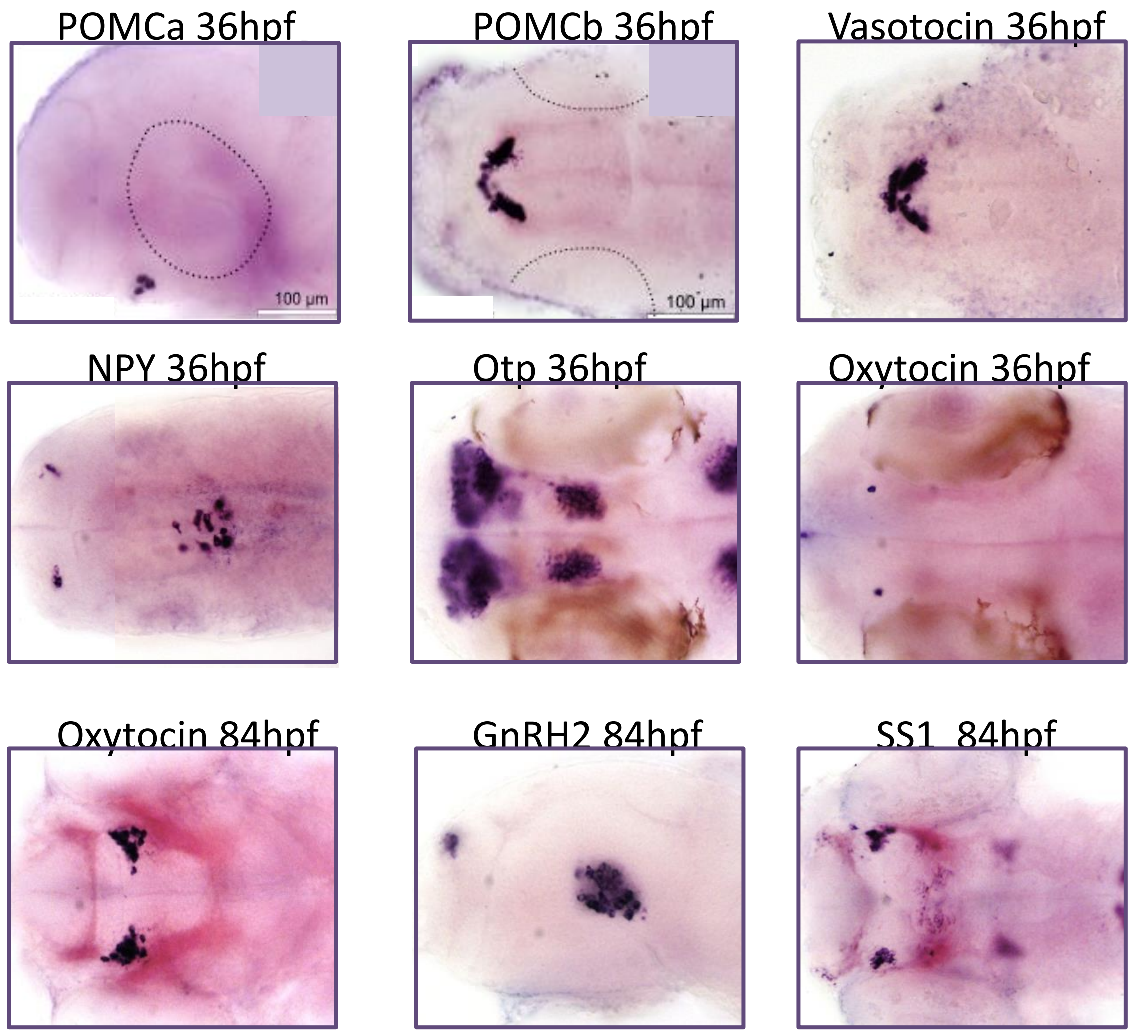


- The cavefish neural plate is modified, particularly at the midline
- The medial part of the neural plate gives rise to the hypothalamus

Pottin et al, Development, 2011

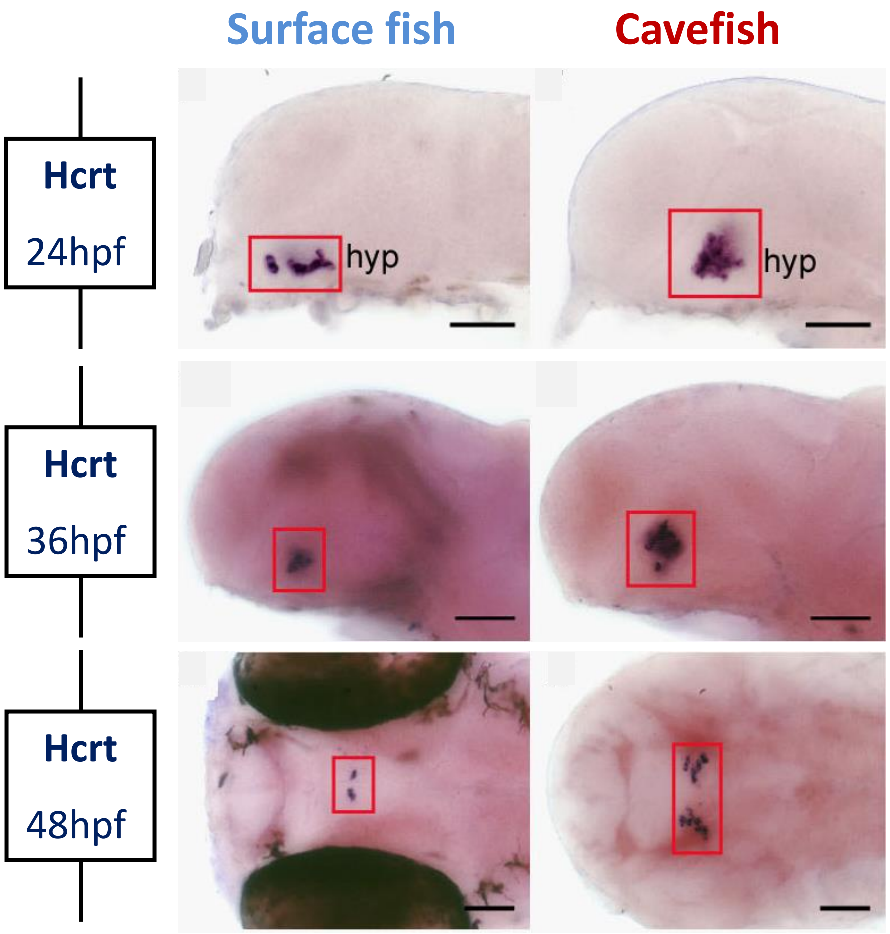
Hypothalamic development

- ✓ NPY
- ✓ Hcrt
- ✓ AgRP
- ✓ POMC a
- ✓ POMC b
- ✓ AVT/vasotocin
- ✓ IT/oxytocin
- ✓ CART3
- ✓ MCH
- ✓ GnRH2
- ✓ Somatostatin 1
- ✓ Somatostatin 2
- ✓ Otpa, Otpb
- ✓ Lhx7, Lhx9



- Comparative mapping of the development of neuropeptidergic cell groups in surface fish and cavefish

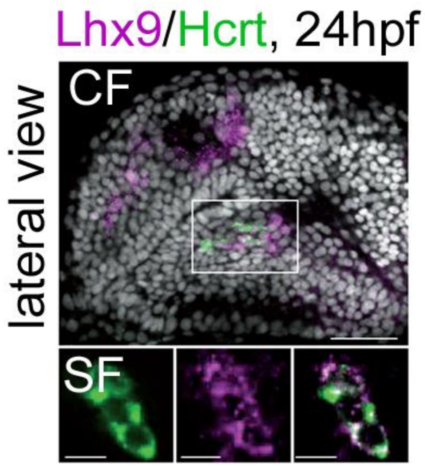
Hypocretin neurons of the hypothalamus



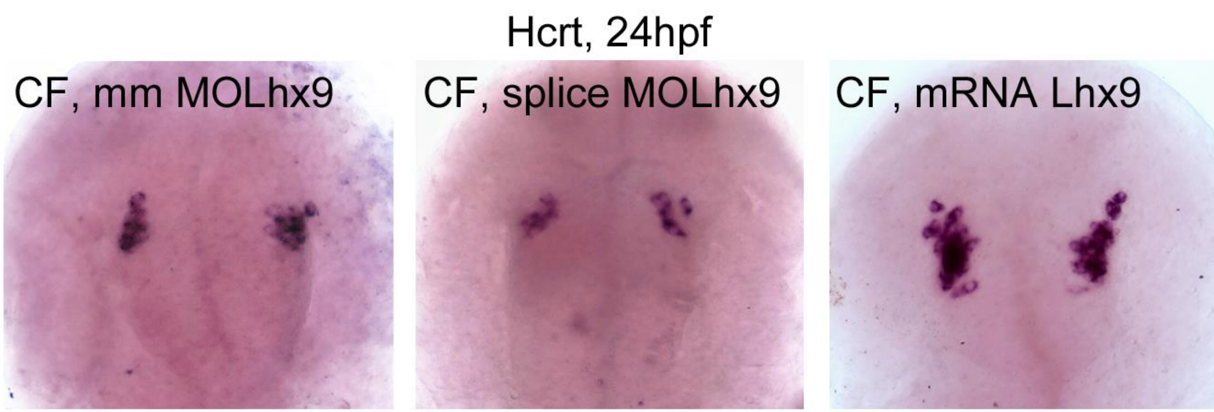
- More Shh-dependent Hcrt neurons in cavefish

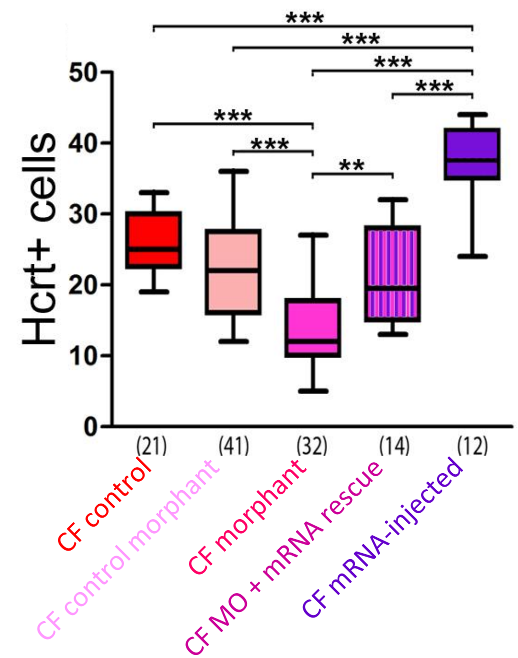
Alié*, Devos*, Torres-Paz* et al., eLife 2018

Lhx9 controls hypocretin specification



- All Hcrt neurons express *Lhx9*



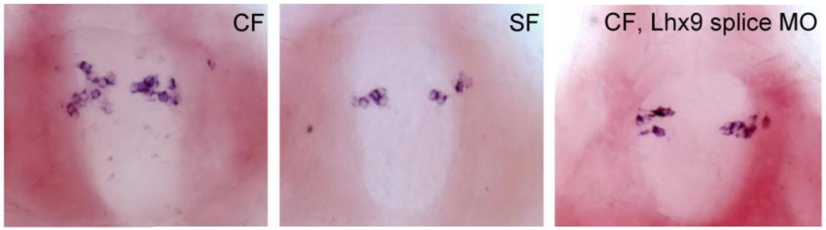


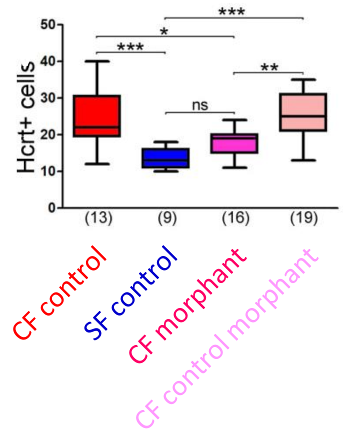
- Lhx9 is necessary and sufficient to induce Hcrt specification

Jorge Torres Paz

Hypocretin neurons and loss of sleep in cavefish

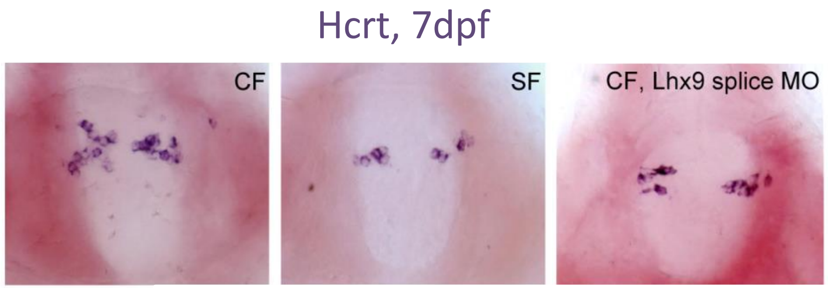
Hcrt, 7dpf

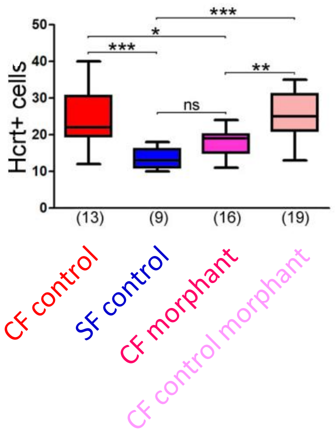




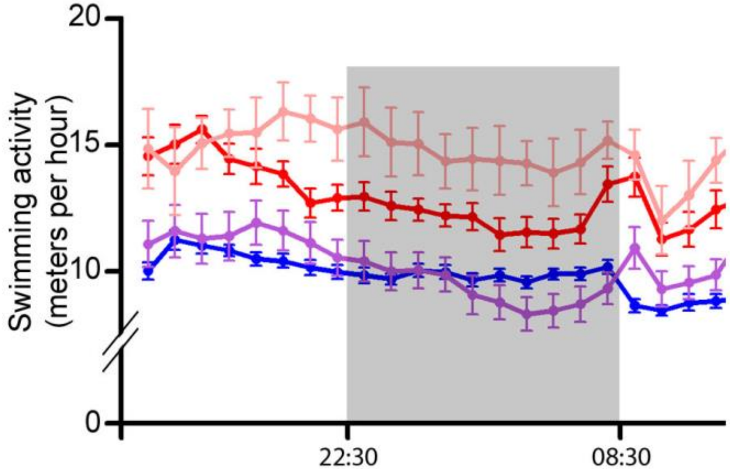
Alié*, Devos*, Torres-Paz* et al., eLife 2018

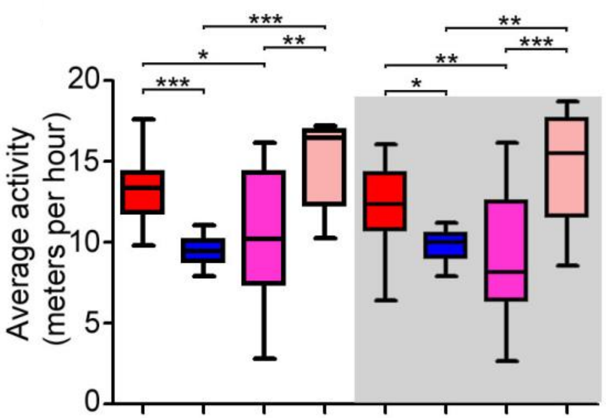
Hypocretin neurons and loss of sleep in cavefish





Locomotor activity



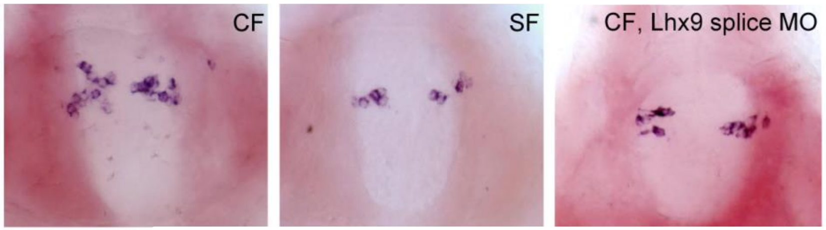


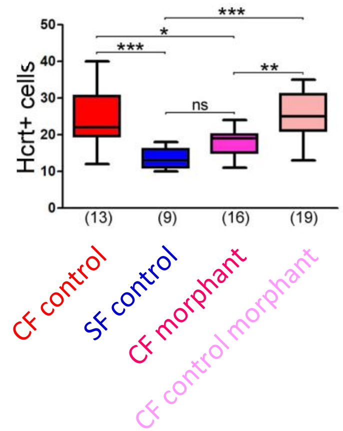
cavefish
cavefish *Lhx9* morphant
surface fish

Alié*, Devos*, Torres-Paz* et al., eLife 2018

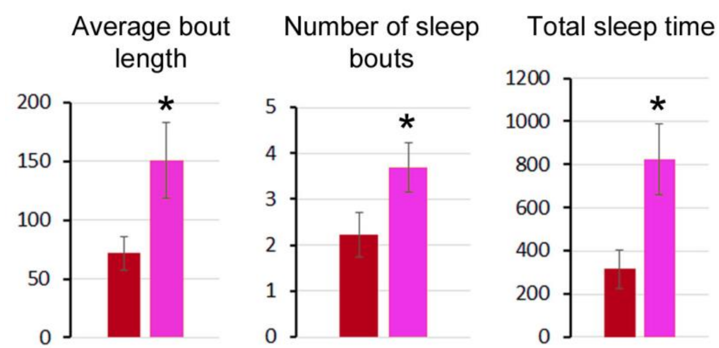
Hypocretin neurons and loss of sleep in cavefish

Hcrt, 7dpf





Sleep



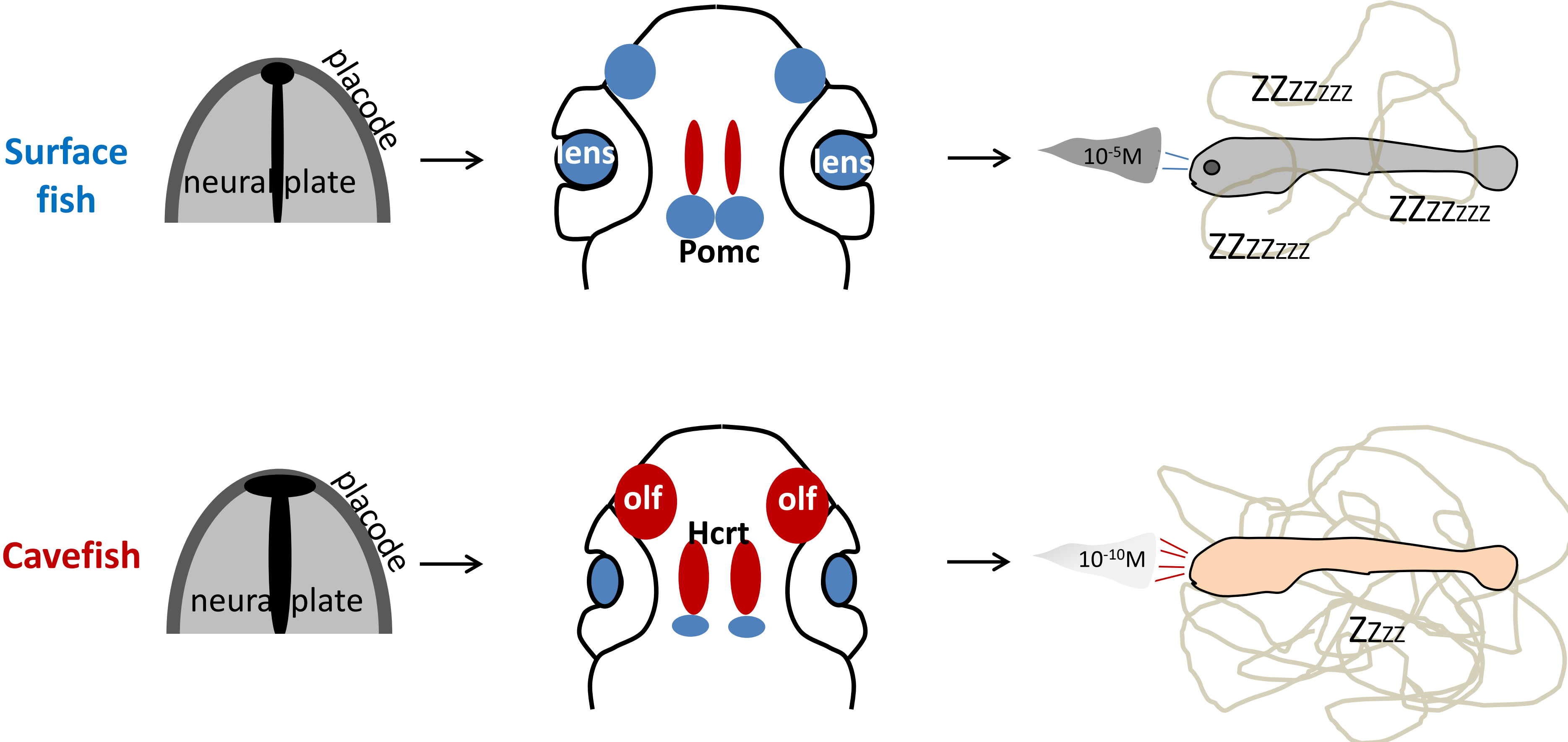
CF control

CF *Lhx9* morphant

- Developmental evolution of the number of hypothalamic Hcrt neurons participates to the elevated locomotor activity and the reduction of sleep in cavefish

Alié*, Devos*, Torres-Paz* et al., eLife 2018

Summary - Conclusion



- From early developmental evolution to adaptive behavioral evolution

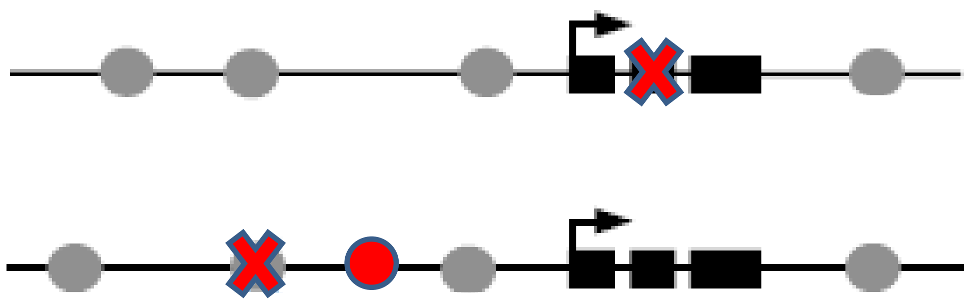
Genotype-phenotype relationship

- Changing the size, shape, number, or color of physical traits is fundamentally different from changing the chemistry of physiological processes.

- Relative contributions of changes in **coding** versus **regulatory** sequences ?
  (Carroll 2005, 2008; Wittkopp and Kalay 2012).

!!! Nothing known in cavefish, but bet on regulatory change !!!

« Developmental genes »



LOF mutation,
lethal

regulatory mutation,
viable / adaptive

The **modular nature of *cis*-regulatory elements and pleiotropy of gene products** allows for selective spatio-temporal changes of expression patterns and morphological changes

Sean Carroll

Genotype-phenotype relationship

- Changing the size, shape, number, or color of physical traits is fundamentally different from changing the chemistry of physiological processes.

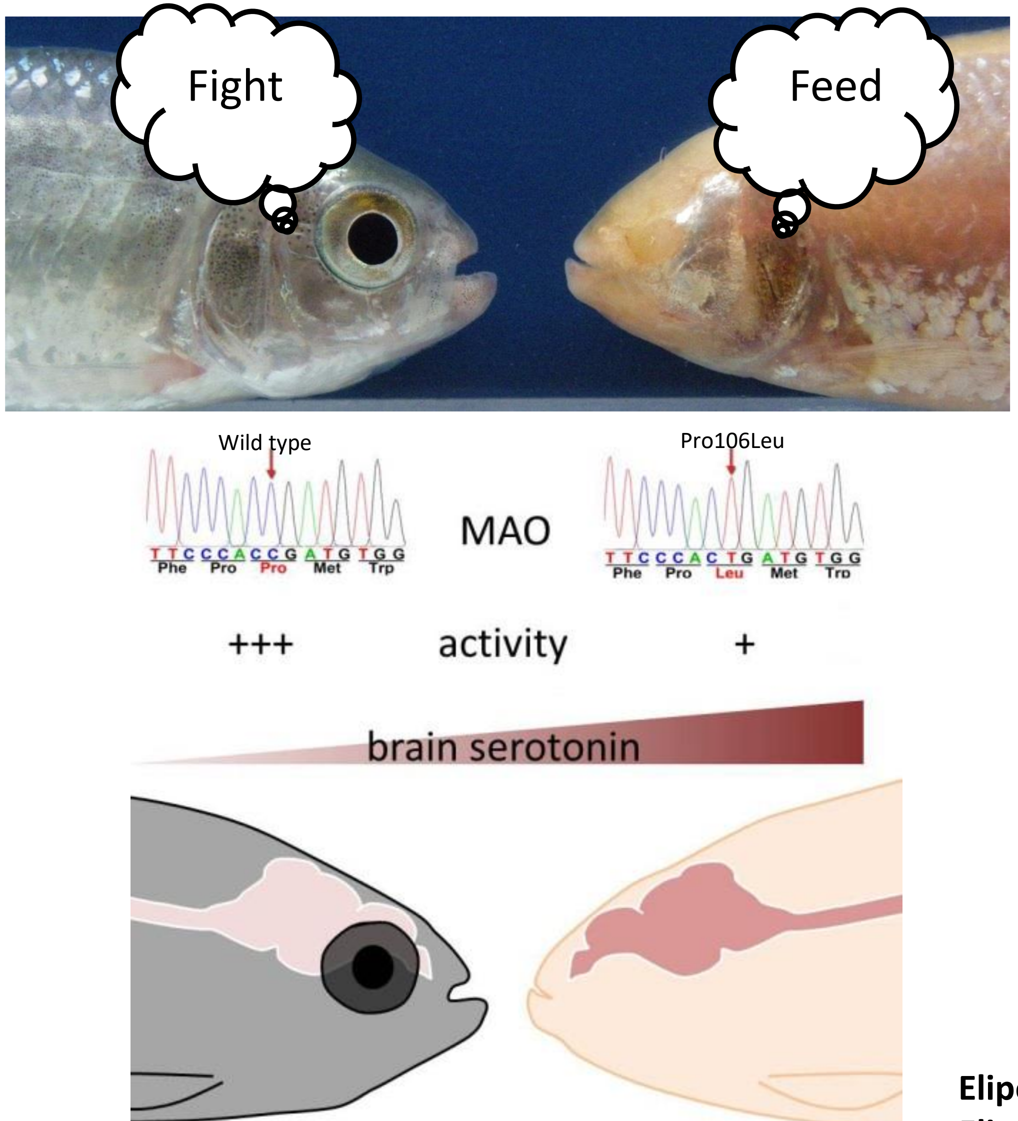
- Relative contributions of changes in **coding** versus **regulatory** sequences ? (Carroll 2005, 2008; Wittkopp and Kalay 2012).

« Chemistry genes »

Oca2 (Ocular and Cutaneous Albinism 2)	➡	Albinism/pigmentation
Mc4R (Melanocortin Receptor4)	➡	Increased appetite
InsR (Insulin receptor)	➡	Insulin resistance/diabetes
MAO (Mono Amine Oxidase)	➡	Serotonin/behavior

Protas et al. *Nat Genet* 2006
Gross et al. *PLoS Genet* 2009
Aspiras et al. *PNAS* 2014
Riddle et al. *Nature* 2018

MAO mutation and loss of aggressiveness in cavefish



Elipot et al. Current Biology 2013
Elipot et al. Nature Comms 2014

Thank you


Carole Hyacinthe
Jorge Torres-Paz
Victor Simon
Yannick Elipot
Eugène Tine
Lucie Devos
Laurent Legendre
Alexandre Alié
Stéphane Père
Marilyne Blin
Hélène Hinaux
Luis Espinasa
Joel Attia
Didier Casane
Julien Fumey
Karen Pottin
Yoni Bibliowicz
Constance Pierre