Gene-environment interactions underpinning temperature induced sex reversal in a dragon lizard (*Pogona vitticeps*)

SCAN ME

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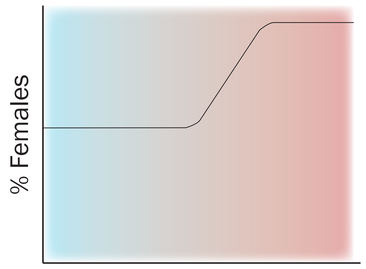
Did you know that the bearded dragon can reverse sex from male to female during embryonic development under the influence of high temperatures?

We use this species to understand the epigenetic mechanisms by which environmental factors, such as temperature, can influence gene expression and determine sexual fate.

It is unknown how temperature influences sex during embryongensis, but there are promising candiates[1]. CLK1/4and CIRBP are highly conserved genes shown to respond to changes in environmental conditions[2]. Chromatin remodelling genes JARID2 and KDM6B have unique splicing patterns in association with temperature across evolutionarily disparate lineages[3].

What is sex reversal?




Concordant Males
ZZ genotype


Concordant Females
ZW genotype


Sex Reversed Females
ZZ genotype

High incubation temperatures experienced during development can cause ZZ males to reverse sex and develop as females.

Sex reversed females can breed successfully, generating all ZZ offspring whose sex is determined only by incubation temperature[4]

What did we do?

Does CLK1/4 interference at high temperatures disrupt sex reversal?


1. Incubate eggs at high temperatures to induce sex reversal


2. Explant urogen-ital system and culture *ex vivo*

3. Treat with CLK1/4 inhibitor TG003

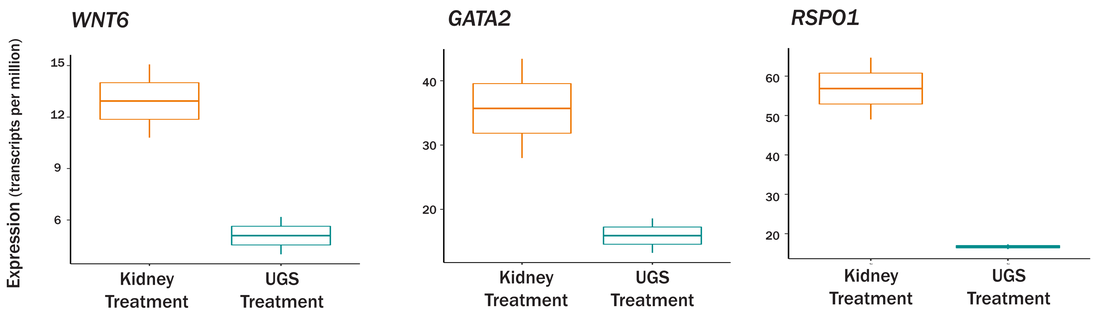
How is gene expression and splicing altered by high incubation temperatures? Are the transcriptoional signatures of sex reversal shared with other species?


1. Incubate eggs at high and low temperatures

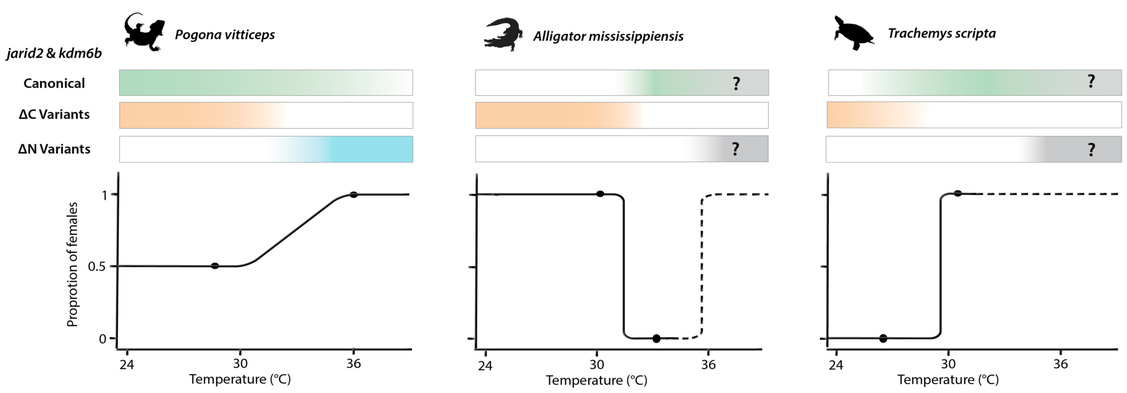

2. Dissect isolated gonads at different developmental stages


3. Use RNA-seq to assess changes in gene expression and splicing[5]

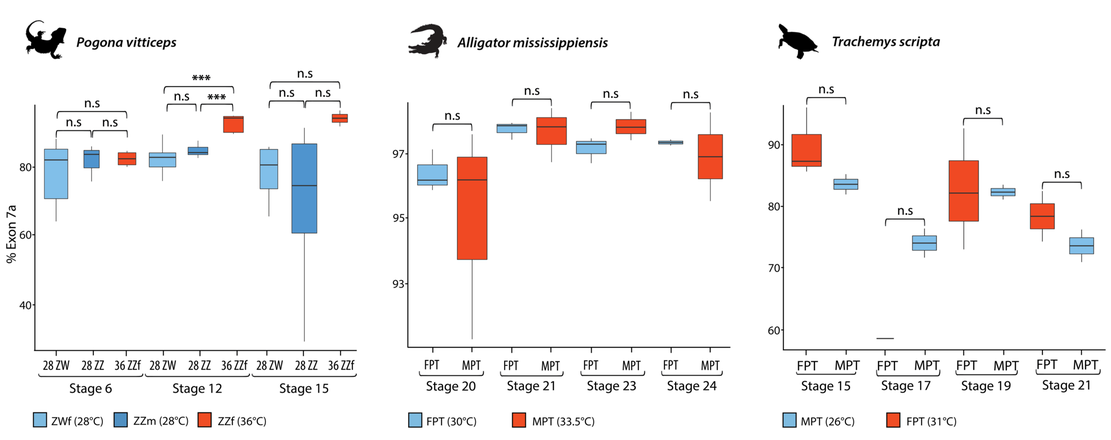
What did we find?



Treatment with CLK1/4 inhibitor drug TG003 interferes with sex reversal pathway via downregulation of female genes. *WNT6*, *GATA2* and *RSPO1* show a nearly two-fold decrease.



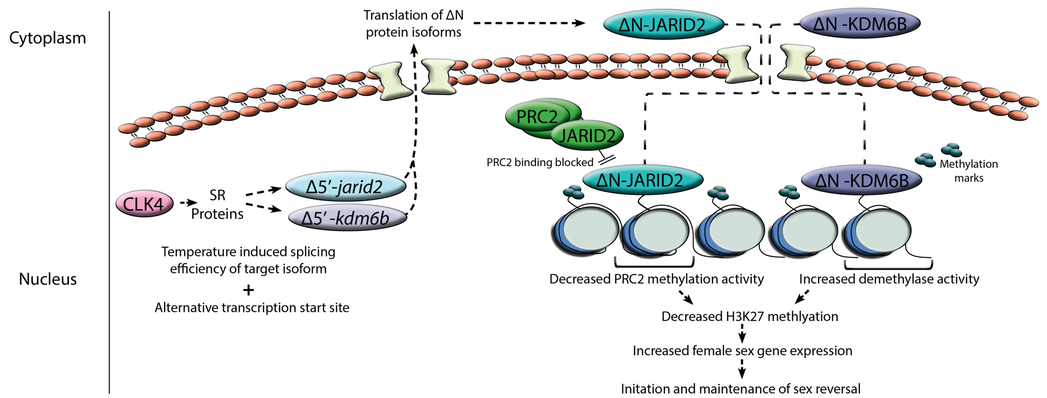
Unique variants of chromatin remodelling genes *jarid2* and *kdm6b* are associated with sex reversal in *Pogona vitticeps* that are not shared with other species with thermosensitive sex determination systems



Splicing of thermally stable *cirbp* variant containing exon 7a[2] increases during sex reversal in *Pogona vitticeps*. *Cirbp* is not differentially spliced at different incubation temperatures in other species

Is this how sex reversal works?

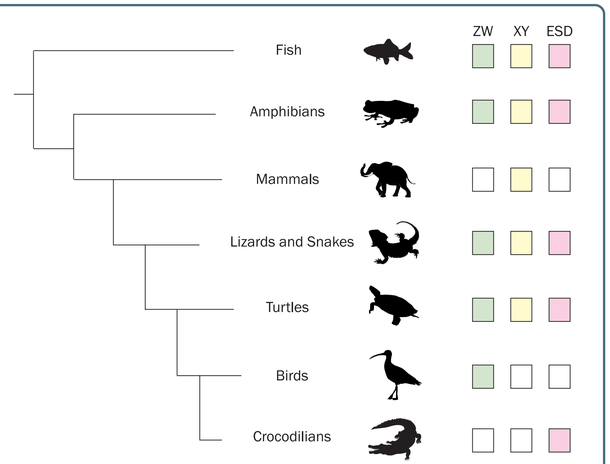
Temperature induced sex reversal pathway requires complex multi-gene cascades mediated by genes with inherent temperature sentivitiy



What now?

Sex determination systems with gene-environment interactions are very complex, and we still know very little about how they work at the molecular level.

A huge diversity of species have various types of environmentally sensitive sex determination systems. It is important to understand the processes driving the evoltuion of these systems



For illustrative purposes only. Adapted from Gamble & Zarkower 2012

As for our dragon, we are working on using gene editing techniques to switch sex reversal off at high temperatures, and switch it on at low temperatures

References

[1]Castelli et al., 2020. Biological Reviews, doi:10.1111/brv.12582

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[3]Deveson et al., 2017. Science Advances, doi: 10.1126/sciadv.1700731

[4]Holleley et al., 2015. Nature, doi:10.1038/nature14574

[5]Whiteley et al., 2021, PLoS Genetics, doi:10.1371/journal.pgen.1009465

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If you are interested in our research. check out other work from our lab. We also work on two other species with environmental sex determination.

http://georges.biomatix.org/