Androgen Receptor β Modulates Female Reproductive Physiology in Cichlid Fish

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INTRODUCTION
In vertebrates, androgens regulate the development and maintenance of reproductive traits, which ultimately indicates the evolutionary fitness of an individual.

In Astatotilapia burtoni, androgens act through two receptors (ARα & ARβ) play a key role in male aggression and courtship. We have previously shown that male ARβ mutants have larger testes than WT, and male ARβ mutants have smaller testes than WT. However, the role of the androgen receptor in females is still largely unknown.

How does a nonfunctional ARβ affect female physiology in this model species? Specifically, how do gonad morphology and neural activity of ARβ female mutants differ from those of WT fish?

METHODS

ARβ mutants created through CRISPR-Cas9

**ARβ +/-**
ARβ +/-
ARβ -/

**RESULTS**

Qualitative Differences in Reproductive Physiology

Dark, hard masses found growing in the ovaries of some mutants

Numerous eggs found in abdominal cavity of some mutants, likely released from ovaries

ARβ Mediates Ovary Size

GSI (gonad mass / body mass x 100) is significantly higher in both ARβ+/+ and ARβ/- than in WT females

ARβ mutants demonstrate more robust GnRH neurons

DISCUSSION AND FUTURE DIRECTIONS

We have shown that mutation of ARβ leads to striking differences in female reproductive physiology of Astatotilapia burtoni.

Both heterozygous and homozygous mutants demonstrated significantly higher GSI than WT females, implicating a possible functional difference in reproductive success.

Abnormal growths:
Polycystic ovarian syndrome patients have been shown to have increased levels of androgens, raising the question of whether similar mechanisms led to this phenotype in the fish.

High egg production:
We have previously found differential levels of the steroid hormone 11-Ketotestosterone (11KT) in male ARβ mutants, and 11KT has been shown to contribute to oocyte growth.

Difference in the GSI measurements between Cohort 1 and Cohort 2:

- Timing in reproductive cycle: It is possible that the females in Cohort 1 were dissected at the peak of their cycle, and that the females in Cohort 2 had already released their eggs.
- Behavioral suppression: It has been shown in zebrafish that dominant females can suppress the reproductive success of other females

Future experiments:
- Measure 11KT levels
- Stain for GnRH in non-GFP brains
- Look at ARα female physiology
- Behavioral assays with ARα and ARβ female mutants
  - Male ARβ mutants shown to be hyperaggressive and have higher 11KT

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