Transcriptional rewiring, post-transcriptional regulation and neo-functionalization: how the master sex-determining gene of medaka was born

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OR 53

Transcriptional rewiring, post-transcriptional regulation and neo-functionalization: how the master sex-determining gene of medaka was born.

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In medaka, *dmrt1bY*, the duplicated copy on the Y-chromosome of *dmrt1a*, became the master regulator of male development after acquiring an upstream position in the sex-determining cascade. Remarkably this evolutionary novelty, requiring a rewiring of the regulatory network, was brought about by co-optation of pre-existing *cis*-regulatory elements contributed by transposable elements. To another level of regulation, differential gene expression of the two dmrt1 co-orthologs seems to be also mediated by post-transcriptional regulation through a highly conserved cis-regulatory motif that directs differential gonadal synexpression of Dmrt1 transcripts during gonad development.
While the autosomal *dmrt1a* is essential for testis maintenance, in contrast, *dmrt1bY* was shown to be responsible for male-specific primordial germ cell (PGC) mitotic arrest in the developing gonad at the sex-determination stage. Accordingly, the onset of *dmrt1bY* expression was recorded exactly at this stage in the Sertoli cell precursors only.
For a detailed analysis of expression, regulation and function of Dmrt1 and other gonadal genes we generated several transgenic fluorescent reporter lines (BAC clones). Strikingly, we observed a very early expression of *dmrt1bY* in the PGCs long before the somatic gonadal primordium is committed. This PGC-specific expression then progressively vanishes while the somatic expression of *dmrt1bY* rises only at hatching stage. Concomitantly we observed that an HMG-box gene shows a strictly inverse PGC-specific expression pattern in relation to *dmrt1bY*. Interestingly, also some other gonad development genes showed transient sex-specific expression in the pre-committed gonad primordium. Using *in vivo* whole tissue ChIP and *in vitro* gene regulation assays, we found clear evidences that the specific expression pattern of *dmrt1bY* is controlled by differential cross-regulations of *dmrt1a, dmrt1bY* and the HMG-box gene as well as by specific stabilization and translational control of dmrt1 transcripts *via* an RNA-binding protein.

OR 54

The sexual fate of the gonad in the protandrous fish

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Gonadal sex determination and differentiation is important for gonadal development, reproduction and sex manipulation in animals. Various mechanisms may exist in different species. Sex change occurs in a variety of fish and invertebrates. This ability is lost in amphibians, reptiles, birds and mammals. Furthermore, no ancient ancestry and no single sex-determining mechanism are involved in the hermaphroditic fish. However, the origins and evolution of hermaphroditism in fish are far from understood. Protandrous hermaphroditic fish (black porgy, *Acanthopagrus schlegelii*) is a unique to study sex differentiation and development of gonad especially due to the interaction between testicular and ovarian tissues. Gene profiles in the testis (male-related genes) and ovary (female-related genes) during sex differentiation and sex change were characterized. The sex switch is controlled by male fate that testis is a dominant ovary-suppressing factor. Sertoli cell Dmrt1 is a key regulator for testis development and regulates spermatogonia proliferation through Amh during testis development. Knockdown of *dmrt1* and *amh* resulted in the female fate. Estradiol treatment induced the ectopic oocytes in the regenerated testis and then sex change to a female gonad. Furthermore, the cells surrounding the oocytes are Dmrt1-positive cells (Sertoli cells) in the oocytes at an early stage (with a robust Fig1a staining) and change to Cyp19a1a-positive follicle cells. Fig1a and Amh play important roles in the development of somatic cell transdifferentiation (Sertoli cells to follicle cells). These results shed light on the understanding for the appearance of more than one sex at the life time and also for the evolutionary transition from gonochorism to hermaphroditism in fish.