Medaka mutant of *cyp21a2* with the loss of cortisol reveals presence of two populations of *pomca*-expressing cells in pituitary and the defect in reproduction – a new disease model

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Cortisol is a critical steroid hormone indispensable for sustaining life in various vertebrates. In human being, an impaired synthesis of cortisol has been well documented as Congenital Adrenal Hyperplasia (CAH) which shows manifesting life-threatening symptoms such as salt-wasting and dehydration accompanied with hyperandrogenism. The defect of *CYP21A2* is identified as the most common genetic causes of CAH. Using the teleost fish, medaka (*Oryzias latipes*), we have disrupted the gene of *cyp21a2*. The homozygous mutant does not show any apparent defect during embryogenesis, but after hatching, only 10% reaches adulthood. No cortisol was detected in whole embryos and blood samples by liquid chromatography-mass spectrometry. The mutant exhibits hyperplastic interrenal (adrenal-equivalent organ in teleost) and pituitary, which is recovered upon administration of cortisol during embryogenesis. We found two populations of *pomca* (precursor transcripts of ACTH)-expressing cells which responds differently to a level of cortisol. Interestingly, the homozygous mutants of adult males (XY) are fertile while no spawning of eggs is observed. We will describe the critical role of cortisol on ovulation and meiotic arrest along with analysis of an HPG axis.