Requirements for maintenance and differentiation of germline stem and progenitor cells

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Emperor Yu Tames the Flood. The cover adopts the concept of ancient Chinese

myth and legend "Emperor Yu Tames the Flood". Yellow River, the "mother river of China" represents the germline which is the vehicle of reproduction. The artifact leisi handheld by Dayu represents the mitochondrial fusion factor in germline-Pld6. Emperor Yu governances mitochondrial fusion by Pld6 in the germline (Yellow River), thus ensuring the balance of self-renewal and differentiation of GSPCs. Credit: IHB

Germline stem and progenitor cells (GSPCs), including primordial germ cells (PGCs) and germline stem cells (GSCs), generate various states of germ stem cells and then differentiate into specialized cells, while self-renewing to generate more stem cells. The formation, maintenance and differentiation of GSPCs are essential for the animal reproduction process and are regulated by a multitude of mechanisms.

In addition to their long-recognized role in energy production, mitochondria may also regulate cell fate determination. The balance of mitochondrial fusion and fission, namely mitochondrial dynamics, is closely related to cellular physiology and even cell fate. However, whether and how mitochondrial dynamics participate in GSPCs development and gonadal differentiation remain unknown.

Recently, a research group led by Prof. Sun Yonghua from the Institute of Hydrobiology (IHB) of the Chinese Academy of Sciences, in collaboration with Prof. Chen Zhenxia from Huazhong Agricultural University, demonstrated the novel mechanisms used in germline-specific mitochondrial organization are necessary for the maintenance and differentiation of GSPCs. This study was published in *Advanced Science*.

By cross-analyzing the RNA sequencing results of zebrafish juvenile testes and ovaries, the researchers found that the mitochondrial

organization process was significantly enriched by gene ontology analysis, and they identified mitoPLD (zebrafish pld6) as a novel germline-specific gene related to mitochondrial fusion.

By generating pld6-knockout mutants, the researchers found that zygotic disruption of pld6 did not affect the initial number of GSPCs, whereas the mutants had a small size in gonads at 25 dpf and the GSPCs failed to differentiate into early oocytes thereafter. The germ cells disappeared in the mutants after 35 dpf, eventually leading to masculinization and infertility of the mutants. Mitochondrial fusion in the pld6-depleted GSPCs was also severely impaired.

These findings reveal zebrafish Pld6 as a novel germline-specific regulator of mitochondrial fusion, and highlight its essential role in the maintenance and differentiation of GSPCs as well as in gonadal development and gametogenesis.

More information: Ru Zhang et al, A Germline-Specific Regulator of Mitochondrial Fusion is Required for Maintenance and Differentiation of Germline Stem and Progenitor Cells (Adv. Sci. 36/2022), *Advanced Science* (2022). DOI: 10.1002/advs.202270233

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