



BIOLOGY COLLOQUIUM

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Hosted by A/P Liou Yih Cherng

Transposon-activated Immune Signaling in the Aged Niche Drops Germline Stem Cells

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*I obtained PhD training from National Defense Medical Center, Taiwan in 2005, and joined Dr. Daniela Drummond-Barbosa's lab in US for postdoc. training from 2006 to 2010, and then joined institute of Cellular and Organismic Biology, Academia Sinica. I am interested to know the regulation of stem cells in response to diet and aging. Adult stem cells perform asymmetrical division to self-renew and to produce differentiating cells to replenish lost cells in tissues. Stem cells reside in a specialized environment, or niche, which provides tissue-intrinsic signals that regulate stem cell function. Stem cell behavior is also modulated by tissue-extrinsic factors that mediate the effects of changes of environmental and physiological status, for instance nutritional inputs and aging, respectively. We are interested in how stem cells adjust their division rates and lifespan to maintain tissue homeostasis in response to external environments and physiological status, and intend to investigate the mechanisms underlying this process using the fruit fly, *Drosophila melanogaster*.*

Transposons participate in tissue aging, but the impacts on stem cells remain unclear. Here, we report that in the *Drosophila* ovarian germline stem cell (GSC) niche, aging reduces expression of Piwi (a transposon silencer) to derepress retrotransposons. This derepression activates Glycogen synthase kinase 3 (GSK3) to impair β -catenin-E-cadherin-mediated GSC anchorage, leading to GSC loss. Supplementation of Piwi in the aged niche delays age-dependent GSC loss, while elimination of Piwi in the young niche accelerates this loss. In the piwi-knockdown niche, suppressing GSK3-dependent β -catenin degradation or inhibiting retrotransposon duplication restores GSC anchorage. We also report that the gypsy retrotransposon generates endogenous virus to activate GSK3 via Toll-mediated immune signaling. Suppression of virus generated by retrotransposons or disruption of Toll signaling in the piwi-knockdown niche decreases GSK3 activity and prevents GSC loss. Our results document that during aging, retrotransposon-mediated GSK3 activation impairs stem cell maintenance, a finding that may have relevance to aging-related processes in many tissues.