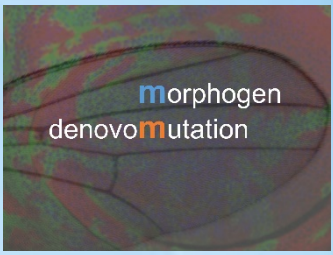
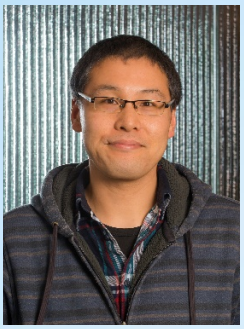
生命科学研究科セミナー

New genetics from *Drosophila*: Impacts of *de novo* mutations in animal development





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Date : December 15, 2017 (Fri) 15:00～

Place : Lecture Room A (104), Life Science Project Research Laboratory (Katahira Campus)

Alteration of genetic information is a cause of a variety of diseases. Although pathogenesis associated with inherited mutations has been extensively studied, how *de novo* mutations during development and homeostasis lead to disease conditions remains elusive. To address this question, we establish an inducible allele switch system at the endogenous locus that allows replacement of *wild-type* coding sequence with its mutants via *flippase recognition target* (*FRT*)-mediated recombination. As a model system, we employ the *Drosophila BMPR1A thickveins* (*tkv*). In the developing wing disc, the Tkv receptor complex activates the *Drosophila* BMP2/4-like ligand Decapentaplegic (DPP) morphogen pathway by phosphorylating a downstream signaling transducer, Mothers against DPP (p-Mad), and directs wing pattern formation. we found that inherited heterozygous *tkv* mutants exhibit little effect of p-Mad expression and develop normal adult wings. In contrast, *de novo tkv* heterozygous mutations generating wing discs with both *wild-type* and heterozygous clonal cell populations disrupt proper p-Mad expression in a clone-size dependent manner, leading to wing patterning defects. We term this phenomenon “deleterious heteromosaicism.” In this seminar, I would like to discuss previously unrecognized impacts of *de novo* recessive heterozygous mutations in animal development and provide a new concept to understand genetic mechanisms underlying disease initiation.

References: Akiyama & Gibson, *Nature* 2015; 527: 375-8.
Akiyama et al., *Sci Signal* 2012; 5(218):ra28.

* This seminar will be held in English. (質疑は日本語可)

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