

【Grant-in-Aid for Scientific Research(S)】

Biological Sciences (Medicine, dentistry, and pharmacy I)



Title of Project : Regulation of developmental robustness by cell death signaling

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Research Area : Developmental Genetics

Keyword : development, robustness, caspase, stress, genetics and biochemistry, imaging

【Purpose and Background of the Research】

A developing animal is exposed to both intrinsic and extrinsic stresses. Even in these stressful environmental conditions, animal development is achieved with the surprisingly robust patterns. We thought that stress response in developing animal is a key for the regulation of robustness of development. One important stress response will be caspase activation. Caspase activation is not only observed in apoptosis but also in non apoptotic condition. Non apoptotic caspase function includes cell proliferation, migration and differentiation. We will study the dynamics and roles of caspases and other stress signaling molecules that play crucial roles for developmental robustness.

【Research Methods】

Our previous study indicated the involvement of caspases in the regulation of the robustness of sensory organ precursor (SOP) development. It is also suggested that caspase plays important roles for the regeneration of imaginal discs. Caspase mutant mice show neural tube closure defects. We will perform genetic, biochemical, and live imaging approaches to dissect the signaling pathways required for the achievement of the robustness of development.

【Expected Research Achievements and Scientific Significance】

Our research will establish the fundamental mechanisms for developmental robustness that is regulated by stress signaling. Our research also provides the new insight for teratology.

【Publications Relevant to the Project】

Nakajima, Y-I, Kuranaga, E., Sugimura, K., Miyawaki, A., and Miura, M.: Non-autonomous apoptosis is triggered by local cell cycle progression during epithelial replacement in *Drosophila*. *Mol. Cell Biol.*, 31 2499-2512, 2011
Koto, A., Kuranaga, E., and Miura, M.: Apoptosis ensures spacing pattern formation of

Drosophila sensory organs. *Current Biol.*21, 278-287, 2011

Ohsawa, S., Hamada, S., Kuida, K., Yoshida, H., Igaki, T., and Miura, M.: Maturation of the olfactory sensory neurons by Apaf-1/caspase-9-mediated caspase activity. *Proc. Natl. Acad. Sci. USA.* 107, 13366-13371, 2010

Kondo, S., Senoo-Matsuda, N., Hiromi, Y., and Miura, M.: Dronc coordinates cell death and compensatory proliferation. *Mol. Cell Biol.* 26, 7258-7268, 2006.

Kuranaga, E., Kanuka, H., Tonoki, A., Takemoto, K., Tomioka, T., Kobayashi, M., Hayashi, S., and Miura, M.: *Drosophila* IKK-related kinase regulates nonapoptotic function of caspases via degradation of IAPs. *Cell* 126, 583-596, 2006

Kanuka, H., Kuranaga, E., Takemoto, K., Hiratou, T., Okano, H., and Miura, M.: *Drosophila* caspase transduces Shaggy/GSK-3b kinase activity in neural precursor development. *EMBO J.* 24, 3793-3806, 2005

【Term of Project】 FY2011-2015

【Budget Allocation】 165,200 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.f.u-tokyo.ac.jp/~genetics/index.html>