

# Applied Genetics

## 1. Staffs and Students (April, 2009)

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Research Student	Yuya KAGAMI,	Tian Tian GUO

## 2. Purpose of Education

Our research is directed at understanding how cells recognize, assess and respond to lesions in DNA and the molecular mechanisms by which a damaged cell can distinguish between continued proliferation, permanent growth arrest and suicide. BRCA2, products of hereditary breast cancer genes, are associated with genome stability through DNA damage repair. We analyze functions of BRCA2 and other related proteins to reveal the mechanism of breast carcinogenesis.

## 3. Research Subject

- 1) Functional analysis of the BRCA2 gene.
  - BRCA2 complexed with plectin is required for centrosome positioning.
- 2) Regulatory mechanisms of tumor cells in the apoptotic response to DNA damage
  - Protein kinase C delta activates RelA/p65 and NF-kappaB signalling in response to TNF-alpha.
  - DNA damage signalling recruits RREB-1 to the p53 tumor suppressor promoter.
- 3) Analyses of DNA damage repair mechanisms
  - Cooperation of DNA polymerases delta, epsilon and kappa in the gap-filling synthesis step of nucleotide excision repair in human cells, recruited by different mechanisms.
  - Analyses of molecular domains of translesion DNA polymerases by introducing a point mutation by homologous recombination in vertebrates.
  - DNA double-strand break repair through homologous recombination by means of PTIP.

## 4. Publication

### Original Article

1. Takenaka, K. and Miki, Y. Introduction and characterization of a polymerase-dead point mutation into the POLK gene in vertebrates. *FEBS Lett*, 583, 661-4, 2009
2. Liu, H., Hew, H.C., Lu, Z.G., Yamaguchi, T., Miki, Y.\* and Yoshida, K. DNA damage signalling recruits RREB-1 to the p53 tumour suppressor promoter. *Biochem J*, 422, 543-51, 2009 \*Corresponding author
3. Lu, Z.G., Liu, H., Yamaguchi, T., Miki, Y.\* and Yoshida, K. Protein kinase Cdelta activates RelA/p65 and nuclear factor-kappaB signaling in response to tumor necrosis factor-alpha. *Cancer Res*, 69, 5927-35, 2009
4. Nihira, K., Ando, Y., Yamaguchi, T., Kagami, Y., Miki, Y. and Yoshida, K. Pim-1 controls NF-kappaB signalling by stabilizing RelA/p65. *Cell Death Differ.* 2009 [Epub ahead of print]
5. Niwa, T., Saito, H., Imajoh-ohmi, S., Kaminishi, M., Seto, Y., Miki, Y.\* and Nakanishi, A. BRCA2 interacts with the cytoskeletal linker protein plectin to form a complex controlling centrosome localization. *Cancer Sci*, 100, 2115-25, 2009
6. Taira, N., Yamamoto, H., Yamaguchi, T., Miki, Y.\* and Yoshida, K. (2009) ATM augments nuclear stabilization of DYRK2 by inhibiting MDM2 in the apoptotic response to DNA damage. *J Biol Chem.* 2009 [Epub ahead of print] \*Corresponding author
7. Takenaka, K.; Miki, Y. Introduction and characterization of a polymerase-dead point mutation into the POLK gene

in vertebrates. FEBS Lett 583:661-664; 2009.