

# Applied Genetics

## 1. Staffs and Students (April, 2010)

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## 2. Purpose of Education

Our research is directed at understanding the molecular mechanism of carcinogenesis, based on basic molecular cell biology and molecular genetics. We have applied new findings and information obtained by basic research to develop the new diagnosis, treatment, and prevention of cancer. Our objective in the graduate course is to provide students opportunity to study basic science and applied genome science for cancer research.

## 3. Research Subject

- 1) Functional analysis of the BRCA2 gene.
  - ① BRCA2 binds to motor domain of myosin IIC
  - ② Identification of a cleavage product of BRCA2 in cancer cell lines
  - ③ Identification of novel BRCA2-associated proteins and analyses of functions of their association in numerical integrity of centrosomes.
- 2) Regulatory mechanisms of tumor cells in the apoptotic response to DNA damage
  - ① Pim-1 activates RelA/p65 and NF-kappaB signaling in response to TNF-alpha.
  - ② ATM augments nuclear stabilization of DYRK2 by inhibiting MDM2 in the apoptotic response to DNA damage.

## 4. Publication

### Original Article

1. Hirono, S., Yamaue, H., Hoshikawa, Y., Ina, S., Tani, M., Kawai, M., Ushijima, M., Matsuura, M., Saiki, Y., Saiura, A., Yamamoto, J., Miki, Y. and Noda, T. (2010) Molecular markers associated with lymph node metastasis in pancreatic ductal adenocarcinoma by genome-wide expression profiling. *Cancer Sci*, **101**, 259-66.
2. Ito, Y., Nagasaki, K., Miki, Y., Iwase, T., Akiyama, F., Matsuura, M., Horii, R., Makita, M., Tokudome, N., Ushijima, M., Yoshimoto, M., Takahashi, S., Noda, T. and Hatake, K. (2011) Prospective randomized phase II study determines the clinical usefulness of genetic biomarkers for sensitivity to primary chemotherapy with paclitaxel in breast cancer. *Cancer Sci*, **102**, 130-6.
3. Kimura, J., Kudoh, T., Miki, Y. and Yoshida, K. (2011) Identification of dihydropyrimidinase-related protein 4 as a novel target of the p53 tumor suppressor in the apoptotic response to DNA damage. *Int J Cancer*, **128**, 1524-31.
4. Kudoh, T., Kimura, J., Lu, Z.G., Miki, Y. and Yoshida, K. (2010) D4S234E, a novel p53-responsive gene, induces apoptosis in response to DNA damage. *Exp Cell Res*, **316**, 2849-58.
5. Nihira, K., Ando, Y., Yamaguchi, T., Kagami, Y., Miki, Y. and Yoshida, K. (2010) Pim-1 controls NF-kappaB signalling by stabilizing RelA/p65. *Cell Death Differ*, **17**, 689-98.
6. Ogi, T., Limsirichaikul, S., Overmeer, R.M., Volker, M., Takenaka, K., Cloney, R., Nakazawa, Y., Niimi, A., Miki, Y., Jaspers, N.G., Mullenders, L.H., Yamashita, S., Fousteri, M.I. and Lehmann, A.R. (2010) Three DNA polymerases, recruited by different mechanisms, carry out NER repair synthesis in human cells. *Mol Cell*, **37**, 714-27.
7. Taira, N., Yamamoto, H., Yamaguchi, T., Miki, Y. and Yoshida, K. (2010) ATM augments nuclear stabilization of DYRK2 by inhibiting MDM2 in the apoptotic response to DNA damage. *J Biol Chem*, **285**, 4909-19.

8. Tanaka, S., Mogushi, K., Yasen, M., Noguchi, N., Kudo, A., Nakamura, N., Ito, K., Miki, Y., Inazawa, J., Tanaka, H. and Aii, S. (2010) Gene-expression phenotypes for vascular invasiveness of hepatocellular carcinomas. *Surgery*, **147**, 405-14.
9. Wang, H.F., Takenaka, K., Nakanishi, A. and Miki, Y. (2011) BRCA2 and nucleophosmin coregulate centrosome amplification and form a complex with the Rho effector kinase ROCK2. *Cancer Res*, **71**, 68-77.
10. Yamaguchi, T., Miki, Y. and Yoshida, K. (2010) The c-Abl tyrosine kinase stabilizes Pitx1 in the apoptotic response to DNA damage. *Apoptosis*, **15**, 927-35.
11. Wang, X., Takenaka, K., Takeda, S. (2010) PTIP promotes DNA double-strand break repair through homologous recombination. *Genes to Cells*, **15**, 243-54.

#### Review Article

1. Yoshida, K. and Miki, Y. The cell death machinery governed by the p53 tumor suppressor in response to DNA damage. *Cancer Sci*, **101**, 831-5. (2010)
2. Miki, Y. Gene expression-based diagnosis of efficacy of chemotherapy for breast cancer. *Breast Cancer*, **17**, 97-102. (2010)