

Molecular Oncology

1. Staffs and Students (April, 2010)

Professor	Yasuhito YUASA	
Lecturer	Yoshimitsu AKIYAMA,	Hiroshi FUKAMACHI
Secretary	Yoshiko Abe	
JSPS Research Fellow	Takeshi OTSUBO	
Graduate Student	Shu SHIMADA,	Ayako MIMATA,
	Yutaka HASHIMOTO,	Pichayanoot ROTKRUA,
	Aika HIRATSUKA,	Ayuna SAKAMOTO
Visiting Professor	Masabumi SHIBUYA	
Tokunin Assistant Professor	Feng WANG,	Tsuyoshi OSAWA,
	Rika TSUCHIDA	

2. Purpose of Education

• Undergraduate course:

Hygiene is our charge. The undergraduate curriculum of hygiene includes lectures, small-group seminars, and laboratory studies. Topics of lectures consist of environmental pollution and human health, world-wide environmental problems, carcinogen and occupational cancer, smoking-related diseases, infectious diseases including AIDS and hepatitis, food poisoning, anoxia and heat-related diseases.

• Graduate course:

The graduate students pursue their own projects associated with one of researches being in progress in the division. Every student can learn the basic scientific techniques, such as genetic engineering, cell culture and biochemical procedures. There are also many special lectures on cancer, gene, cell biology and biochemistry for the graduate students. On weekly seminars, the students present their own research data and introduce important papers from newly-arrived journals. Once the students get new findings, they are encouraged to present them at the domestic or international meeting and write manuscripts.

3. Research Subjects

- 1) Cellular and molecular analyses of cancer-related genes, such as oncogenes and tumor suppressor genes, in gastroenterological cancers
- 2) Molecular mechanism of cell growth, differentiation and apoptosis
- 3) Involvement of differentiation-related genes in gastroenterological diseases
- 4) Cancer stem cells
- 5) DNA methylation and cancer
- 6) Transcription factors and cancer
- 7) Mouse model of gastric cancer
- 8) Effect of environmental factors on gene expression and DNA methylation
- 9) Involvement of microRNA in gastric carcinogenesis
- 10) Involvement of VEGF receptors in tumor growth and metastasis
- 11) Mechanism of tumor resistance to anti-angiogenesis therapy

4. Publications

Original Article

1. Wada R, Akiyama Y, Hashimoto Y, Fukamachi H, Yuasa Y: miR-212 is down-regulated and suppresses methyl-CpG-binding protein MeCP2 in human gastric cancer. *Int. J. Cancer* 2010;127:1106-1114.
2. Hashimoto Y, Akiyama Y, Otsubo T, Shimada S, Yuasa Y: Involvement of epigenetically silenced microRNA-181c in gastric carcinogenesis. *Carcinogenesis* 2010;31:774-784.
3. Yuasa Y: Epigenetics in molecular epidemiology of cancer: A new scope. *Adv. Genet.* 2010;71:211-235.
4. Wen XZ, Akiyama Y, Pan KF, Liu ZJ, Lu ZM, Zhou J, Gu LK, Dong CX, Zhu BD, Ji JF, You WC, Deng DJ: Methylation of GATA-4 and GATA-5 and development of sporadic gastric carcinomas. *World Journal of Gastroenterology*, 2010;16:1201-1208.
5. Chang, T. L., Ito, K., Ko, T. K., Liu, Q., Salto-Tellez, M., Yeoh, K. G., Fukamachi, H., and Ito, Y: Claudin-1 has tumor

- suppressive activity and is a direct target of RUNX3 in gastric epithelial cells. *Gastroenterology*, 2010;138:255-265.
6. Beck H, Raab S, Copanaki E, Heil M, Scholz A, Shibuya M, Deller T, Machein M, Plate KH. VEGFR-1 signaling regulates the homing of bone marrow derived cells in a mouse stroke model. *J. Neuropathol. Exp. Neurol.* 69:168-175, 2010.
 7. Murohashi M, Nakamura T, Tanaka S, Ichise T, Yoshida N, Yamamoto T, Shibuya M, Schlessinger J, Gotoh N. An FGF4-FRS2 α -Cdx2 axis in trophoblast stem cells induces BMP4 to regulate proper growth of early mouse embryos. *Stem Cells.* 28:113-121, 2010.
 8. Huusko J, Merentie M, Dijkstra MH, Ryhänen MM, Karvinen H, Rissanen TT, Vanwildemeersch M, Hedman M, Lipponen J, Heinonen SE, Eriksson U, Shibuya M, Ylä-Herttuala S. The effects of VEGF-R1 and VEGF-R2 ligands on angiogenic responses and left ventricular function in mice. *Cardiovasc Res.* 86:122-130, 2010.
 9. Bais C, Wu X, Yao J, Yang S, Crawford Y, McCutcheon K, Tan C, Kolumam G, Vernes JM, Eastham-Anderson J, Haughney P, Kowanetz M, Hagenbeek T, Kasman I, Reslan HB, Ross J, Van Bruggen N, Carano RA, Meng YJ, Hongo JA, Stephan JP, Shibuya M, Ferrara N. PlGF Blockade Does Not Inhibit Angiogenesis during Primary Tumor Growth. *Cell.* 141:166-177, 2010.
 10. Zhang L, Zhou F, Han W, Shen B, Luo J, Shibuya M, He Y. VEGFR-3 ligand-binding or kinase activity is required for lymphangiogenesis but not for angiogenesis. *Cell Res.* 20:1319-1331, 2010.
 11. Muramatsu M, Yamamoto S, Osawa T, Shibuya M. VEGFR-1 signaling promotes mobilization of macrophage-lineage cells from bone marrow and stimulates solid tumor growth. *Cancer Res.* 70: 8211-8221, 2010.
 12. Kusaba T, Okigaki M, Matui A, Murakami M, Ishikawa K, Kimura T, Sonomura K, Adachi Y, Shibuya M, Shirayama T, Tanda S, Hatta T, Sasaki S, Mori Y, Matsubara H. Klotho is associated with VEGF receptor-2 and the transient receptor potential canonical-1 Ca²⁺ channel to maintain endothelial integrity. *Proc Natl Acad Sci U S A.*, 107: 19308-19313, 2010.
 13. Brave SR, Eberlein C, Shibuya M, Wedge SR, Barry ST. Placental Growth Factor Neutralising Antibodies Give Limited Anti-Angiogenic Effects in an in vitro Organotypic Angiogenesis Model. *Angiogenesis*, 13: 337-347, 2010.
 14. Bry M, Kivelä R, Holopainen T, Anisimov A, Tammela T, Soronen J, Silvola J, Saraste A, Jeltsch M, Korpisalo P, Carmeliet P, Lemström KB, Shibuya M, Ylä-Herttuala S, Alhonen L, Mervaala E, Andersson LC, Knuuti J, Alitalo K. Vascular endothelial growth factor-B acts as a coronary growth factor in transgenic rats without inducing angiogenesis, vascular leak, or inflammation. *Circulation*, 122:1725-33, 2010.