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Research Interests

Bioimaging, Cancer biology, Bone biology, TGF-β signaling

Education

1980- 1987	MD. Graduate School of Medicine, Kagoshima University, Kagoshima, JAPAN.
1989- 1993	Ph.D. Graduate School of Medicine, Kagoshima University, Kagoshima, JAPAN.

Professional Career

1994- 1995	Assistant Professor, Graduate School of Medicine, Kagoshima University. Kagoshima, JAPAN.
1995- 1996	Postdoctoral Fellow, Ludwig Institute for Cancer Research. Uppsala, Sweden.
1996- 2004	Associate, Associate Member & Group Head, The JFCR Cancer Institute. Tokyo, JAPAN
2004- 2010	Department Director, The JFCR Cancer Institute. Tokyo, JAPAN
2010 - present	Professor, Ehime University Graduate School of Medicine. Ehime, JAPAN

Honors

2008	"JSBMR Distinguished Scientist Award" by the Society for Bone and Mineral Research
2000	"Incitement Award of the Japanese Cancer Association" by the Japanese Cancer Association

Publications

1. Inoue M et al. Rational Engineering of XCaMPs, a Multicolor GECI Suite for In Vivo Imaging of Complex Brain Circuit Dynamics. Cell. 177: 1346-60, 2019.
2. Yoon JH et al. Phosphorylation status determines the opposing functions of Smad2/Smad3 as STAT3 cofactors in TH17 differentiation. Nat Commun. 6: 7600, 2015
3. Sakaue-Sawano A, et al., Visualizing spatiotemporal dynamics of multicellular cell-cycle progression. Cell. 132: 487-98, 2008.
4. Yoshida Y et al. Negative regulation of BMP/Smad signaling by Tob in osteoblasts. Cell. 103: 1085-97, 2000.
5. Lu SL et al. HNPCC associated with germline mutation in the TGF-βtype II receptor gene. Nat Genet. 19: 17-8, 1998.
6. Imamura T et al. Smad6 inhibits signalling by the TGF-β superfamily. Nature. 389: 622-6, 1997.

Development of in vivo cancer imaging technique by advanced multi-photon laser excitation microscopy

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Recently, heterogeneity is one of the most popular keywords in cancer research. For instance, resistance to chemotherapy has long been thought to be attributed to the heterogeneity of cancer cells. However, it is difficult to prove this using only molecular biology. The easiest approach to answer this question is in vivo fluorescent imaging. This technique enables the researchers to observe the same cells in living animals for some time. In addition, this allow us to visualize the molecular activity, cellular function and microenvironment.

Fluorescent imaging technique is a promising technique, and has already been applied for in vitro experiments in cellular biology. Recently, there has been a growing interest in applying this fluorescent imaging technique to study different disease process and complex biology such as cancer in vivo. Particularly, the in vivo fluorescent imaging using various fluorophores and/or fluorescent proteins, in conjunction with appropriate microscopy, allows visualization of cell behavior as well as cell function in vivo.

In this talk, I will talk about applications of the fluorescent imaging systems to monitor cancer cell as well as tumor microenvironment such as angiogenesis in vivo. Using the in vivo fluorescent imaging system, we can visualize not only cell behavior but also cell function such as cell cycle and epithelial mesenchymal transition (EMT) [1, 2].

Finally, I would like to talk about a technological development of fluorescent imaging methods including two-photon microscopy and the application of the fluorescent imaging approaches to cancer research. Two-photon microscopy is a powerful method to investigate behavior and function of cells in deep tissues. Moreover, I would like to present the setup and application of infrared-(IR)-two-photon microscopy using excitation wavelengths above 1040 nm [3]. IR-two-photon microscopy enables us the application of red fluorescent proteins/dyes and deeper imaging compared with conventional multi-photon microscopy.

In vivo fluorescent imaging technique is now unravelling the cause and result of the heterogeneity among cancer cells and will pave a way to invent novel approaches for cancer treatment.

References

[1] Sakaue-Sawano A, et al., Visualizing spatiotemporal dynamics of multicellular cell-cycle progression. ***Cell***. 132: 487-98, 2008.

[2] Ieda T et al., Visualization of epithelial-mesenchymal transition in an inflammatory microenvironment-colorectal cancer network. ***Sci Rep***. 9: 16378, 2019.

[3] Grzybowski M et al., A highly photostable near-infrared labeling agent based on a phospharhodamine for long-term and deep imaging. ***Angew Chem Int Ed Engl***. 57: 10137-10141, 2018.