Genomic analysis and simulation to understand principles generating intratumor heterogeneity

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Cancer results from accumulation of mutation in genomes and evolutionary selection for growth advantage. In the evolutionary process, it is assumed that multiple clones appear and intratumor heterogeneity of cancer genomes is generated. To investigate intratumor heterogeneity in colorectal cancer, we dissected a single colorectal tumor and exome-sequenced their DNA. As a result, we found that founder mutations exist, which are shared by all samples and assumed to appear in the early stage of carcinogenesis. In contrast, progresser mutations not shared by all samples also exist. They are assumed to appear in the early late of carcinogenesis, and contribute to intratumor heterogeneity. Next, to understand mechanisms to generate the intratumor heterogeneity, we simulate tumor growth using an agent simulation model, which assumes a cell as an agent. Moreover, using a supercomputer, we run the simulator with various combinations of parameters in searching for conditions that reproduce our experimental data. Our result suggests that the existence of multiple driver genes, cancer stem cell and microenvironmental selection is critical for heterogeneous tumor evolution. Collectively, our study demonstrated that a combination of genome analysis and simulation would be a powerful tool for studying cancer evolution.

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EDUCATIONS/TRAINING

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POSITIONS AND HONORS

2007-2008 Postdoctoral fellow, Department of Molecular and Genetic Information, Institute of Molecular and Cellular Biosciences, The University of Tokyo.

2008-2011 Postdoctoral fellow, Laboratory of DNA Information Analysis, Human Genome Center, Institute of Medical Science, The University of Tokyo.

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RECENT PUBLICATIONS

1. Niida A, Imoto S, Shimamura T and Miyano S. Statistical model-based testing to evaluate the recurrence of genomic aberrations. ***Bioinformatics*** 28: i115-i120, 2012.
2. Niida A, Imoto S, Yamaguchi R, Nagasaki M, Fujita A, Shimamura T and Miyano S. Model-free unsupervised gene set screening based on information enrichment in expression profiles. ***Bioinformatics*** 26: 3090-3097, 2010.
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