医学セミナー・第 18 回分子遺伝疫学セミナー
“Seminars in Medical Sciences” Lecture

ゲノム医科学リサーチユニット　難治性免疫疾患・アレルギーリサーチユニット

Whole-genome sequencing and mutational landscape in cancer genomes

Speaker: **Dr. Akihiro Fujimoto** (Associate Professor, Department of Drug Discovery Medicine, Graduate School of Medicine, Kyoto University)
藤本明洋博士、京都大学大学院医学研究科創薬医学講座　特定准教授

Date:　November 1, 2018 (Thurs)
Time:　17:00-18:15
Venue:　Faculty of Medicine Building, Room 483（医学系学系棟 483）

This seminar is one of the seminars for the subject “Seminar in Medical Sciences” in Doctoral Programs in Biomedical Sciences and Clinical Sciences. The seminar will be given in English, but questions in Japanese are also welcome.

This seminar will NOT be video-recorded. Be sure to attend if interested.

Next generation sequencing technologies enable us to analyze the mutational landscape in cancer genomes. To identify somatic mutation in liver cancer, we constructed an analysis pipeline for mutation detection. Using the method, we analyzed whole genome sequencing of liver cancer genomes. Our comprehensive analysis identified point mutations, structural variations (STVs), and virus integrations, in noncoding and coding regions. We discovered recurrently mutated coding and noncoding regions, promoters, and regulatory regions. STV analysis found a significant association with replication timing and identified known (*CDKN2A*, and *TERT*) and new (*ASH1L*, and *MACROD2*) cancer-related genes.

We next focused on mutations in microsatellite regions. Microsatellites are repeats of 1-6bp units and have been used to detect cancers with mismatch repair deficiency. To detect somatic indels in microsatellite regions, we analyzed ~9 million microsatellites in 2,717 cancer samples across 21 tissue types. Our analysis identified samples with higher microsatellite mutation rate (MSI; microsatellite instability). We found 20 highly-mutated microsatellites which can be used to detect MSI cancers with high sensitivity. Analysis of highly mutated microsatellite found that replication timing and DNA shape were significantly associated with mutation rates. Our analysis reveals possible causes of mutations, as well as provides a useful marker set for MSI detection.

References

1. Fujimoto A, Furuta M, Totoki Y, Tsunoda T, Kato M, et al. (2016) Whole genome mutational landscape and characterization of non-coding and structural mutations in liver cancer. **Nat Genet** 48: 500-509
2. Fujimoto A, Totoki Y, et al. (2012) Whole-genome sequencing of liver cancers identifies etiological influences on mutation patterns and recurrent mutations in chromatin regulators. **Nat Genet** 44: 760-76
3. Fujimoto A, et al. (2010) Whole-genome sequencing and comprehensive variant analysis of a Japanese individual using massively parallel sequencing. **Nat Genet** 42: 931–936

【contact】Naoyuki Tsuchiya, Molecular and Genetic Epidemiology Laboratory
tsuchiya@md.tsukuba.ac.jp