セミナーのお知らせ

Bioscience & Biotechnology Topics II 2010
生命理工学トピックスII 2010

Title: **Inverted gene duplications in the human genome**

Speaker: **Dr. Hisashi Tanaka** (Assistant Professor, Department of Molecular Genetics, Cleveland Clinic Foundation, Cleveland, OH, USA)

November 19 (Fri) 16:00-17:30 @ B2 棟 4 階 大会議室

Duplication of genomic segments that occurs close to the parental segments in an inverted orientation (inverted duplication) is an important DNA structure in both cancer and normal genomes. When inverted duplication occurs in cancer cells, it can initiate a series of DNA rearrangements that eventually establish a highly amplified genomic segment. Such an amplified segment harbors a gene (gene amplification), the overexpression of which drives adverse impacts on cancer phenotypes, such as abnormal cell growth and resistance to anti-cancer drugs. Thus, inverted duplication in cancer cells represents an early, critical process in genome instability.

Inverted gene duplication can also be found in the normal genomes and is often highly conserved between closely related species. Good examples for such duplication is several, very large (~1 million bases) conserved inverted duplications in Y chromosomes of humans and chimpanzees. However, it is also well-documented that inverted duplication is an unstable DNA structure and causes DNA rearrangements. For example, the large part of above-mentioned duplications in Y chromosomes is susceptible to deletion, and such deletion causes infertility in men. Furthermore, we have shown that the 36-kb large inverted duplication of a histone gene cluster plays a key role in establishing somatic, high-level gene amplification in cancer cells. How inverted duplication initiates genomic instability in cancer genomes, and how such unstable structure is maintained in normal genomes, will be discussed.

Ref)

Tanaka et al. (2005) Widespread and non-random distribution of DNA palindromes provides a structural platform for subsequent gene amplification. Nat. Genet. 37, 320-327.

Tanaka & Yao (2009) Palindromic gene amplification – an evolutionarily conserved role for DNA inverted repeats in the genome. Nat. Rev. Cancer 9, 216-224.

Zhao et al. (2009) Linkage disequilibrium between two high-frequency deletion polymorphisms: implication for association studies involving the glutathione-S transferase (GST) genes. PLoS Genet. 5, e10000472.

Masayuki Komada (駒田 雅之 x5703)