



Title of Project : Integrative Systems Understanding of Cancer for Advanced Diagnosis, Therapy and Prevention

Term of Project : FY2010-2014

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【Purpose of the Research Project】

Cancer is an extremely complex, heterogeneous disease caused by mutations on the genome. Furthermore, each individual is exposed to different environmental factors that can affect genome aberrations. In fact, the cancer genome has a multitude of mutations on genes which are related to cancer pathways. These mutations on our genome make our cell system uncontrollable.

Recent advances in cutting-edge technologies, such as next-generation sequencers, enable us to analyze omics data in an unprecedented manner. However, the labour intensive paradigm of molecular biology in conjunction with the computational power of ordinary PCs is insufficient to challenge the complex task of comprehending cancer as a system.

This project aims to create a new paradigm in cancer research. By extensive omics analysis based on systems biology, cancer biology and supercomputing, an integrative systems understanding of cancer shall be realized. Systems biology approaches are essential to elucidate the disease mechanisms of cancer. In conjunction with the supercomputer system (75 TFLOPS) at the Human Genome Center, this new approach will bring us closer to the understanding of cancer than any paradigm before.

【Content of the Research Project】

The systems biology strategy in this project comprises the association study of cancer pathogenesis and SNVs, mining/modeling drug response dynamics of cancer systems, digitalizing personal cancer systems together with their characteristics and heterogeneity, prediction of personal cancer systems (Fig. 1). This strategy will be applied to:

【A01】 Understanding molecular pathogenesis of cancer with systems biology approaches

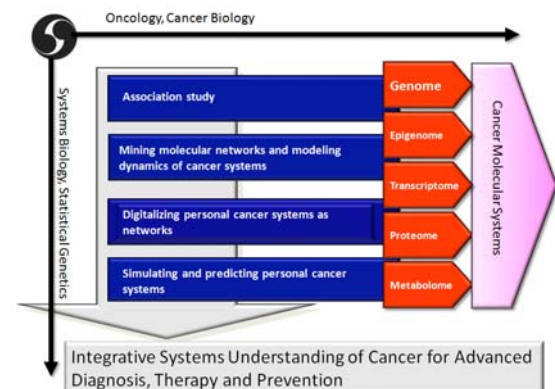
Based on genome-wide genomic and epigenomic data, integrative analysis of gene expressions, protein functions, cancer specific chromatic structures and gene knock-downs will be conducted. We explore essential genes and their networks/pathways across a diversity of cancers with a systems perspective. Detection of biomarkers for personalized

diagnosis is also an aim of our analysis.

【A02】 Innovative cancer therapeutics towards clinical applications

Through the analysis of functional RNAs, e.g. microRNAs, we are going to identify cancer specific pathways. Furthermore, we will perform high resolution analyses of genomic aberrations and allelic imbalances. Finally, we will build predictive network models for therapeutics development and molecular target discovery.

Figure 1 Strategic view of systems biology.



【Expected Research Achievements】

Our integrative systems approach of understanding cancer will identify the “Achilles' heels” of cancer systems which cannot be uncovered by conventional molecular analysis. This will lead to the identification of cancer biomarkers at a very early stage, molecular targets for innovative therapeutics and mechanisms of drug resistance by molecular network modeling and mining. Furthermore, the prediction accuracy of prognosis and drug-sensitivity will be increased.

【Key Words】

Cancer Systems Biology: An interdisciplinary field to understand cancer as system disease by combining mathematical modeling/simulation and experimental systems analysis.

【Homepage Address】

<http://cancersystem.hgc.jp/en/>