

General Summary of Division of Translational and Clinical Oncology

The mission of the division centers on laboratory and clinical research to develop the novel strategies and modalities for clinical management (diagnosis and treatment) and prevention of cancer in the gastrointestinal and respiratory tracts. Research projects are based on molecular and cellular characteristics of individual tumor types that are relevant to their biological properties including metastatic potential, recurrence and outcome. Our current efforts are focused on the following projects. We are intended to translate as much the achievements created from these studies as possible to the fields responsible for diagnosis and treatment of cancer patients in clinical setting.

A) Molecular pathology and translational research for oncogenic signaling networks

(1) Novel mechanisms underlying deregulated Wnt/ β -catenin signaling

RNA *trans*-factor CRD-BP (coding region determinant-binding protein) is a previously unrecognized transcription target of β -catenin/Tcf complex, and stabilizes mRNA of β -TrCP (β -transducin repeats-containing protein), NF- κ B and c-Myc. CRD-BP is a novel cancer target that integrates multiple oncogenic signaling pathways.

(2) Pathologic properties of glycogen synthase kinase 3 β (GSK3 β)-mediated cellular signaling

GSK3 β supports and promotes tumor cells' survival and proliferation, and protects them from undergoing apoptosis in cancers of the major digestive organs. The results warrant proposing this kinase as a novel target in cancer treatment (PCT/JP 2006/300160).

B) Development of tailored chemotherapy based on pharmacogenetics

Thymidylate synthase (TS) is a target of fluoropyrimidines including 5-FU. TS has the unique gene polymorphisms (VNTR and SNP) in the 5' -UTR. Frequent LOH has been found in TS locus. TS gene polymorphisms and LOH are linked with the gene expression and can be of clinical use for tailored chemotherapy.

C) Translational research of DNA methylation markers

Both promoter hypermethylation and global hypomethylation occur simultaneously in cancer. The profile of the DNA methylation is characteristic as molecular signature in individual cancer, influencing patients' outcome. Tailored medicine (diagnosis, treatment and prevention) can be developed using the methylation markers.

D) Establishment of tissue material resources of human gastrointestinal cancer

The material resource is important for all types of translational research for diagnosis, treatment as well as molecular, cellular and biological cancer research.