

IMSUT Hospital

Department of Applied Genomics

ゲノム診療科

Department of Clinical Genomics

ゲノム診療部

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Projects

Our department has been working on the application of human genome information in clinics. As clinical services in IMSUT Hospital, we provide genetic counseling, genetic tests for human diseases, and a surveillance program for patients with hereditary colorectal cancer. In addition, we have been carrying out two research projects; 1) determination of genetic alterations in human tumors, and elucidation of the mechanisms underlying their development, and 2) clinical sequence for the implementation of genomic medicine.

1. Genetic test of human neoplasms

Yoichi Furukawa

As a part of clinical service, we have performed genetic analysis of human neoplasms including colorectal cancer. A total of 11 cases were analyzed by WGS in 2025. The results were utilized for the precise classification of neoplasms, evaluation of disease status, selection of therapeutic drugs, and evaluation of the response to treatment.

2. Genetic counseling and related activities

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In IMSUT hospital, we provided genetic counseling and genetic tests to clients who visited our counseling clinic. In 2025, we had a total of 41 counseling cases with various hereditary diseases such as muscular dystrophy, spinal and bulbar muscular atrophy, achondroplasia, hereditary breast and ovarian cancer, and Lynch syndrome. In the counseling, we provided appropriate information about the diseases to the clients and took their psychological care in collaboration with a clinical psychologist. Genetic testing was performed in cases with informed consent after thoughtful discussion about its merit and demerit.

Systematic surveillance programs are provided for the patients susceptible to hereditary tumors.

3. Identification of pathogenic germline variants in patients with biliary tract cancer: insights from 799 Japanese cases

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Biliary tract cancer (BTC) is a group of malignancies that include intrahepatic cholangiocarcinoma (ICC), extrahepatic cholangiocarcinoma (ECC), gallbladder carcinoma (GBC), and ampulla of Vater carcinoma (AVC). Although BTC is relatively rare, it is a highly aggressive disease with a poor prognosis, largely due to its frequent diagnosis at late-stages and limited treatment options. The incidence of BTC is particularly high in East Asia and South America, likely due to a combination of environmental, lifestyle, and genetic factors. Despite advances in diagnostic technologies and treatment modalities, the overall survival rates for BTC patients remain dismal compared to other gastrointestinal cancers.

Recent studies suggest that germline variants in homologous recombination repair (HR) genes may contribute to BTC development. Therefore, in this study, we analyzed 799 Japanese BTC cases from Biobank Japan using amplicon sequencing, focusing on key HR genes including *BRCA1*, *BRCA2*, *PALB2*, *BARD1*, *BRIP1*, *RAD51C*, *RAD51D*, *RAD50*, *FANCM*, *ATM*, *CHEK2*, and *NBN*. Germline variants were assessed using ClinVar, gnomAD, and TOGOvar databases, and consequently pathogenic variants were identified in 30 cases. The variants included those in *BRCA1* (8 cases), *BRCA2* (5 cases), *PALB2* (6 cases), *BRIP1* (2 cases), *RAD51D* (2 cases), *RAD50* (1 case), *FANCM* (1 case), *ATM* (4 cases), and *CHEK2* (1 case). As we expected, a significant correlation between pathogenic HR variants and family history of cancer was observed. This finding underscores the potential importance of hereditary cancer predisposition in BTC and highlights the need for genetic screening in patients with family history of malignancies. Such efforts may allow earlier detection of BTC and more personalized therapeutic interventions.

4. Clinical sequencing for the implementation of genomic medicine

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The application of Next-Generation Sequencing (NGS) technology in clinical medicine has revolutionized molecular diagnostics by enabling multiple gene testing, or analysis of the entire exon or whole genome with a limited amount of DNA. In collaboration with Human Genome Center and Advanced Clinical Research Center, we have been working on the genetic diagnosis of patients with suspected hereditary cancer predisposition, and the implementation of precision medicine for patients with rare or intractable cancer.

We have applied NGS technology for molecular diagnostics of hereditary colon cancer syndromes such as familial adenomatous polyposis (FAP), Lynch syndrome (LS), and polymerase proofreading-associated polyposis (PPAP). In addition to short read-sequencing, we took advantage of PromethION, a long-read sequencer of Oxford Nanopore Technologies, for the detection of pathogenic structural variants (SVs). In 2025, we analyzed several cases of hemophilia, a hereditary disease caused by genetic alterations in coagulation factor VIII (*F8*) or coagulation factor IX (*F9*) using PromethION. As a result, we successfully identified complex SVs that will not be determined by short-read sequencing technology alone.

We have been also working on the implementation of genomic data in clinics. Patients with various types of cancer who gave written informed consent for genetic analysis were enrolled in this study. Genetic alterations in their tumors were identified using NGS, and the data were subsequently analyzed by QIAGEN Clinical Insights (QCI). Actionable variants were reviewed and discussed in a tumor board to determine recommended therapeutic options. This multidisciplinary board comprised physicians, medical oncologists, genetic counselors, geneticists, bioinformaticians, and ethics experts, and convened online every two weeks.

Publications

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