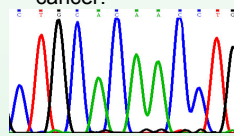


Genetic Diagnosis of Hereditary Cancers & Disorders

We provide genetic testing services to various disciplines of clinical medicine. Our services include symptomatic testing of the proband and carrier/presymptomatic testing/predictive testing for the other family members. We also provide consultation services and clinical interpretation of test results.

A) BRCA1/2 Mutation Screening for Breast and/or Ovarian Cancers

BRCA1 and BRCA2 are breast cancer susceptibility genes. Loss of the normal function of the genes conveys an increased risk of breast and ovarian cancer. Inherited alterations in these genes are involved in many cases of hereditary breast and ovarian cancer.



Test:

✘ Identification of germline mutation that may be transmitted to other family members by direct nucleotide sequencing.

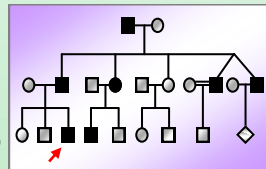
Applications:

- ✘ Testing should begin by identification of a specific mutation in affected family members.
- ✘ Once such mutation is identified, "carrier" testing is possible for family members who wish to learn whether or not they have inherited that mutation and the associated cancer risks.

Individuals are recommended to receive genetic counseling prior to testing.

B) Cardiovascular, Developmental, Endocrine, Metabolic, Neurological, & Skin Disorders

Genetic testing of various human diseases. Urgent consultation is also available on request. For examples:



- ✘ Familial endocrine tumors and disorders
- ✘ Inborn errors of metabolism and development: carnitine-acylcarnitine translocase deficiency and fatty acid oxidation defects, citrin deficiency and other causes of neonatal jaundice, Gitelman syndrome, glucose-6-phosphate dehydrogenase deficiency, glycogen storage disease, lysosomal storage disease, mitochondrial diseases, mucopolysaccharidosis and mucopolidosis, ornithine transcarbamylase deficiency and other urea cycle defects, porphyria, and Wilson disease
- ✘ Long-QT syndrome, cardiomyopathy
- ✘ Neurogenetic and neuromuscular disorders, and Parkinson's disease
- ✘ Sudden infant death

C) Multiple endocrine neoplasia (MEN) syndromes

The MEN syndromes comprise 3 genetically distinct familial diseases involving hyperplasia and cancer in several endocrine glands.

Genetic testing of the MEN1 and RET genes for the MEN1 and MEN2/Familial Medullary Thyroid Carcinoma (FMTC) syndromes respectively can be used for pre-symptomatic identification of at-risk individuals for early interventional management.

Viruses & Cancer

A) Hepatitis B virus (HBV)

Test:

- ✘ Viral load by qPCR and HBV DNA mutants detection

Applications:

- ✘ Guide to anti-HBV viral therapy and monitoring of response
- ✘ Assessment of liver disease and cancer development

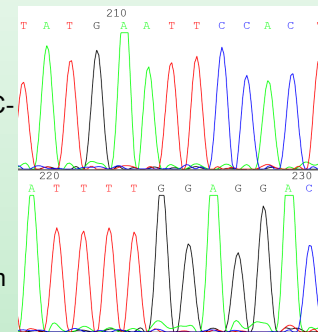
B) Human Papillomavirus (HPV) & Cervical Lesion/ Cancer

Tests (can be applied on Liquid-Based Cytology):

- ✘ Digene Hybrid Capture II (detect 13 HR HPV)
- ✘ Cobas HPV test - PCR-based test (detect 14 HR HPV and identification of HPV 16 and 18)
- ✘ Linear Array HPV Genotyping Test (identify 37 HPV genotypes, designed to detect multiple infections)
- ✘ HPV Genotyping by Sequencing

Applications:

- ✘ Reflex HPV detection test for atypical squamous cells of undetermined significance (ASC-US)
- ✘ Screening for cervical cancer and precursors
- ✘ Monitoring for disease recurrence (Test of Cure)
- ✘ Quality control for HPV test from



Enquiries

For any enquiries and bookings, please contact our reception:

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Email: UPL@pathology.hku.hk
Website: <http://www.hku.hk/patho/UPL>

Address: Room 129, University Pathology Building,
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Queen Mary Hospital, 102 Pokfulam Road,
Hong Kong, China

Business Hours: Monday - Friday, 8:30AM - 5:00PM
(except Saturdays, Sundays and Public Holidays)



Department of Pathology
The University of Hong Kong

University
Pathology
Laboratory



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Queen Mary Hospital
Hong Kong, China

For further information, please visit
<http://www.hku.hk/patho/UPL>

Our Mission

The University Pathology Laboratory (UPL), HKU is the state-of-the-art laboratory committed to providing excellent diagnostic service specially tailored for serious and common disorders in Hong Kong and the region. We employ cutting-edge technologies and are staffed by a comprehensive panel of professoriate grade clinical pathologists for consultation and clinical interpretation of tests. Samples referred to UPL will be assured of early and accurate diagnoses, enabling clinicians timely and optimal management of their patients.

Head of Department: Prof LC Chan
Directors: Prof AN Cheung
Prof CW Lam

Scope of Services

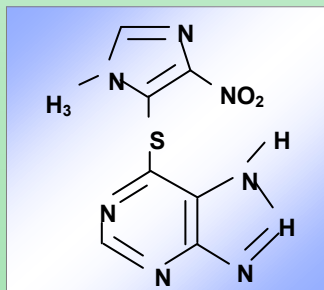
The University Pathology Laboratory was established to provide cutting-edge technologies for diagnosis and management of human diseases along the main themes of:

- ✘ Diagnosis of Metabolic & Endocrine Disorders
- ✘ Cancer Molecular Prognostic Marker for "Personalized Medicine"
- ✘ Toxicology & Pharmacogenomics
- ✘ Early bladder Cancer Detection
- ✘ Genetic Diagnosis of Hereditary Cancers & Disorders
- ✘ Viruses & Cancer

Toxicology & Pharmacogenomics

We provide a comprehensive pharmacogenetic testing for personalized, individualized therapy. These molecular diagnostic assays can provide guidance to treatment of diseases. For examples:

- ✘ Selecting drug with the greatest efficacy in managing the disease
- ✘ Predicting adverse drug reaction for individual patients for a given drug therapy



Cancer Molecular Prognostic Marker For "Personalized Medicine"

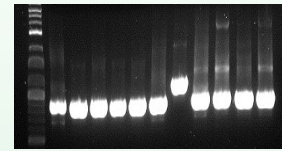
A) BCR/ABL kinase mutation detection for chronic myelogenous leukaemia and related disorders

Test:

- ✘ BCR/ABL mutation detection by semi-nested PCR and subsequent sequencing of cDNA extracted from patients' peripheral blood

Application:

- ✘ Patients with the diseases which harbour BCR/ABL gene fusion respond to targeted therapy using specific tyrosine kinase inhibitors. Resistance to this therapy can be due to mutations in the ABL domains. Detection of these mutations can guide further management such as switching to alternative tyrosine kinase inhibitors or discontinuation of drugs.



B) KRAS mutation detection for colorectal cancer

Test:

- ✘ Microdissection in paraffin tumour blocks (including small biopsies) to enrich for tumour cells, followed by PCR and DNA sequencing to detect for KRAS mutation

Applications:

- ✘ Metastatic colorectal cancers that harbour KRAS mutations do not respond to therapy using anti-EGFR antibodies (e.g. Cetuximab).
- ✘ Presence of KRAS mutation also predicts lack of response to EGFR inhibitors in other types of cancers.
- ✘ This test can help clinicians in the choice of treatment strategy.

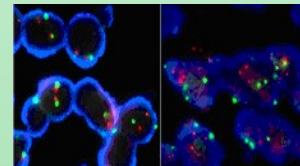
C) HER2 amplification test for breast cancer

Tests:

- ✘ HER2 fluorescent-in-situ hybridization (FISH) test using PathVysion® HER2-DNA Probe Kit (FDA approved prediction test)
- ✘ Performed on formalin-fixed, paraffin-embedded tissue samples; it utilizes a built-in control probe that enables direct counting of HER2 gene copies and control probes simultaneously, providing more accurate results.

Application:

- ✘ Helping oncologists to determine the appropriate use of systemic adjuvant therapy such as Trastuzumab (Herceptin)



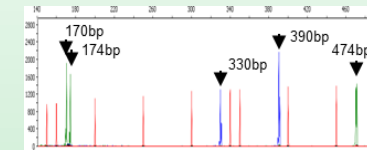
D) NPM1/FLT3-ITD mutation test

Tests:

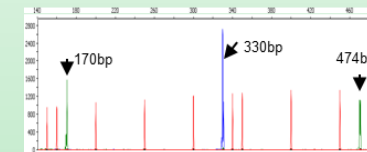
- ✘ Multiplex PCR for amplification of exon 12 of NPM1 and exons 14 and 15 (juxtamembrane domain) of FLT3, followed by capillary electrophoresis to detect the mutant amplicons in the bone marrow or peripheral blood

Application:

- ✘ For prognostication of cytogenetically normal acute myeloid leukaemia patients at diagnosis
- ✘ For obtaining adjunctive information when considering allogeneic haematopoietic stem cell transplantation in cytogenetically normal acute myeloid leukaemia patients in first complete remission
- ✘ For consideration of using experimental tyrosine kinase inhibitor therapy in persistent or relapsed acute myeloid leukaemia patients (FLT3-ITD component of the test)

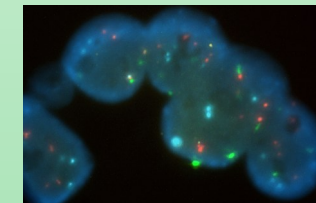


Sample #23 - NPM1 & FLT3 mutations
NPM1 (-HEX): w.t. = 170bp, mutant allele = 174bp
FLT3 (-FAM): w.t. = 330bp, mutant allele = 390bp
HBG (-HEX): internal control = 474bp
GeneScan™500ROX™ : Internal size standard



Sample #24 - wild-type for NPM1 & FLT3
NPM1 (-HEX): w.t. = 170bp
FLT3 (-FAM): w.t. = 330bp
HBG (-HEX): internal control = 474bp
GeneScan™500ROX™ : Internal size standard

Early Bladder Cancer Detection



Test:

- ✘ A set of molecular tests using the FISH technique to detect aneuploidy for chromosomes 3, 7, 17, and loss of the 9p21 locus in urine specimens from persons with haematuria sus-

Application:

- ✘ Useful for early detection of recurrent urothelial carcinoma and screening of urothelial cancer