

DIVISION OF MOLECULAR PATHOLOGY AND THERAPY BIOMARKERS

Molecular Pathology and Therapy Biomarkers

- Molecular Hematopathology
- Molecular Solid Tumors
- Molecular Genetic Testing
- Molecular Microbiology
- Cytogenetics Hematopathology
- Cytogenetics Solid Tumors
- Cytogenetics Enumeration Probes

Consultation Services:

- Hematopathology, Cytopathology, Dermatopathology and Surgical Pathology Subspecialties
- Immunohistochemistry (IHC) and Special Stains
- Flow Cytometry Immunophenotyping

MOLECULAR HEMATOPATHOLOGY

HopeSeq Heme Comprehensive Panel

Next generation sequencing (NGS) analysis of mutations (full exon of 523 genes), copy number variations (CNV), tumor mutation burden (TMB), gene fusions (>5,000 selected rearrangements in 165 genes) and gene expressions (71 genes).

For gene list, see sections A, B and C on the last page.

AML Rapid Genomic Assay

Simultaneous testing of: FLT3, NPM1, IDH1, IDH2, CEBPA, KIT, TP53, CBFB/MYH11 translocation (inv(16)), RUNX1/RUNX1T1 translocation (t(8;21)), BCR/ABL translocation (t(9;22)).

Individual Molecular Hematologic Malignancies testing

ABL1 kinase domain	FLT3-TKD and ITD with signal ratio	KIT	NPM1
CALR	IDH1/IDH2 mutations	MPL	TP53
CEBPA	JAK2		

Gene Rearrangement, B and T-cell Clonality Assays

IGH and IGK gene arrangements by PCR	TCR-γ and TCR-β gene rearrangements by PCR
IGHV Hypermutation analysis by NGS	TCR-γ and TCR-β gene rearrangement by NGS

Quantitative RT-PCR Assays

BCR/ABL translocation (t(9;22))	CBFB/MYH11 inversion (inv(16))	PML/RARA translocation (t(15;17))
• p190 BCR/ABL • p210 BCR/ABL (reporting on International Scale)	Minimal residual disease (MRD) NPM1 known mutations	RUNX1/RUNX1T1 translocation (t(8;21))

MOLECULAR SOLID TUMORS

HopeSeq Solid Tumors Comprehensive Panel

Mutations (full exon of 523 genes), CNV, microsatellite instability (MSI), TMB, gene fusions (>5,000 selected rearrangements in 165 genes) and PD-L1 IHC (upon request).

For gene list, see sections A and B on the last page.

HopeSeq Glioma Comprehensive

Mutations (full exon of 523 genes), CNV, MSI, TMB, fusions (>5,000 selected rearrangements in 165 genes), MGMT methylation analysis and PD-L1 IHC.

For gene list, see sections A and B on the last page.

HopeSeq FNA Comprehensive Panel (Lung, Thyroid, Upper GI)

Mutations (full exon of 523 genes), CNV, MSI, TMB, fusions (>5,000 selected rearrangements in 165 genes). Expression of epithelial markers will be evaluated for specimen sufficiency prior to NGS testing. Gene expression assay will be performed for adequacy assessment of FNA samples for this panel.

For gene list, see sections A and B on the last page.

Molecular Oncology Methylation Assays

- MGMT promoter methylation
- MLH1 methylation

MOLECULAR GENETIC TESTING

HopeSeq Germline Confirmatory Panel (Hope Hereditary Cancer Predisposition Panel)

This panel confirms the presence of any suspicious cancer predisposition/germline alterations identified by HopeSeq Heme and Solid Tumor panels.
For gene list, see section A on the last page.

MOLECULAR MICROBIOLOGY

Quantitative Viral Assays by PCR

- Adenovirus (ADV)
- BK virus (BKV)
- Cytomegalovirus (CMV)
- Epstein Barr virus (EBV)

CYTOGENETICS HEMATOPATHOLOGY

Whole-Genome Oncology Microarray (SNP-Array) for Hematological Malignancies (CytoScan HD)*

The CytoScan HD microarray provides high resolution whole-genome interrogation of newly diagnosed or relapse neoplastic specimens, including genome-wide copy number and copy-neutral loss of heterozygosity (CN-LOH) analyses.

Enumeration Probes

FISH probes are available to detect aneuploidy of chromosomes 1-22, X and Y.

* Currently available to City of Hope patients only. Please contact lab outreach for non-City of Hope availability status.

- City of Hope Cytogenetics Laboratory is a Children's Oncology Group (COG)-approved lab for conventional cytogenetic and FISH analyses.
- Most commonly known designations are used here to indicate each abnormality identified by the FISH probes.

G-banded Chromosome Analysis

Conventional cytogenetic studies to detect chromosomal gains, losses and rearrangements such as inversions and translocations for a variety of neoplasms including hematological malignancies and solid tumors

Fluorescence In Situ Hybridization (FISH) Panels

Molecular cytogenetic FISH assays to detect or confirm previous or applicable abnormalities for a variety of neoplasms. Available FISH probes and panels are listed below.

- **Chronic Lymphocytic Leukemia (CLL):** del(11q) ATM, Trisomy 12 DDIT3, -13/del(13q) D13S319/LAMP1, del(17p) TP53; t(11;14) IGH::CCND1
- **Targeted Plasma Cell FISH:** 1q/1p (CKS1B/CDKN2C), +5/+9/+15 (for hyperdiploidy), MYC, -13/del(13q) D13S319/LAMP1, del(17p) TP53, IGH break-apart [with reflex to t(4;14), t(11;14) and t(14;16)]
- **Double/Triple Hit Lymphoma:** BCL6 break apart, MYC break apart, t(8;14) IGH::MYC and t(14;18) IGH::BCL2

Individual FISH Probes for Myeloid and Lymphoid Lineage Abnormalities

- | | | |
|--|---------------------------------|--|
| • 1q/1p (CKS1B/CDKN2C) gain/loss | • +8 (CEP 8/MYC) | • -13/del(13q) (D13S319/LAMP1) |
| • ABL2 (1q25.2) rearrangement | • 8q24.21/MYC rearrangement | • 14q32.33/IGH rearrangement |
| • 2p/ALK rearrangements (lymphoma) | • +8, del(20q) (CEP 8/D20S108) | • t(14;16) IGH::MAF fusion |
| • inv(3)/t(3;3) MECOM | • t(8;21) RUNX1::RUNX1T1 fusion | • t(14;18) IGH::BCL2 fusion |
| • 3q/BCL6 rearrangement | • t(8;14) IGH::MYC fusion | • t(15;17) PML::RARA fusion |
| • +4/+10 (CEP 4/10) | • ABL1 (9q34.1) rearrangement | • inv(16)/t(16;16) CBFβ |
| • 4q12 rearrangement | • t(9;22) BCR::ABL1/ASS1 | • del(17p) TP53/CEP 17 |
| • CHIC2 deletion/FIP1L1::PDGFRA fusion | • del(9p) CDKN2A/CDKN2B | • 17q/RARA rearrangement, e.g., t(15;17) |
| • t(4;14) IGH::FGFR3 fusion | • t(11;14) IGH::CCND1 fusion | • 18q21.3/MALT1 rearrangement |
| • -5/5q- (EGR1) | • del(11q22.3) ATM/CEP 11 | • 19p/TCF3 rearrangement, e.g., t(1;19) |
| • PDGFRB (5q32) rearrangement | • 11q23/KMT2A rearrangement | • CRLF2 (Xp22.33/Yp11.32) |
| • del(6q21) FOXO3 | • 12p/ETV6 rearrangement | • P2RY8 (Xp22.33/Yp11.32) |
| • t(6;9) DEK::NUP214 fusion | • t(12;21) ETV6::RUNX1 fusion | |
| • -7/7q- (CEP 7/D7S486) | • Trisomy 12 (DDIT3) | |

CYTOGENETICS SOLID TUMOR

Individual Probes

- MYCN amplification (neuroblastoma)
- FOXO1 rearrangement (alveolar rhabdomyosarcoma)
- SS18 rearrangement (synovial sarcoma)
- EWSR1 rearrangement (Ewing sarcoma/PNET)
- ERBB2 (HER2) amplification (breast, gastroesophageal and other cancers)*
- MYC amplification/rearrangement
- del(9p) CDKN2A/CDKN2B, del(10q) PTEN, del(17p) TP53/CEP 17 (various tumor types; fresh tissue is required for deletion probes)

CONSULTATION SERVICES: HEMATOPATHOLOGY, CYTOPATHOLOGY, DERMATOPATHOLOGY AND SURGICAL PATHOLOGY SUBSPECIALTIES

Consultation services at City of Hope combine an extensive array of diagnostic expertise into a single customer-focused consultation program. A comprehensive integrated report with the diagnosis, phenotype and genotype is provided for each case as required.

IMMUNOHISTOCHEMISTRY AND SPECIAL STAINS

- Comprehensive menu of over 150 immunohistochemical, cytochemical and histochemical stains:

IHC (88341/88342)

AE1/AE3 (Pancytokeratin), AFP, ALK, AMACR (P504S), AR (Androgen Receptor), Annexin A1, Arginase, ATRX, BCL1, BCL2, BCL6, BEREPA (ESA), Beta-catenin, BOB1, CAIX (Carbonic Anhydrase IX), Calcitonin, Caldesmon, Calponin, Calretinin, CAM5.2, CD1A, CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD15, CD19, CD20, CD21, CD23, CD25, CD30, CD31, CD33, CD34, CD43, CD45 (LCA), CD56, CD57, CD61, CD68, CD79A, CD99, CD117, CD123, CD138, CD163, CD278 (ICOS), CDK4, CDX2, CEA (MONO), CEA (POLY), Chromogranin, CK5/6, CK7, CK8/18, CK17, CK19, CK20, CMV, C-MYC, OSCAR (Pancytokeratin), D2-40, DBA44, Desmin, DOG1, E-Cadherin, EBV-LMP, EMA, ER (Estrogen Receptor), ERG, FLI1, FXIIIA, GATA3, GCDFP15, GFAP, Glypican3, Granzyme-B, H3K27ME3, HBME1, HCG, H. Pylori, Hemoglobin-A, HepPar1, HER2, HMB45, 34BE12 (HMW Keratin), IDH1, IGA, IGD, IGG, IGG4, IGM, IL13RA, INHIBIN, INI1, Kappa, Keratin (MCK/AE1/AE3), Ki67, KSHV (HHV8), Lambda, Langerin, Lysozyme, Mammaglobin, MDM2, Melan-A (MART1), MOC31, MPO, MSA, MUC1, MUC2, MUC4, MUC5AC, MUM1, Myogenin, Napsin-A, NeuN, NF, NKX3.1, OCT2, OTC4, PAX2, PAX5, PAX8, PD1, Perforin, PIN4, PSA, PTEN, P120, P16, P40, P53, P63, P501S, PHH3, RCC, ROS1, S100, SALL4, SATB2, SF1, SMA, SM-Myosin, SOX10, SOX11, Synaptophysin, TCL1, TCR-Beta-F1, TCR-Delta, TDT, TGB (Thyroglobulin), TIA1, TRAP, Tryptase, TTF1, Vimentin, WT1

ISH (88364/88365)

EBER (EBV), HPV-High Risk Cocktail, Kappa, Lambda

MMR Panel (88341)

MLH1, MSH2, MSH6, PMS2

Breast Panel FDA (88360)

ER (Estrogen Receptor), HER2, Ki67, PR (Progesteron Receptor)

PD-L1 FDA (88360)

PD-L1 (SP142), PD-L1 (SP263)

SPECIAL STAINS (88312/88313)

AFB, Alcian Blue pH2.5, Colloidal Iron, Congo Red, Elastic, Fite, Fontana Masson, GMS, Gram, Iron (Prussian Blue), Mucicarmine, PAS, Periodic Acid Schiff with Digestion (PASD), Periodic Acid Schiff for Fungus (PASF), Reticulin, Trichrome, Warthin Starry (Spirochete)

FLOW CYTOMETRY IMMUNOPHENOTYPING

- Comprehensive and targeted panels for characterization and follow-up of hematopoietic malignancies, including lymphoma, leukemia and related disorders
- Lymphocyte subset analysis
- Quantitative stem cell analysis

HopeSeq Comprehensives Panels Gene List

Section A: Full-length mutation and CNV analysis of 523 genes

ABL1, ABL2, ACVR1, ACVR1B, AKT1, AKT2, AKT3, ALK, ALOX12B, ANKRD11, ANKRD26, APC, AR, ARAF, ARFRP1, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKB, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BBC3, BCL10, BCL2, BCL2L1, BCL2L11, BCL2L2, BCL6, BCOR, BCORL1, BCR, BIRC3, BLM, BMPR1A, BRAF, BRCA1, BRCA2, BRD4, BRIP1, BTG1, BTK, C11orf30, CALR, CARD11, CASP8, CBF, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CD74, CD79A, CD79B, CDC73, CDH1, CDK12, CDK4, CDK6, CDK8, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CEBPA, CENPA, CHD2, CHD4, CHEK1, CHEK2, CIC, CREBBP, CRKL, CRLF2, CSF1R, CSF3R, CSNK1A1, CTCF, CTLA4, CTNNA1, CTNNB1, CUL3, CUX1, CXCR4, CYLD, DAXX, DCUN1D1, DDR2, DDX41, DHX15, DICER1, DIS3, DNAJB1, DNMT1, DNMT3A, DNMT3B, DOT1L, E2F3, EED, EGFL7, EGFR, EIF1AX, EIF4A2, EIF4E, EML4, EP300, EPCAM, EPHA3, EPHA5, EPHA7, EPHB1, ERBB2, ERBB3, ERBB4, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERG, ERFF1, ESR1, ETS1, ETV1, ETV4, ETV5, ETV6, EWSR1, EZH2, FAM123B, FAM175A, FAM46C, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FAS, FAT1, FBXW7, FGF1, FGF10, FGF14, FGF19, FGF2, FGF23, FGF3, FGF4, FGF5, FGF6, FGF7, FGF8, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FH, FLCN, FLI1, FLT1, FLT3, FLT4, FOXA1, FOXL2, FOXO1, FOXP1, FRS2, FUBP1, FYN, GABRA6, GATA1, GATA2, GATA3, GATA4, GATA6, GEN1, GID4, GLI1, GNA11, GNA13, GNAQ, GNAS, GPR124, GPS2, GREM1, GRIN2A, GRM3, GSK3B, H3F3A, H3F3B, H3F3C, HGF, HIST1H1C, HIST1H2BD, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I, HIST1H3J, HIST2H3A, HIST2H3C, HIST2H3D, HIST3H3, HLA-A, HLA-B, HLA-C, HNF1A, HNRNP, HOXB13, HRAS, HSD3B1, HSP90AA1, ICOSLG, ID3, IDH1, IDH2, IFNGR1, IGF1, IGF1R, IGF2, IKBKE, IKZF1, IL10, IL7R, INHA, INHBA, INPP4A, INPP4B, INSR, IRF2, IRF4, IRS1, IRS2, JAK1, JAK2, JAK3, JUN, KAT6A, KDM5A, KDM5C, KDM6A, KDR, KEAP1, KEL, KIF5B, KIT, KLF4, KLHL6, KMT2B, KMT2C, KMT2D, KRAS, LAMP1, LATS1, LATS2, LMO1, LRP1B, LYN, LZTR1, MAGI2, MALT1, MAP2K1, MAP2K2, MAP2K4, MAP3K1, MAP3K13, MAP3K14, MAP3K4, MAPK1, MAPK3, MAX, MCL1, MDC1, MDM2, MDM4, MED12, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLL, MLLT3, MPL, MRE11A, MSH2, MSH3, MSH6, MST1, MST1R, MTOR, MUTYH, MYB, MYC, MYCL1, MYCN, MYD88, MYOD1, NAB2, NBN, NCOA3, NCOR1, NEGR1, NF1, NF2, NFE2L2, NFKB1A, NKX2-1, NKX3-1, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NPM1, NRAS, NRG1, NSD1, NTRK1, NTRK2, NTRK3, NUP93, NUTM1, PAK1, PAK3, PAK7, PALB2, PARK2, PARP1, PAX3, PAX5, PAX7, PAX8, PBRM1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDK1, PDPK1, PGR, PHF6, PHOX2B, PIK3C2B, PIK3C2G, PIK3C3, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R1, PIK3R2, PIK3R3, PIM1, PLCG2, PLK2, PMAIP1, PMS1, PMS2, PNRC1, POLD1, POLE, PPARG, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PREX2, PRKAR1A, PRKCI, PRKDC, PRSS8, PTCH1, PTEN, PTPN11, PTPRD, PTPRS, PTPRT, QKI, RAB35, RAC1, RAD21, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RANBP2, RARA, RASA1, RB1, RBM10, RECQL4, REL, RET, RFWD2, RHEB, RHOA, RICTOR, RIT1, RNF43, ROS1, RPS6KA4, RPS6KB1, RPS6KB2, RPTOR, RUNX1, RUNX1T1, RYBP, SDHA, SDHAF2, SDHB, SDHC, SDHD, SETBP1, SETD2, SF3B1, SH2B3, SH2D1A, SHQ1, SLIT2, SLX4, SMAD2, SMAD3, SMAD4, SMARCA4, SMARCB1, SMARCD1, SMC1A, SMC3, SMO, SNCAIP, SOCS1, SOX10, SOX17, SOX2, SOX9, SPEN, SPOP, SPTA1, SRC, SRSF2, STAG1, STAG2, STAT3, STAT4, STAT5A, STAT5B, STK11, STK40, SUFU, SUZ12, SYK, TAF1, TBX3, TCEB1, TCF3, TCF7L2, TERC, TERT, TET1, TET2, TFE3, TFRC, TGFB1, TGFB2, TMEM127, TMPRSS2, TNFAIP3, TNFRSF14, TOP1, TOP2A, TP53, TP63, TRAF2, TRAF7, TSC1, TSC2, TSHR, U2AF1, VEGFA, VHL, VTCN1, WISP3, WT1, XIAP, XPO1, XRCC2, YAP1, YES1, ZBTB2, ZBTB7A, ZFH3, ZNF217, ZNF703, ZRSR2

Section B: Fusion Analysis of 165 Genes (>5,000 selected rearrangements)

ABL1, ABL2, AKT3, ALK, ARHGAP26, AXL, BCL11B, BCL2, BCL6, BCOR, BCR, BIRC3, BRAF, BRD3, BRD4, CAMTA1, CBF, CCNB3, CCND1, CCND2, CD151, CDK6, CHD1, CHIC2, CIC, CIITA, CREBBP, CRLF2, CSF1R, DEK, DUSP22, EBF1, EGFR, EIF4A1, EPC1, EPOR, ERG, ESR1, ESRRA, ETV1, ETV4, ETV5, ETV6, EWSR1, FGFR1, FGFR2, FGFR3, FGR, FOSB, FOXO1, FUS, GLI1, GLIS2, HMGA2, IKZF1, IKZF2, IKZF3, IL2RB, INSR, JAK2, JAZF1, KAT6A, KLF2, KMT2A, LMO2, LYN, MALT1, MAML2, MAN2B1, MAST1, MAST2, MBTD1, MEAF6, MECOM, MEF2D, MET, MGEA5, MKL1, MKL2, MLF1, MLLT10, MLLT4, MN1, MSMB, MUSK, MYB, MYC, MYH11, NCOA1, NCOA2, NF1, NFKB2, NOTCH1, NOTCH2, NPM1, NR4A3, NRG1, NTRK1, NTRK2, NTRK3, NUMBL, NUP214, NUP98, NUTM1, P2RY8, PAG1, PAX3, PAX5, PAX7, PBX1, PDCD1LG2, PDGFB, PDGFRA, PDGFRB, PHF1, PICALM, PIK3CA, PKN1, PLAG1, PML, PPARG, PRDM16, PRKCA, PRKCB, PRKD1, PRKD2, PRKD3, PTK2B, RAF1, RANBP17, RARA, RBM15, RECK, RELA, RET, ROS1, RSPO2, RSPO3, RUNX1, RUNX1T1, SEMA6A, SETD2, SS18, STAG2, STAT6, STIL, TAF15, TAL1, TCF12, TCF3, TERT, TFE3, TFEB, TFG, THADA, TMPRSS2, TP63, TSLP, TYK2, USP6, YAP1, YWHAE, ZCCHC7, ZMYND11, ZNF384

Section C: Expression Analysis (RNA Sequencing) of 71 genes

ASB13, BAALC, BAX, BCL2A1, BCL2, BCL3, BCL6, BMPR1B, CA6, CCDC50, CCND1, CCND2, CCND3, CD274, CD97, CDK3, CDK4, CDK6, CHN2, CREB3L2, CRLF2, CTLA4, CYB5R2, DENND3, DNMT3B, EGFL7, EPOR, ERG, FLT1, FLT3, FLT4, FOXP1, GPR110, HOXA9, ID4, IGF1, IL2RA, IRF4, ITPKB, JAK2, KDR, LIMD1, LMO1, LMO2, MAML3, MCL1, MECOM, MME, MUC1, MUC4, MYBL1, MYC, NRXN3, PAX5, PDGFRA, PIM2, PTPN1, RAB29, RARA, S1PR2, SEMA6A, SERPINA9, SH3BP5, SOX11, SPARC, SPATS2L, SPRED1, TAL1, TNFRSF13B, TP53INP1, WT1

For all inquiries about
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