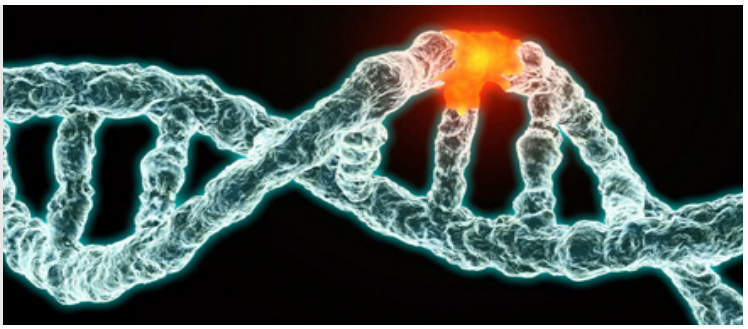
Experience.

MPLN MOLECULAR DIAGNOSTICS

Molecular Pathology Laboratory Network, Inc. (MPLN) has been on the forefront of laboratory medicine since its inception. Our molecular diagnostics laboratory performs quantitative polymerase chain reaction (PCR), mutation analysis and gene sequencing to support therapy selection, treatment monitoring and minimal residual disease detection. Experience. MPLN.



Companion Diagnostics

Advances in pharmacogenetics, along with the design and development of targeted cancer therapies, have led to an increasing number of companion diagnostic assays.

Whereas pharmacogenetics explores a patient's specific genotype and response to a drug, companion diagnostics is a broader application that includes the association of biomarkers and genetic mutations that predict treatment outcomes.

Using molecular technology, we can identify patients who may experience adverse drug interactions or those who may be unresponsive to certain medications due to genetic variations or expression of specific hormones, proteins and/or enzymes.

Mutation Analysis

Identifying gene mutations and specific markers prior to initiating therapy can result in better patient outcomes as well as substantial cost savings by avoiding poor drug choices and needless over prescribing.

For example, colorectal cancer (CRC) patients with KRAS or BRAF mutations are less likely to respond to anti-EGFR therapy. Therefore, ASCO recommends patients with metastatic CRC who are candidates for anti-EFGR therapy be tested for KRAS gene mutations prior to initiating treatment. Also, when the KRAS gene is not mutated, NCCN guidelines recommend determination of BRAF gene status as part of their workup, although this recommendation is currently based on inconsistent field data.

Clonality and Gene Rearrangements

T-cell receptor and B-cell immunoglobulin heavy chain (IgH) or light chain (Igk) gene rearrangement studies can be supportive of a lymphoma diagnosis with identification of monoclonality in a morphologically suspicious lymphoid infiltrate.

Molecular immunoglobulin kappa (Igk) light chain testing is also a useful complement to B-cell heavy chain (IgH) gene rearrangement analysis. Igk gene rearrangement can provide confirmation of clonality in post-germinal center (mature) neoplasms where clonotypic IgH signatures may not be detected due to somatic hypermutation of VH genes.

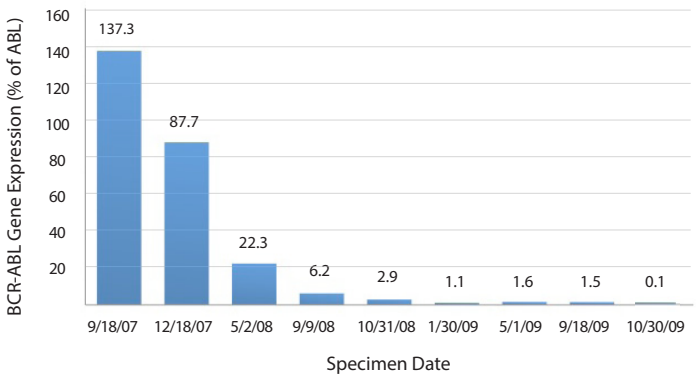
The Igk assay, in addition to identifying clonality in atypical lymphoproliferative disorders, can also support a differential diagnosis between reactive lesions and hematologic malignancies, and assign presumptive lineage in mature monoclonal lymphoproliferative disorders.

Minimal Residual Disease Detection

Detection and monitoring of minimal residual disease can be accomplished by quantitative PCR, specifically in chronic myelogenous leukemia and acute prolymphocytic leukemia. Quantitative PCR provides at least 100 to 1000 times greater sensitivity than fluorescent in situ hybridization (FISH). Measurements are taken at baseline in newly diagnosed cases and at regular intervals to monitor for evidence of molecular remission in response to chemotherapy or allogeneic stem cell transplantation.

Studies using gene sequencing can also assist in identifying patients with an acquired drug resistance to tyrosine kinase inhibitor (TKI) therapy, and NCCN guidelines recommend consideration of ABL Kinase domain sequencing for these patients.

Serial evaluation for quantitative BCR/ABL in a case of chronic myelogenous leukemia on Gleevec® treatment



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Molecular Diagnostic Oncology Testing

Molecular Oncology Test	Diagnostic Condition & Companion Therapy
ABL kinase mutation analysis	Philadelphia positive leukemia (CML, ALL, AML) and tyrosine kinase inhibitor resistance
AML mutation profile: FLT3 and NPM1 mutations with reflex to CEBPA mutation	AML
BCR/ABL quantitative PCR major and minor	Philadelphia positive leukemia (CML, ALL, AML), baseline, and monitoring minimal residual disease
B-cell heavy chain gene rearrangement B-cell kappa light chain gene rearrangement	B-cell clonality
BRAF V600E mutation	EGFR inhibitor response in metastatic Colorectal Cancer (CRC): Erbitux® (cetuximab), and Vectibix™ (panitumumab)
c-kit mutation	AML
JAK2 V617F mutation	PV
KRAS mutation	EGFR inhibitor response in metastatic CRC: Erbitux, and Vectibix
MPL W515/S505N mutation	EV, PMF
PML/RARA t(15;17) quantitative PCR short and long form	APL, baseline and monitoring minimal residual disease
T-cell gamma receptor gene rearrangement	T-cell clonality
UGT1A1 genotype	Camptosar® (Irinotecan) toxicity and drug dosage in metastatic or recurrent CRC
*Fluorescence in situ hybridization (FISH) assays	*Complement molecular PCR assays for diagnosis, prognosis and minimal residual disease detection

NCCN Guideline

*Fluorescence in situ hybridization (FISH) assays performed in our Cytogenetics Laboratory complement molecular PCR assays for diagnosis, prognosis and minimal residual disease detection of hematological malignancies and solid tumors. Clinical indications and/or results from previous testing are utilized to select specific gene locations for investigation. FISH uses fluorescent probes that bind to only those parts of the chromosome with which they show a high degree of sequence similarity.

For a complete list of FISH probes available to detect and localize the presence or absence of specific DNA sequences on chromosomes in metaphase, interphase cells or in tissue, visit us online at www.MPLNET.com.

References

1. Ross J S et al. (2004). Targeted Therapies for Cancer 2004. Am J Clin Pathol.122(4):598-609.

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(Rev 12/2018)