



CASE STUDIES

Comprehensive Cancer Gene Set



Genomic Tests for Personalized Patient Care

Complementing our close partnership with Siteman Cancer Center, **Genomics and Pathology Services (GPS)** at Washington University offers an integrated approach to disease-specific genomic testing including the use of **clinical next generation sequencing** methodologies. Although our primary focus area is cancer, we also offer tests and expertise in other areas.



Comprehensive Cancer Gene Set

This tumor sequencing test offers a **cost-effective** and **efficient analysis** of clinically actionable genetic biomarkers spanning a **wide range of cancers**. It is widely used by oncologists at **Siteman Cancer Center** and is also available to any interested physician.

Below are examples of clinical cases that demonstrate the clinical utility of tumor sequencing.

Case 1: Make a Diagnosis

Presentation - 12-day-old infant presented with low platelet count (thrombocytopenia) and hepatosplenomegaly. Broad differential diagnosis was bone marrow failure, juvenile myelomonocytic leukemia (JMML), hemophagocytic lymphohistiocytosis and autoimmune lymphoproliferative syndrome.

NGS Test Utility / Results - Comprehensive cancer sequencing was performed to aid in diagnosis and a *KRAS* p.G13D alteration was detected.

Actions / Outcomes - Based on molecular findings the infant was diagnosed with JMML, an uncommon cancer type. Management included evaluation for hematopoietic stem cell transplant, splenectomy and chemotherapy, as well as parental counseling and follow-up.

Case 2: Refine a Prognosis

Presentation - 45-year-old female presented with cytogenetically normal acute myelogenous leukemia (AML). Routine molecular testing revealed *NPM1* insertion and *FLT3* internal tandem duplication by PCR. She was started on chemotherapy.

NGS Test Utility / Results - Comprehensive cancer sequencing was performed to assess for mutational status of critical hematologic disease associated genes. A *DNMT3A* p.R882H mutation was identified, which is associated with poor prognosis in AML and myelodysplastic syndromes.

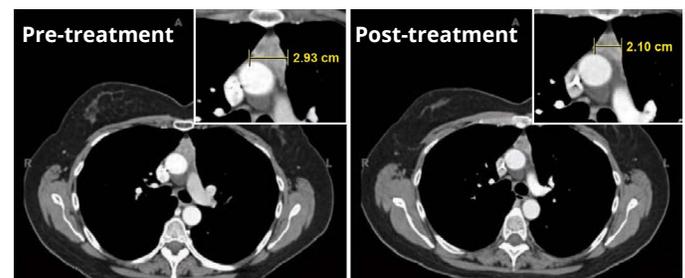
Actions / Outcomes - In concert with other cytogenetic and molecular findings the patient was determined to have an unfavorable prognosis with high risk of relapse. She was treated for aggressive disease with plans for allogeneic bone marrow transplantation.

Case 3: Identify a Targeted Treatment

Presentation - 58-year-old female presented with metastatic thymic carcinoma. Disease was rapidly growing in chest cavity and liver.

NGS Test Utility / Results - Comprehensive cancer sequencing detected a *KIT* p.D579del deletion, which is uncommon in this cancer type.

Actions / Outcomes - This mutation is predicted to respond to a drug in the expanding class of tyrosine kinase inhibitors (TKI), so a daily dose of the TKI imatinib was initiated. After one month of treatment, significant radiologic response was noted. Patient remains well with stable disease two years later.





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Case 4: Eliminate Unsuitable Treatment

Presentation - 67-year-old male presented with metastatic rectal adenocarcinoma. Routine molecular testing at diagnosis was negative for *KRAS* mutations in codons 12 and 13 by allele-specific PCR.

NGS Test Utility / Results - Comprehensive cancer sequencing detected *KRAS* p.Q61H alteration, which is uncommon and not tested in routine workup.

Actions / Outcomes - *KRAS* mutations confer resistance to anti-EGFR therapy, so patient therapy was adjusted to eliminate this treatment.

Case 5a: Identify a Clinical Trial

Presentation - 53-year-old female presented with metastatic colon adenocarcinoma. She was treated with standard of care including FOLFOX/Avasin and received a right hemicolectomy. However, disease recurrence was observed.

NGS Test Utility / Results - Comprehensive cancer sequencing detected *PIK3CA* p.H1047L alteration, which results in increased catalytic activity and enhanced signaling. Patient was wildtype for *KRAS*, *BRAF* and *NRAS*.

Actions / Outcomes - Due to this alteration in *PIK3CA*, the patient is being screened to determine eligibility for enrollment in *PIK3CA* colon cancer clinical trial.

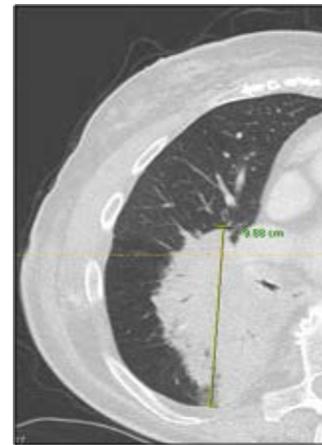
Case 5b: Identify a Clinical Trial

Presentation - 71-year-old female presented with mucinous lung adenocarcinoma. Routine molecular testing was negative for *ALK*, *EGFR*, and *KRAS*. Patient was treated with multiple chemotherapeutic agents but she experienced disease recurrence and progression over a period of three years.

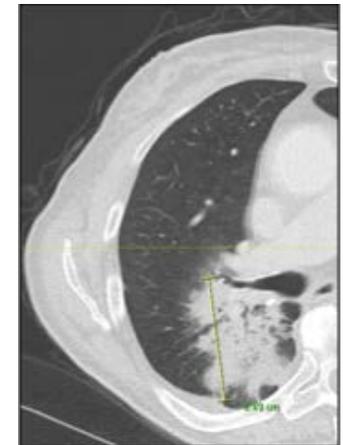
NGS Test Utility / Results - Comprehensive cancer sequencing detected a 12 base pair insertion in codon 20 of *ERBB2* (*HER2*). *ERBB2* mutations are not extensively reported in non-small cell lung cancer (2-4 percent).

Actions / Outcomes - *ERBB2* exon 20 insertions have been shown to be sensitive to *EGFR/ERBB2* TKIs and *ERBB2* monoclonal antibody (mAb) therapy. The patient was enrolled in a phase I study of neratinib with temsirolimus to study the effect of a targeted treatment option. She responded favorably to treatment with a decrease in pulmonary mass and remains well with stable disease 10 months later.

Pre-treatment



Post-treatment (4 mo)



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