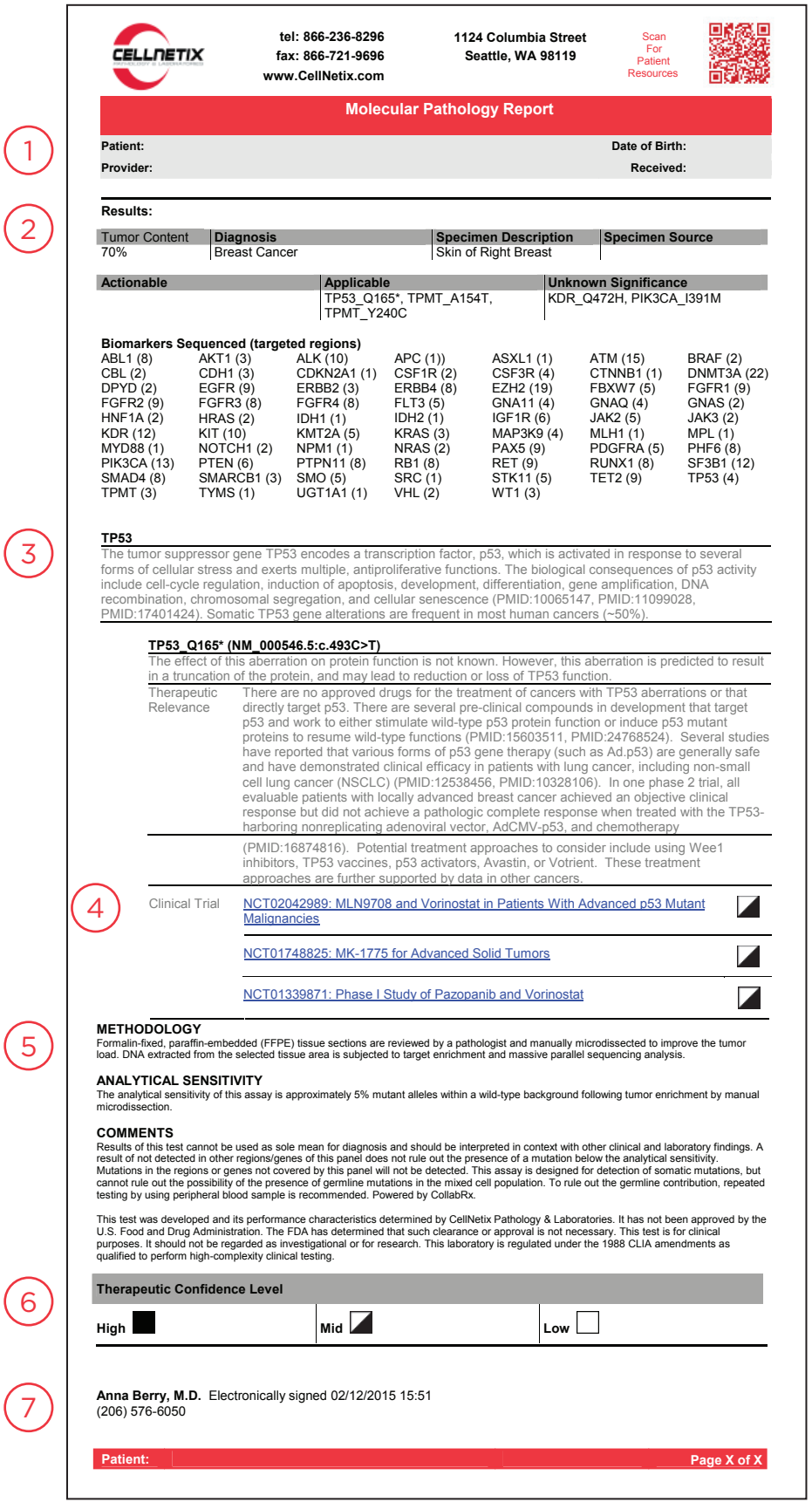
A Guide to Your Report Page

To help you understand how to find information on your Pathology Report page, below are descriptions and corresponding annotations of the different sections that may appear.



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Scan For Patient Resources

Molecular Pathology Report

1

Patient: **Date of Birth:**
Provider: **Received:**

2

Results:

Tumor Content	Diagnosis	Specimen Description	Specimen Source
70%	Breast Cancer	Skin of Right Breast	

Actionable	Applicable	Unknown Significance
	TP53_Q165*, TPMT_A154T, TPMT_Y240C	KDR_Q472H, PIK3CA_I391M

Biomarkers Sequenced (targeted regions)

ABL1 (8)	AKT1 (3)	ALK (10)	APC (1))	ASXL1 (1)	ATM (15)	BRAF (2)
CBL (2)	CDH1 (3)	CDKN2A1 (1)	CSF1R (2)	CSF3R (4)	CTNNB1 (1)	DNMT3A (22)
DPYD (2)	EGFR (9)	ERBB2 (3)	ERBB4 (8)	EZH2 (19)	FBXW7 (5)	FGFR1 (9)
FGFR2 (9)	FGFR3 (8)	FGFR4 (8)	FLT3 (5)	GNA11 (4)	GNAQ (4)	GNAS (2)
HNF1A (2)	HRAS (2)	IDH1 (1)	IDH2 (1)	IGF1R (6)	JAK2 (5)	JAK3 (2)
KDR (12)	KIT (10)	KMT2A (5)	KRAS (3)	MAP3K9 (4)	MLH1 (1)	MPL (1)
MYD88 (1)	NOTCH1 (2)	NPM1 (1)	NRAS (2)	PAX5 (9)	PDGFRA (5)	PHF6 (8)
PIK3CA (13)	PTEN (6)	PTPN11 (8)	RB1 (8)	RET (9)	RUNX1 (8)	SF3B1 (12)
SMAD4 (8)	SMARCB1 (3)	SMO (5)	SRC (1)	STK11 (5)	TET2 (9)	TP53 (4)
TPMT (3)	TYMS (1)	UGT1A1 (1)	VHL (2)	WT1 (3)		

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TP53

The tumor suppressor gene TP53 encodes a transcription factor, p53, which is activated in response to several forms of cellular stress and exerts multiple, antiproliferative functions. The biological consequences of p53 activity include cell-cycle regulation, induction of apoptosis, development, differentiation, gene amplification, DNA recombination, chromosomal segregation, and cellular senescence (PMID:10065147, PMID:11099028, PMID:17401424). Somatic TP53 gene alterations are frequent in most human cancers (~50%).

TP53_Q165* (NM_000546.5:c.493C>T)

The effect of this aberration on protein function is not known. However, this aberration is predicted to result in a truncation of the protein, and may lead to reduction or loss of TP53 function.

Therapeutic Relevance: There are no approved drugs for the treatment of cancers with TP53 aberrations or that directly target p53. There are several pre-clinical compounds in development that target p53 and work to either stimulate wild-type p53 protein function or induce p53 mutant proteins to resume wild-type functions (PMID:15603511, PMID:24768524). Several studies have reported that various forms of p53 gene therapy (such as Ad.p53) are generally safe and have demonstrated clinical efficacy in patients with lung cancer, including non-small cell lung cancer (NSCLC) (PMID:12538456, PMID:10328106). In one phase 2 trial, all evaluable patients with locally advanced breast cancer achieved an objective clinical response but did not achieve a pathologic complete response when treated with the TP53-harboring nonreplicating adenoviral vector, AdCMV-p53, and chemotherapy (PMID:16874816). Potential treatment approaches to consider include using Wee1 inhibitors, TP53 vaccines, p53 activators, Avastin, or Votrient. These treatment approaches are further supported by data in other cancers.

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Clinical Trial
- NCT02042989: MLN9708 and Vorinostat in Patients With Advanced p53 Mutant Malignancies
- NCT01748825: MK-1775 for Advanced Solid Tumors
- NCT01339871: Phase I Study of Pazopanib and Vorinostat

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METHODOLOGY

Formalin-fixed, paraffin-embedded (FFPE) tissue sections are reviewed by a pathologist and manually microdissected to improve the tumor load. DNA extracted from the selected tissue area is subjected to target enrichment and massive parallel sequencing analysis.

ANALYTICAL SENSITIVITY

The analytical sensitivity of this assay is approximately 5% mutant alleles within a wild-type background following tumor enrichment by manual microdissection.

COMMENTS

Results of this test cannot be used as sole mean for diagnosis and should be interpreted in context with other clinical and laboratory findings. A result of not detected in other regions/genes of this panel does not rule out the presence of a mutation below the analytical sensitivity. Mutations in the regions or genes not covered by this panel will not be detected. This assay is designed for detection of somatic mutations, but cannot rule out the possibility of the presence of germline mutations in the mixed cell population. To rule out the germline contribution, repeated testing by using peripheral blood sample is recommended. Powered by CollabRx.

This test was developed and its performance characteristics determined by CellNetix Pathology & Laboratories. It has not been approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is for clinical purposes. It should not be regarded as investigational or for research. This laboratory is regulated under the 1988 CLIA amendments as qualified to perform high-complexity clinical testing.

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Therapeutic Confidence Level

High ■ Mid ◪ Low □

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Anna Berry, M.D. Electronically signed 02/12/2015 15:51
(206) 576-6050

Patient: **Page X of X**

1. Find patients and provider information here, as well as when we received the specimen for testing.

2. Overview of results from the diagnosis, to the biomarker's used during the analysis that have significance in the results.

   Actionable = An approved therapy is available
   Applicable = An off-label drug or a clinical trial may be available.
   Unknown Significance = No clear therapy at this time.

3. Here you will find information regarding the applicable genes specific to this case.

4. There are hundreds of clinical trials available to which a patient may apply. Our systems cross reference a clinical trial database to find relevant clinical trials specific to the patients genes. Links in the report take you directly to www.clinicaltrials.gov.

5. This methodology section provides a brief transparent snapshot of the way we prepare each sample.

6. The therapeutic confidence level is our summation of how effective we believe that the clinical trials will be for the targeted gene therapy.

7. We always include the direct contact information of the pathologists who diagnosed the case if you have any questions or need further explanation on the diagnosis.

