PRECISION INSIGHTS

GPS Cancer

Molecular Insights You Can Rely On

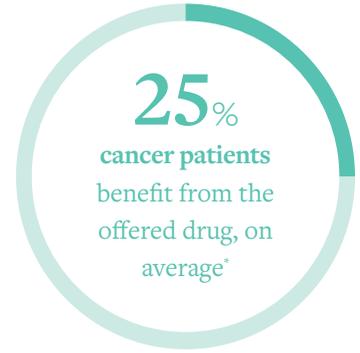*Tumor-normal sequencing of DNA + RNA expression*

NantHealth®

Cancer Care is Evolving

Oncologists use all the information available to make the best decisions for their patients. And yet, response rates for most cancer therapies remain low, with only 25% of cancer patients benefiting from the offered drug.

What if you could know more about each patient's tumor? Could you drive up that 25%, and give your patients better outcomes?

We can now know more about each patient's tumor than ever before – knowledge that may help oncologists prescribe a more effective treatment and avoid treatments that likely won't be effective.

25%
cancer patients benefit from the offered drug, on average[*]

GPS Cancer - Tumor-Normal Sequencing of DNA + RNA Expression

How Precise Is Your Precision Medicine?

When striving to deliver precision cancer care, it's essential to have precise information. When a test identifies a target for a drug, you need to be confident that the target is there.

At NantHealth, we believe that looking at tumor DNA is not enough. Increasingly, research is showing that tumor-only sequencing can allow false positive mutation calls by not adequately filtering out germline mutations. Likewise, alterations in DNA are sometimes not transcribed into altered RNA or expressed as protein, and as such, may not be viable targets for drug treatment.

Molecular Insights You Can Rely On

GPS Cancer provides a precise and comprehensive molecular profile, equipping oncologists with insights that they can rely on to inform their personalized treatment strategies.

Whole genome sequencing and whole exome sequencing equips doctors with information on DNA alterations located throughout the genome, including non-coding regions, which can harbor actionable alterations (e.g. RET, TRK rearrangements), as well as mutations in promoter and enhancer sequences.

Whole transcriptome (RNA) sequencing may help avoid inappropriate therapies by confirming genomic alterations that may result in expression of abnormal protein. RNA sequencing provides a quantitative measure of gene expression, and identifies gene fusions resulting from genomic translocations.

Tumor-normal sequencing may help avoid inappropriate therapies due to misinterpretation of inherited mutations as somatic and confirms provenance — i.e., that the tumor being tested comes from that patient.

In a NantHealth and NantOmics study comparing tumor-only to tumor-normal sequencing in 621 patients across 30 different cancer types, "filtering for common SNPs still resulted in as high as 48% false positive variant calling."[*]

*Rabizadeh et al. Comprehensive genomic transcriptomic tumor-normal gene panel analysis for enhanced precision in patients with lung cancer. Oncotarget. 2018; 9:19223-19232. This is an open-access article distributed under the terms of the Creative Commons Attribution License 3.0 (CC BY 3.0).

1-on-1 Physician Consultants

Peer-To-Peer Collaboration

Tumor Board Access

Actionable Reports to Inform Oncologists' Treatment Strategies

The GPS Cancer report — accessible through NantHealth's web-based Precision Insights Portal – offers insight into therapies that may have potential benefit and therapies to which the cancer may be resistant.

Based on genomic and transcriptomic analysis, the report provides clear information on:

- FDA-approved therapies with potential clinical benefit
- Active clinical trials for investigational therapies
- Therapies to which the tumor may be resistant

Other detailed information within the report includes:

- Tumor mutational burden (TMB)
- Microsatellite instability (MSI)
- Provenance
- Germline mutations in cancer predisposition genes

Informing Your Personalized Treatment Strategies

Targeted Therapy – By integrating tumor-normal sequencing of DNA with RNA sequencing, GPS Cancer provides precise information on clinically relevant mutations to inform use of targeted therapies.

Immunotherapy – GPS Cancer assesses true TMB based on assessment of nearly 20,000 genes, as well as MSI and PD-L1, informing use of checkpoint inhibitors.

Chemotherapy – Unlike most DNA-only gene panels, GPS Cancer utilizes RNA sequencing and leverages NantHealth's deep understanding of biological pathways to inform use of common chemotherapies.

NantHealth Precision Insights

GPS Cancer
Precise and comprehensive tissue-based profiling

Liquid GPS
Blood-based tumor profiling and quantitative monitoring

Precision Insights Portal
Bringing precision insights to evidence-based care

Why Tumor-Normal Sequencing

2015 | **John Hopkins** – "a tumor-only sequencing approach could not definitively identify germline changes in cancer-predisposing genes and led to additional false-positive findings comprising 31% and 65% of alterations identified in targeted and exome analyses, respectively, including in potentially actionable genes."*

2017 | **Moffitt Cancer Center** – "Matched tumor/normal mutation detection is more appropriate for applications requiring high precision such as novel mutation detection and mutation signature analysis and remains the optimal approach."†

2018 | **NantOmics and NantHealth** – With tumor-only sequencing, 29% of lung cancer patients included in the study had at least one false-positive variant in a druggable gene.‡

Why RNA

DNA

Advancements in genome (DNA) sequencing have been instrumental in understanding genomic alterations that may drive a patient's cancer, but genomic sequencing alone is only part of the story.

RNA

DNA is the blueprint for RNA. Emerging research** shows that alterations in DNA are sometimes not transcribed into altered RNA or expressed as protein. Likewise, alterations are sometimes introduced at the RNA or protein level that are not detectable at the DNA level.
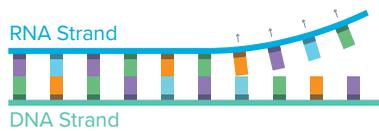
PROTEIN

RNA is the blueprint for protein. To make the most informed treatment decisions, it is essential to understand the impact of genomic alterations on RNA expression and protein.
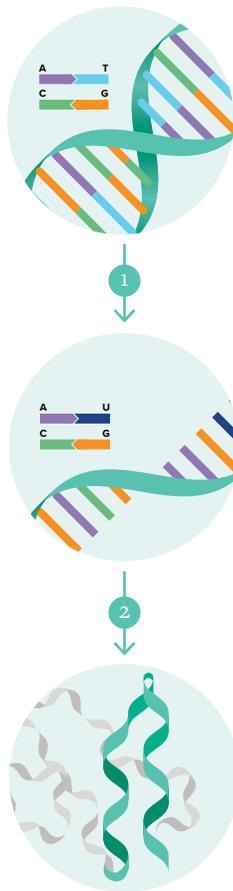
1 TRANSCRIPTION

Genetic information stored in DNA is copied into a complementary strand of RNA.
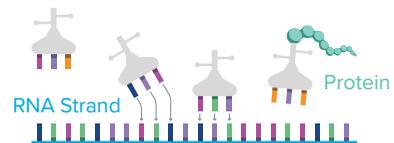
RNA Strand

DNA Strand

Mutations may not be transcribed due to:

- DNA methylation
- Defective DNA replication/transcription machinery
- Post-transcriptional modification processes (splicing, RNA editing, etc.)

2 TRANSLATION

The gene sequence in the RNA strand is decoded to form strings of amino acids that fold into proteins.

RNA Strand

Protein

* Jones et al. Personalized genomic analyses for cancer mutation discovery and interpretation. Sci Transl Med. 2015 April 15; 7(283): 283ra53.

† Teer JK et al. Evaluating somatic tumor mutation detection without matched normal samples. Human Genomics. 2017;11:22.

‡ Rabizadeh et al. Comprehensive genomic transcriptomic tumor-normal gene panel analysis for enhanced precision in patients with lung cancer. Oncotarget. 2018; 9:19223-19232. This is an open-access article distributed under the terms of the Creative Commons Attribution License 3.0 (CC BY 3.0).

** Wang Q, Xia J, Jia P, Pao W, Zhao Z. Application of next generation sequencing to human gene fusion detection: computational tools, features and perspectives. Briefings in Bioinformatics. 2013;14(4):506-519.

Bringing Precision Insights to Evidence-Based Care

Although genomic information is increasingly important to an oncologists' treatment strategies, it can be challenging to integrate this personalized information into established clinical practice and pathways.

In addition to offering web-based ordering and results for NantHealth molecular tests, the **Precision Insights Portal** is the only solution available to blend guidelines-based regimen information powered by Eviti with personalized insights from GPS Cancer, providing oncologists an integrated view of treatment options informed by both standard of care and patient-specific molecular insights.

Highlights of this web-based portal include:

- **Tools to move from test results to treatment insights:**
  When viewing GPS Cancer results within the Precision Insights Portal, oncologists have one-click access to treatment options, physician consultations, and tumor boards to enable informed treatment decisions for each patient.

- **Standard-of-care regimens prioritized by personalized results from GPS Cancer:**
  Oncologists can leverage GPS Cancer results to prioritize among a potentially long list of standard regimens and quickly identify those regimens that are most likely to benefit the patient based on their unique tumor. Standard regimen information is powered by NantHealth's Eviti Evidence-based Medicine Library, a curated knowledgebase of over 3,000 multi-modality oncology regimens, aggregated through comprehensive surveillance of national oncology consensus group guidelines, peer-reviewed journal articles, and federally-registered clinical trials.

- **Easy access to supporting information to enable data-driven decision-making:**
  On-screen details with drill-down capability gives oncologists clarity to compare regimen options. Regimen information available at-a-glance includes molecular target drug associations, level of evidence, reported outcomes, toxicity prevalence, estimated cost, and supporting literature.

NantHealth | ORDER ▾ | Dr. Arthur Johnson | Support

◀ Back to GPS Cancer® Results

Treatment Options (*Powered by Eviti®*) | **Western University Cancer Center**

Order ID: KE4p2m4JT4d91AWd830BOut

| Cancer Type: Colon | Pathology: Adenocarcinoma ✕ | Stage: Recurrent ✕ | Line of Treatment: First Line ✕ | Goal of Treatment: Non-curative ✕ |
| Performance Status: 0-Normal Activity (asymptomatic) ✕ | Adult/Pediatric: Adult ✕ | MSI Level: Low | K-ras Gene: Mutant | N-ras Gene: Wildtype |

EDIT

Evidence-Based Regimens - 8 ⌃

Select a treatment, and then select Save to link this treatment to the patient. Modify your search using the fields above.

NOTE: Omics information provided on this screen was generated via the GPS Cancer® laboratory developed test and has been imported to NantHealth's Eviti® solution.

✔ Support ✕ Opposition — None

REGIMEN NAME	OMICS GUIDANCE ❓	OMICS RATIONALE	LEVEL OF EVIDENCE	UNSELECTED OUTCOME ❓	ESTIMATED COST
☐ Fluorouracil, Leucovorin, and Irinotecan (FOLFIRI)	✔	Overexpression of TOPO1 has been associated with improved response to Irinotecan.	A4	Median OS: 23.1 months	$9,545.92
☐ Fluorouracil, Leucovorin, Irinotecan (FOLFIRI) and Bevacizumab	✔	Overexpression of TOPO1 has been associated with improved response to Irinotecan.	A4	Median OS: 25.8 months	$44,146.56
☐ Capecitabine	—	N/A	A4	Median OS: 13.2 months	$4,490.96
☐ Capecitabine and Bevacizumab	—	N/A	B1	Median OS: 16.6 months	$23,134.84
☐ Capecitabine and Oxaliplatin	✕	Overexpression of ERCC1 can cause resistance to platinum-based therapies.	A5	Median OS: 17.2 months	$10,051.64
☐ Capecitabine, Oxaliplatin and Bevacizumab	✕	Overexpression of ERCC1 can cause resistance to platinum-based therapies.	A5	Median OS: 24.6 months	$42,165.69
☐ Fluorouracil, Leucovorin, and Oxaliplatin (FOLFOX)	✕	Overexpression of ERCC1 can cause resistance to platinum-based therapies.	A4	Median OS: 19.5 months	$7,143.96

NantHealth®

ABOUT NANTHEALTH

NantHealth's Mission is to improve the delivery of healthcare and optimize patient outcomes by leveraging the latest advancements in precision medicine and software technologies to enable true value based care.

TO LEARN MORE ABOUT NANTHEALTH PRECISION INSIGHTS:

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TO LEARN MORE ABOUT OTHER NANTHEALTH SOLUTIONS, INCLUDING EVITI, NAVINET, AND CONNECTED CARE:

1.855.WHY.NANT | www.nanthealth.com