GPS Cancer
The Era of Complete Genomics and Proteomics is Here
Advanced molecular profiling to inform personalized treatment strategies

www.nanthealth.com
What information do you need to make more informed treatment decisions for your patients?

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.

Did You Know?

| Gene panels without RNA may result in false positives† |
| Gene panels without tumor-normal comparison may result in 65% inaccuracy‡ |
| IHC for determining trastuzamab use was invented in the 1940s and is qualitative |

GPS Cancer | DNA + RNA + PROTEIN

Know More Before

When there are many standard treatment options available, which are more or less likely to benefit your patient?

GPS Cancer precisely measures expression of protein biomarkers – e.g., hENT1, ERCC1, and TUBB3 – that have been shown to indicate sensitivity or resistance to common chemotherapies.

When there are few standard-of-care options available, or the standard isn’t working, how do you find new options?

GPS Cancer may reveal new treatment options – including active clinical trials – based on the molecular profile of the patient’s tumor.

GPS Cancer is a key enabler of Cancer Breakthroughs 2020, the world’s most comprehensive cancer care initiative, with the ultimate goal of creating a personalized cancer vaccine.

The Era of Complete Genomics and Proteomics is Here

GPS Cancer provides oncologists with unprecedented insights into the molecular signature of each patient’s cancer to inform personalized treatment strategies.

Whole genome (DNA) sequencing of 20,000+ genes equips doctors with information on alterations located throughout the whole genome, including non-coding regions, which can harbor actionable alterations (e.g. RET rearrangements), as well as mutations in promoter and enhancer sequences.

Whole transcriptome (RNA) sequencing confirms genomic alterations that may result in expression of abnormal proteins, and infers expression for proteins that cannot be directly measured.

Quantitative proteomics measures amount of clinically relevant proteins to provide insight into how well therapies may work.

Tumor-normal matching helps 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.

Confirmation of provenance is important to prevent the clinical challenges posed by switching of patient specimens. A study of 13,000 prostate biopsies found that 0.26% of specimens were completely switched with that of another patient*; when applied to the 1 million prostate biopsies performed each year, this suggests 2,600 mismatched prostate biopsies annually.*

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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 GPS Order and Results app – offers insight into therapies that may have potential benefit and therapies to which the cancer may be resistant.

<table>
<thead>
<tr>
<th>Patient is LIKELY to benefit from</th>
<th>Based upon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin, Cisplatin, Oxaliplatin</td>
<td>ERCC1 (Protein−)</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>KRAS Mutation (No Evidence)</td>
</tr>
<tr>
<td>EGFR Expression (RNA+)</td>
<td></td>
</tr>
<tr>
<td>Docetaxel, Paclitaxel, nab-Paclitaxel</td>
<td>TUBB3 (Protein+)</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Patient is UNLIKELY to benefit from</th>
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</thead>
<tbody>
<tr>
<td>Gemcitabine</td>
<td>RRM1 (Protein+)</td>
</tr>
<tr>
<td>Temozolomide</td>
<td>MGMT (Protein+)</td>
</tr>
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Based on the genomic and proteomic biomarkers, the report provides clear information on:

- FDA-approved therapies with potential clinical benefit
- Active clinical trials of therapies that may have clinical benefit
- 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
Beyond DNA sequencing:

Why RNA & Protein Are So Important

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

PROTEIN
Cancer drugs act on proteins, not DNA. To make the most informed treatment decisions, it is essential to understand the impact of genomic alterations on protein expression. With quantitative proteomics, it is now possible to precisely measure protein expression levels that may predict patient response to a given treatment.

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Errors can be caused by:
- DNA methylation
- Defective DNA replication/transcription machinery
- Post-transcriptional modification processes (splicing, RNA editing, etc.)

Defective transcription (DNA-to-RNA) and translation (RNA-to-Protein) processes can lead to mutations, insertions, deletions, amplifications, losses, and rearrangements/translocations that can affect protein structure, function, and expression levels.

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Absence of \( \text{ERCC1} \) protein expression may predict benefit of platinum therapy

Analysis of \( \text{ERCC1} \) protein, as assessed by GPS Cancer, is capable of predicting survival among patients treated with cisplatin. Although the difference was statistically nonsignificant, in a cohort of 121 patients treated with cisplatin-based therapy 27 patients with undetectable \( \text{ERCC1} \) protein expression levels (blue line) had higher overall survival (OS) than 94 patients with detectable levels of \( \text{ERCC1} \) protein (pink line).

GPS Cancer’s quantitative proteomic analysis confirmed IHC is not a reliable method to measure expression of \( \text{ERCC1} \) protein.

**Study:** Reevaluation of the TASTE (Tailored Postsurgical Therapy in Early-Stage NSCLC) adjuvant trial; 121 NSCLC patients retrospectively analyzed with mass spectrometry-based proteomics to quantitate \( \text{ERCC1} \) protein.


Low \( \text{TUBB3} \) protein expression may predict benefit from taxane therapy

GPS Cancer allowed precise identification of a subset of patients who benefited from the addition of docetaxel to adjuvant chemotherapy in a retrospective analysis of a 125 gastric cancer patient cohort.

Patients with \( \text{TUBB3} \) expression levels <750 amol/µg (blue line) had nearly twice the median overall survival (OS) compared to patients with expression levels >750 amol/µg (pink line) \( (p=0.04) \). A cutoff for \( \text{TUBB3} \) was prospectively defined based on the proteomic assay’s limit of detection.

**Study:** Reevaluation of ITACA-S (Intergroup Trial of Adjuvant Chemotherapy in Adenocarcinoma of the Stomach) trial; 125 gastric cancer patients retrospectively analyzed with mass spectrometry-based proteomics to quantitate \( \text{TUBB3} \) protein.

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.

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