NCI COMPASS

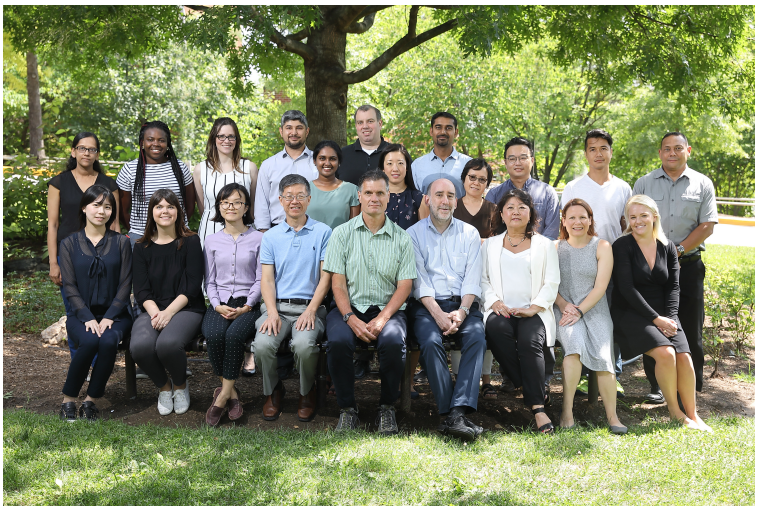
NCI COMPASS

Comprehensive **O**ncologic **M**olecular **P**athology **a**nd **S**equencing **S**ervice

The Laboratory of Pathology (LP), NCI, has implemented the Comprehensive Oncologic Molecular Pathology and Sequencing Service (NCI-COMPASS). The goal of NCI-COMPASS is to provide state of the art clinical sequencing services to CCR PIs. To this end, the NCI-COMPASS program is developing large NGS panels, as well as additional cancer -omics technologies to establish a CLIA-certified and College of American Pathologists (CAP)-accredited program to support precision cancer diagnostics (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5707196/). An example of this effort includes the recently established methylation classifier program for cancer diagnostics, first launched for brain tumors, to be extended to additional tumor types in the future.

Services under the NCI COMPASS program includes:

Clinical Molecular Testing Core	**Clinical Next Gen Sequencing Unit**	**Clinical Cancer Epigenetics Unit**	**Clinical Fluorescence In-Situ Hybridization Unit**	**Clinical Bioinformatics Unit**



Whole Exome Sequencing now available in the NCI-COMPASS, Laboratory of Pathology
September 9, 2021

The NCI Laboratory of Pathology NCI-COMPASS Program recently has developed and validated tumor/normal clinical whole exome sequencing which performs whole exome analysis from tumor DNA and normal control DNA in one integrated workflow. During library preparation, enrichment chemistry is optimized to capture nucleic acid targets from formalin-fixed, paraffin-embedded (FFPE) tissue specimens. With the initial release, the molecular pathology report will include single nucleotide variants (SNVs), indels, tumor mutation burden (TMB), copy number variants, and eventually microsatellite instability (MSI) as well. A molecular pathology report will be completed for each order with the findings to clinical actionability based on AMP/ASCO/CAP/ACMG guidelines. Patient consent is required for this test to be performed.

While this test is primarily designed for somatically acquired alterations in tumors, in the analysis of the normal DNA, we will report any clinically significant germline cancer predisposition variants within ~150 cancer predisposition genes, based on the current American College of Medical Genetics and Genomics (ACMG) guidelines will be reported separately from the somatic genomic findings. The germline variant test consent, pre-genetic test education, and post-genetic test counseling are available through the Clinical Cancer Genetics Program, Genetic Branch, CCR (contact to Kathleen Calzone, PhD, RN, AGN-BC, FAAN, 240-760-6178).

The test orders have been released in CRIS. Please refer CCR clinical SOP # ADGC-5 “Tumor/Normal Whole Exome Sequencing: Consenting, Ordering, and Obtaining Results”.

Please contact Dr. Kenneth Aldape or Dr. Liqiang Xi for any questions regarding clinical issues.

Technical Specifications

Technical Information	**Whole Exome DNA and RNA NGS**

Sample Requirements	Tumor specimen: FFPE block or 20 unstained slides with a minimum of 20% tumor cellularity Matched normal specimen: (blood or saliva)
Tumor Enrichment (when necessary)	Macrodissection to isolate and increase the number of tumor cells to improve variant detection sensitivity
Number of Genes	19,433 genes
Capture Content	45 Mb exonic content (=98% of RefSeq, CCDS, and Ensembl coding regions
Unique On-Target Reads	88%
Mean Target Coverage (DNA exome)	140x for tumor and 59x for normal
Variant Limit of Detection	>95% for SNVs and Indels at =10% VAF
Positive Percentage Agreement (PPA) with TSO500 Clinical Samples Pathogenic and Likely Pathogenic Variants Variant Unknown Significant	 98.8% for SNVs and 88.5% for indels at =10% VAF 94.4% for SNVs and 81.3% for indels at =10% VAF

Laboratory of Pathology Participates in NCI-MATCH
October 30, 2019

The Laboratory of Pathology has been accepted as an NCI-MATCH Designated Laboratory. The NCI-MATCH (EAY131) phase 2 precision medicine clinical trial (NCT02465060) is evaluating the effectiveness of treatment that is directed by genomic profiling in patients with solid tumors, lymphomas or myelomas that have progressed following standard treatments expected to prolong survival, or for rare cancer types for which there is no standard treatment. Hopefully this will provide you and your patients more options or opportunities beyond your clinical studies at the CCR.

The Laboratory of Pathology, ECOG-ACRIN and the NCI-MATCH study team are collaborating to identify eligible patients for NCI-MATCH, based on genomic profiling results from the Laboratory of Pathology. Effective immediately, all our Oncomine Comprehensive Assay results are to be screening for MATCH variants (the eligibility of TSO500 assay is in review process). If a variant(s) is found to be a qualifying tumor gene variant, the variant will be sent to the MATCH study team for further review and you as an NIH clinician will received a referral letter from the Laboratory of Pathology.

To learn more about NCI-MATCH, including clinical trial sites across the country, visit www.ecog-acrin.org/nci-match-eay131 and https://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match. Please contact Dr. Mark Raffeld if there are any questions.

TruSight Oncology ~500 Gene Panel (TSO500) is now available
October 17, 2019

The TSO500 is our next-generation sequencing (NGS) assay that analyzes cancer-relevant genes from both DNA and RNA in one integrated workflow. During library preparation, enrichment chemistry is optimized to capture nucleic acid targets from formalin-fixed, paraffin-embedded (FFPE) tissues. With simultaneous analysis of both DNA and RNA, various types of biomarkers relevant to a given tumor type (single nucleotide variants (SNVs), indels, fusions, splice variants, tumor mutation burden (TMB), and microsatellite instability (MSI)) can be assessed from the same sample in a single assay. The RNA panel uses a probe design that enables capture of both known fusions and novel fusion partners. The TSO500 panel includes 523 genes for DNA mutation detection and 55 genes for fusion and splice variant detection.

The new molecular pathology report is also incorporated with reporting software for clinical actionability as Tier levels of FDA-approved drug and clinical trials, and pathogenicity based on AMP/ASCO/CAP/ACMG guidelines.

Please refer to the CRIS ordering instructions and full gene list of TSO500 attached. There will be no need to order the Oncomine assay in the future if the TSO500 panel is requested. Although the Oncomine Assay is still available in the CRIS menu temporarily, the TSO500 will replace the Oncomine Assay for all tumor types given that it has added features including TMB score, and MSI for most applications. In the near future, copy number variation (CNV) will also be available.

Please contact Dr. Liqiang Xi if there are any questions regarding this assay.

Methylation Classifier in use as a Clinical Diagnostic Tool
May 24, 2019

The NCI Laboratory of Pathology has recently begun to use a new clinically-reportable diagnostic tool that uses genome-wide DNA methylation profiling as a diagnostic for tumors of the central nervous system. The validated tool is based, in part, on data published in a recent *Nature* study that showed tumor methylation profiles can provide definitive evidence to complement and refine morphology-based diagnostics in tumors of the brain and spinal cord. In the study, methylation data resulted in a change in diagnosis for 129 cases (12%) of the cohort.

The NCI Laboratory of Pathology is poised to become a diagnostic reference center to implement this tool for diagnostically challenging neuropathology cases. Going forward, it is likely that new methylation-based classifiers will emerge for additional tumor types and we are poised to lead in this area. Areas of future growth include the implementation of clinical whole-exome sequencing, RNAseq gene expression diagnostics, and a dynamic liquid biopsy program.

For more information about this assay please contact Dr. Zied Abdullaev for questions about ordering Methylation profiling test.

Resources:

NCI COMPASS Organization Chart