Develop and Implement Clinical-Grade Genomic Assays in Clinical Trials

The Clinical Molecular Genetics Laboratory at University of North Carolina offers a range of laboratory assays and services supporting clinical trials (prospective or retrospective).

DNA and RNA or microRNA-based tests are developed to:
1. Understand tumor biology,
2. Answer questions of medical importance (e.g. to diagnose, classify, assign prognosis, predict response to specific intervention, confirm, screen, prevent).

Services Include:
1. Prepare a tissue section or a cytology slide; obtain pathologist's estimate of the percent lesional cells (e.g. malignant/stromal/necrosis). Enrich by dissection, if indicated.
2. Design and apply a molecular test, such as Deep Sequencing, RNAseq, SNP chip, or 384-well Q-rtPCR panel.
3. Devise quality assurance measures (e.g. specimen collection and handling, pathologist vets input tissue, acceptance limits on spiked/endogenous/exogenous controls).
4. Prepare spreadsheet of pertinent results for statistical analysis and clinicopathologic correlation. Determine analytic and clinical performance characteristics of the new test system compared to the standard way of addressing the clinical situation.
5. Establish indications for testing, and define intended use of test in patient management.
6. Ready the test system for transition to routine patient care, once it is vetted as being analytically sound and clinically useful by a CLIA-certified testing laboratory.

Specimen Requirements: Formalin-fixed paraffin-embedded tissue, fresh tissue (about the size of a baby green pea) stabilized upon collection (e.g. freeze at -80^{0}C, or immerse in RNALater), blood, marrow, fine needle aspirate, or DNA/RNA from pathologist-vetted specimens.

Protocols and costs: The investigator consults with Clinical Lab personnel to establish a protocol, including pre- and post-analytic phases, as well as a *standard operating procedure* including quality assurance parameters that are suited to the specimen type and to intended use of results. Charges are per specimen, with a prorated charge for specimens not tested by virtue of exceeding pre-defined quality limits.

Technologies and instrument platforms that simultaneously measure multiple human and/or pathogen DNAs, RNAs, or microRNAs:
1. DNA sequencing (MiSeq, NextSeq 500, Ion Torrent PGM or Proton, Sanger, or pyrosequence).
2. RNA & microRNA profiles (Agilent, Affymetrix, NanostringDx, Exiqon, Illumina or Roche systems)
3. Gene copy number variation (Agilent, Affymetrix 6.0 or CytoScan SNP chip, Nanostring, or Roche LC480 platforms).

CLIA-certified, clinical-grade testing: Many assays can be provided in an analytically valid form, thus permitting consented patients to be managed based on test results (e.g. qualify for enrollment, assign study arm, select dose). Before use in routine patient care, assays must be vetted as having adequate analytic and clinical performance by a CLIA-certified, CAP-accredited clinical laboratory or by an equivalent clinical facility.

References: Tang W, Hu Z, Muallem H, Gulley ML: Quality Assurance of RNA Expression Profiling in Clinical Laboratories. J Molec Diagnostics, 14(1): 1-11, 2012

Jennings L, VanDeerlin VM, Gulley ML: Recommended Principles and Practices for Validating Clinical Molecular Pathology Tests. Arch Pathol Lab Med, 133: 743-755, 2009

Aziz N, et al. College of American Pathologists' laboratory standards for next-generation sequencing clinical tests. Arch Pathol Lab Med, 139:481-93, 2015. PMID: 25152313

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A list of clinical grade assays is found at:
http://www.uncmedicalcenter.org/uncmc/professional-education-services/mclendon-clinical-laboratories/directory/molecular-pathology-and-genetics