

THE BIOLOGICAL SAMPLES PLATFORM AT THE BROAD – A COMMERCIAL-SCALE BIOREPOSITORY IN AN ACADEMIC SETTING



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INTRODUCTION

The Broad Institute is a research collaboration involving faculty, professional staff and students from MIT, and the Harvard academic and medical communities. The Institute is organized around Scientific Programs and Scientific Platforms. The Broad's Scientific Platforms are teams of professional scientists with the expertise and organization to carry out major, large scale, projects that could not be done within a single research laboratory. There are currently 8 Platforms at the Broad: the Biological Samples Platform, the Genetic Analysis Platform, the Genome Sequencing Platform, the Proteomics Platform, the RNAi Platform, the Imaging Platform, the Chemical Biology Platform, and the Novel Therapeutics Platform.

The Biological Samples Platform (BSP) is the Broad's sample management platform, with expertise in technologies for sample storage and processing, procedures for collection and use of human samples in biomedical research, histological analyses of normal and abnormal human tissues, and the development of Laboratory Informatics Management Systems for detailed sample tracking. The need for the platform was recognized in 2005 and the platform was initiated and first staffed in early 2006. One of the driving needs in creating the platform was to support the increasingly large numbers of, primarily human, samples (frequently tens of thousands of samples in any given study) routinely used in research undertaken in collaboration with the Broad's Genetic Analysis and Genome Sequencing Platforms. The platform's mission is to establish a sample repository to centralize sample admission, processing, QC, storage and identification, and ultimately to support all sample projects within the Broad, and Broad-affiliated communities.

In the short span of time since the platform was initiated, it has grown rapidly and currently manages over 182,000 stock samples from 152,400 separate participants. That number is expected to double over the next two years. Sample types now include DNA, RNA, fresh blood, serum and plasma samples, cell cultures, fresh frozen and FFPE tissue specimens, along with viral and yeast isolates and plasmodium specimens. The platform has also begun to support and process cell lines from chemical screening from the Therapeutics Platform, and peptide storage for the Proteomics Platform. The platform follows all 'best practices' and guidelines for sample management. It was developed at the outset with extensive use of barcoding and automation and the ability to integrate with other platforms across the Broad.

SAMPLE MANAGEMENT AND WORKFLOW

Example Sample Workflows

RTS Automated Storage and Retrieval of DNA at -20°C



DNA/RNA Receipt & Storage: 2D barcodes with readable labels



Initially (and ongoing) the vast majority of samples entering the platform were DNA samples.

Example Ongoing Studies:

- CARE - ~50,000 DNA samples from multi sites for genetic analysis
- TSP and TCGA



• GENEVA
GENE ENVIRONMENT ASSOCIATION STUDIES



- Storage of ~300K samples
- Pick/Load 96 samples in 15 mins
- Prioritize multiple picking orders
- Cherry picking via random order or fixed order (key for BSP, given the large number of plating requests)
- Directly interfaced with BSP LIMS to download and receive sample pick lists

PATHOLOGY

Pathology involvement begins with input on prospective collections.

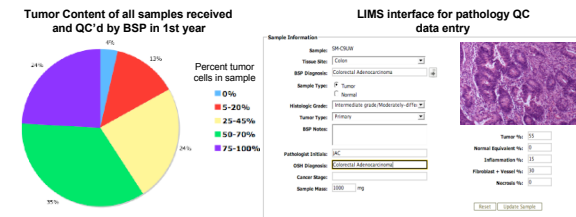
- How much tissue feasible/necessary, which part of organ, appropriate control
- Method of tissue collection and preservation most appropriate for particular scientific question or clinical setting
- Interface with outside tissue sources/collaborators

Quality control of collected tissue by a trained pathologist:

- Verification of Disease State: errors occur during initial sample collection at outside institution (e.g. sample labeling, spreadsheet, diagnostic, tissue allocation errors); up to 4% error in samples submitted to BSP
- Assessment of Purity: diseased tissue content is variable; adequacy of a specimen for downstream analysis is dependent on % tumor vs. stroma
- Assessment of Preservation: samples may be suboptimal depending on amount of tumor necrosis, cautery, or other factors.
- Pathology data into LIMS using standardized vocabulary and QC metrics

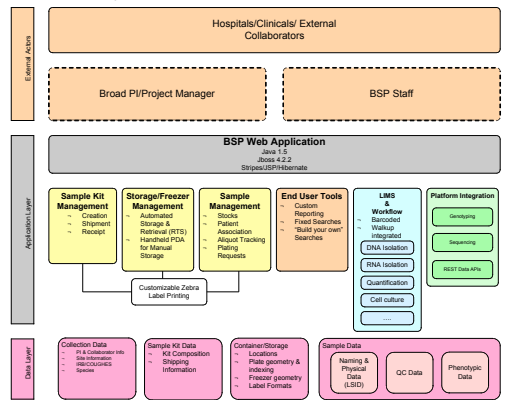
Pathologist involvement in sample processing:

- Macrodissection or microdissection of tissues prior to isolation of DNA/RNA/protein to increase % tumor.



INFORMATICS

Informatics to support the platform have been developed in-house and provide web based interfaces to manage all the needs of the lab staff and researchers within the Broad. The decision to build an in-house system was driven by the lack of commercial products with a good fit, as well as integration requirements with the other platforms at the Broad.



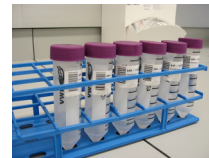
Sample Aliquot Plating



Management of New Sample Collections

- Many samples handled by the platform are DNA samples
- Have seen increasing demand for initiation, management and oversight of fresh sample collections including:
 - Whole Blood for DNA
 - Serum/Plasma
 - RNA PAX
 - Lymphocytes
 - Urine
 - Tissue – Fresh Frozen and FFPE

Automated DNA Isolation



- ~10,000 samples per year (frozen cells &/or buffy coats)
- ~ 60 fresh bloods per week

Renal Donor/Recipient Blood Collection Kit



Example Participant Collections Ongoing:

- MS collection - local hospitals
- Autism Consortium - local hospitals
- Lupus - Rhode Island
- Chronic Kidney Disease - clinical trial
- Renal - donor/recipient pair collection
- Harvard Partners: Discard blood collections for multiple Broad studies
- Malaria – international
- Bipolar Disorder

GATES funded proteomic study HIV, TB, Malaria – Africa/Philippines

