Enabling discovery of novel DNA markers of response to targeted cancer therapeutics

Our service identifies DNA break signatures across the genome. Uses include:

- Characterizing DNA breaks caused by different cancer drugs
- Revealing a drug’s genomic mechanism-of-action
- Discovering a new class of biomarkers to deliver precision medicine

MISSION

Identifying biomarkers that predict response to therapy is critical for precision medicine in the fight against cancer. BreakSight, Inc harnesses new technologies to enable discovery of novel DNA sequence biomarkers based upon DNA break signatures caused by targeted cancer therapeutics and the unique biology of cancer cells.
TARGETED CANCER DRUGS

Many targeted cancer drugs function by inhibiting specific DNA Damage Response (DDR) pathways, or by altering DNA directly. This increases the level of DNA damage and chromosomal breaks in cancer cells that are already defined by genomic instability.

These DNA breaks can occur randomly across the genome or at specific vulnerable sites. By selectively capturing DNA breaks along the cell’s chromosomes, we can discover associated genomic sequences that might serve as biomarkers of response to targeted treatments, such as DDR drugs.

BRITL - BREAKSIGHT’S ASSAY TO CAPTURE DNA DOUBLE-STRANDED BREAKS
Performance of next-generation sequencing on the retrieved DNA break fragments reveals the chromosomal locations and sequences associated with breakage, detected by sequence read build-ups at specific sites across the genome. 

**Chr8: 33,140,000 – 33,200,000 bases**

>50% of breaks in MDA-MB-231 cells treated with a pre-clinical targeted cancer drug, ATRi, occur at unique AT-rich repetitive sequences that form hairpin structures

“Genome-wide identification of structure-forming repeats as principal sites of fork collapse upon ATR inhibition” (Molecular Cell, 2018)

**SITES OF BREAKAGE AS BIOMARKERS OF DRUG EFFICACY**

DDR drugs such as ATRi can therefore be synergistically toxic not only with abnormally expressed proteins in cancer, but also with DNA sequences, particularly in repeat-rich regions that are less well researched.

Pathogenic changes to these sequences in the cancer’s genome may predict sensitivity to targeted treatments.
**PRODUCTS**

**DDsite:**

Performance of our BrITL assay to tag and retrieve DNA double-strand break sites across the genome from cells that acquire DNA damage during proliferation.

Performance of next-generation sequencing (NGS) on captured DNA break fragments from BrITL-processed samples (retrievals and inputs), by an NGS provider (BrITL-Seq).

**DDinsight:**

Analysis of NGS data to identify significant, reproducible peaks of DNA breakage across the genome.

Includes –

- Trimming
- Alignment
- Deduplication
- Quality checks
- Coverage plot generation
- Peak-calling
- Irreproducibility Rate (IDR)
- Identification of differential peaks between conditions

*From cell pellet to sequence data analysis*