BioReliance Genomics

MP-Seq™ Services

"Next Generation" Sequencing Technologies Tailored for Biosafety Testing

BioReliance Genomics offers MP-Seq™ (massively parallel sequencing) services based on the Roche 454 Genome Sequencer FLX™ (GS-FLX) platform. The 454 GS FLX system allows for enormous amounts of genetic data to be generated rapidly from a single sample – as much as 500 million base pairs in one run. This is achieved through coupling the technique of emulsion PCR on microbeads with pyrosequencing at the single-bead level. (For more information, please visit www.454.com.) This, when combined with BioReliance's proprietary algorithms for data assembly and mining, provides clients with an unprecedented ability to interrogate multiple sample types for the purposes of determining nucleic acids sequence.

MP-Seq™ Services Offered by BioReliance

BioReliance has developed a suite of MP-Seq™ services to provide the next level of surveillance for biosafety testing, cell and virus characterization and clinical trial testing:

Transcriptome MP-Seq™

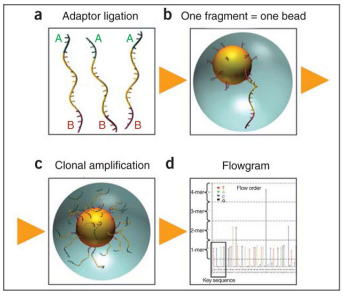
- Provides a complete analysis mRNA transcripts within a cell population – a "snapshot" of transcription – for determining the metabolic state of a cell
- Can be used to find latent virus(es) present in a cell population

Amplicon MP-Seq™

- Proprietary amplification and sequencing of nucleic acids present in the culture fluid of cells (e.g. from a bioreactor).
- Useful for detecting known or unknown adventitious viruses in raw materials used for biomanufacturing
- Can also be used to identify unknown adventitious viruses present in a biological sample (does not require virus sequence to be known prior to analysis)

Genome MP-Seq™

- Whole genome sequencing of cells used as biomanufacturing substrates
- Whole genome sequencing of virus seed stocks as well as virus made during the vaccine manufacturing process
- Useful for detecting known or unknown latent virus sequences
- Can also be used to determine SNP genotypes of cells



*(**a**–**d**) Genome Sequencer process–specific A and B adaptors are appended to each DNA fragment (**a**) to allow binding to DNA capture beads (**b**). The beads are placed into a water-in-oil emulsion that contains hundreds of thousands of PCR microreactors. Each microreactor contains all reagents necessary for PCR. The entire collection of millions of fragments and beads is amplified in parallel (**c**), with each fragment amplified without the introduction of competing or contaminating sequences. When sequenced on the Genome Sequencer FLX, each clonally amplified fragment generates its own unique sequence read, represented by a flowgram (**d**), with over 400,000 reads generated per instrument run. (Image courtesy of Roche.)*

MP-Seq™ (**m**assively **p**arallel **seq**uencing) services can be used for a broad range of applications, including genetic characterization of cell substrates and raw materials used in biomanufacturing.

MP-Seq™ is able to detect and characterize both known and unknown viruses in a sample, thus going beyond primer based amplification technologies.

BioReliance Genomics offers multiple platforms for testing, including microarrays, quantitative PCR (QPCR) and Illumina's BeadXpress™.

BioReliance® by SAFC

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MP-Seq™ Services (continued)

CASE STUDY

Model:
Client A is producing a vaccine in a common cell line. Regulatory authorities asked Client A to provide more data regarding the potential for the cell line to harbor adventitious agents.

Solution:
Client A engaged BioReliance to conduct a Transcriptome MP-Seq™ study of their cell line. Statistics from the study are as follows:

- 195 million total base pairs of data were generated from 746,844 reads
- 5,139 of the reads BLAST to the BioReliance's Reliant Algorithm™, of these
  - 691 were HERVs (Human Endogenous Retroviruses)
  - 2326 were false hits to BVDV (ubiquitin or related)
  - The remainder were repeats and virokines/viroreceptors
- The following genes were monitored as controls for sequence bias:
  - B2M, GAPD, CGI-119, L37a, CALM2, S11, S13, OAZ1
- The following genes were monitored as controls for sensitivity:
  - TUBB ~400 copies/cell
  - CTBP1 ~300 copies/cell
  - GOLGA1 ~100 copies/ cell
- All controls showed that proper sensitivities and breadth of sequence coverage were maintained.

Custom MP-Seq™ Services

BioReliance has been using the GS FLX system for several years and has significant experience with the design and execution of experiments using this platform. To date, we have performed custom studies for numerous pharmaceutical and biotech clients to help fully characterize their raw materials (e.g. cell banks and virus seeds) and their biomanufacturing systems. We have also applied this technology in our own research and development efforts[1]. Our scientists are available for consultation to design and execute the optimal study for data quality as well as for regulatory consultation.

Regulatory Compliant MP-Seq™ Services

Drawing on its 60+ years of experience in providing regulatory compliant testing services, BioReliance has developed the systems and processes necessary to offer MP-Seq™ nucleic acid sequencing services to GMP standards. To do so, we have optimized laboratory workflows and SOPs to ensure that the highest level of quality is maintained. BioReliance also offers MP-Seq™ services for research (non-GMP) purposes.

Please email us at genomicservices@bioreliance.com or call us to discuss your genomics project.

BLAST of read ID with MAX Score vs. nt/nr DB

Unique Accession	Replicates	Max SCORE	GoTo Specific Report Tab	CONCLUSION	Annotation of Read ID with Max Score vs. nt/nr DB
AC091824.3	73	#NAME?	Click here...	Hs	Homo sapiens chromosome 5 clone CTC-455O22, complete sequence
AC013410.5	1	#NAME?	Click here...	Hs	Homo sapiens BAC clone RP11-495I2 from 2, complete sequence
AC006070.1	1	#NAME?	Click here...	Hs	Homo sapiens chromosome 17, clone hRPK.206_C_20, complete sequence
AC097063.2	2	#NAME?	Click here...	Hs	Homo sapiens chromosome 1 clone RP11-430H12, complete sequence
NG_011803.1	2	#NAME?	Click here...	REPEAT	Homo sapiens desmoglein 1 (DSG1) on chromosome 18
AC216174.2	4	#NAME?	Click here...	REPEAT	Homo sapiens FOSMID clone ABC13-961322I20 from chromosome x, complete sequence
AC079623.15	1	#NAME?	Click here...	Hs	Homo sapiens 3 BAC RP11-201D16 (Roswell Park Cancer Institute Human BAC Library) complete seq
AC087632.10	1	#NAME?	Click here...	Hs	Homo sapiens chromosome 15, clone RP11-236P11, complete sequence
AC209277.3	3	#NAME?	Click here...	Hs	Homo sapiens FOSMID clone ABC9-43861300L1 from chromosome 1, complete sequence
AC093217.4	8	#NAME?	Click here...	REPEAT	Homo sapiens chromosome 5 clone CTD-2120M21, complete sequence
AC021549.9	1	#NAME?	Click here...	Hs	Homo sapiens chromosome 18, clone RP11-650P15, complete sequence
AP005327.2	1	#NAME?	Click here...	REPEAT	Homo sapiens genomic DNA, chromosome 18 clone:RP11-231N16, complete sequence
AC079855.8	1	#NAME?	Click here...	Hs	Homo sapiens BAC clone RP11-332L16 from 7, complete sequence
AC020647.9	7	#NAME?	Click here...	Hs	Homo sapiens 12 BAC RP11-922O23 (Roswell Park Cancer Institute Human BAC Library) complete se
AC008868.4	1	#NAME?	Click here...	REPEAT	Homo sapiens chromosome 5 clone CTD-2194F4, complete sequence
AC087590.2	1	#NAME?	Click here...	Hs	Homo sapiens chromosome 3 clone RP11-321I9 map 3p, complete sequence
AC235953.3	139	#NAME?	Click here...	Hs	Homo sapiens BAC clone RP11-520A20 from chromosome x, complete sequence
AL357522.10	277	#NAME?	Click here...	REPEAT	Human DNA sequence from clone RP11-685G11 on chromosome 6 Contains two CpG islands, comple
AC016582.9	1	#NAME?	Click here...	REPEAT	Homo sapiens chromosome 19 clone CTD-2554C21, complete sequence
AC007859.11	8	#NAME?	Click here...	Hs	Homo sapiens, clone RP11-41A1, complete sequence
AC087590.2	22	#NAME?	Click here...	Hs	Homo sapiens chromosome 3 clone RP11-321I9 map 3p, complete sequence
AC138305.2	1	#NAME?	Click here...	Hs	Homo sapiens chromosome 16 clone RP11-2K8, complete sequence
AC084264.7	50	#NAME?	Click here...	REPEAT	Homo sapiens chromosome 2, clone CTB-2122H5, complete sequence
AL139232.13	43	#NAME?	Click here...	Hs	Human DNA sequence from clone RP1-237I15 on chromosome 6 Contains a novel gene, the 5' end of t
AL365367.10	54	#NAME?	Click here...	Hs	Human DNA sequence from clone RP4-736C13 on chromosome 1p32.2-32.3 Contains part of a variant
AC093915.2	149	#NAME?	Click here...	Hs	Homo sapiens BAC clone RP11-785G17 from 2, complete sequence
AC130414.3	1	#NAME?	Click here...	REPEAT	Homo sapiens 12 BAC RP11-15P10 (Roswell Park Cancer Institute Human BAC Library) complete seq
AL445590.4	43	#NAME?	Click here...	Hs	Human DNA sequence from clone RP11-50D16 on chromosome 13 Contains the gene for a novel prote
AC097063.2	97	#NAME?	Click here...	REPEAT	Homo sapiens chromosome 1 clone RP11-430H12, complete sequence

An example of the type of data found in the final report from an MP-Seq™ project.

Ordering Information

Assay Number	Assay Description	Regulatory Compliance	Sample Requirements
Custom	Transcriptome MP-Seq™	GMP	Inquire
Custom	Amplicon MP-Seq™	GMP	Inquire
Custom	Genome MP-Seq™	GMP	Inquire

[1] Onions D, Kolman J, Massively parallel sequencing, a new method for detecting adventitious agents. Biologicals (2010), doi:10.1016/j.biologicals.2010.01.003.

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