Docket #: S15-164

STR-Seq: a technology for massively parallel STR sequencing and genotyping

Researchers in Dr. Hanlee Ji's lab have developed a targeted sequencing method known as short tandem repeat (STR) sequencing (STR-Seq) which improves target selection specificity to generate only the STR spanning reads. STRs are a type of genetic variation which has the fastest mutation rate. As a result, it is one of the most informative parts of the genome and has wide applicability to a variety of fields. However, the analysis of STRs with next generation sequencing methods is limited. There are several major issues with the existing methods including: i) only the reads which encompass an entire STR locus are informative and ii) PCR amplification during library preparation can introduce artifactual “stutter” mutations that confound accurate genotyping. To overcome these limitations, the inventors developed the STR-Seq targeted sequencing technology. This technology includes several features designed to maximize accuracy and throughput including:

- Flow cell engineered to maximize efficiency and specificity of target selection
- Targeted fragmentation process to improve target selection and coverage
- Amplification-free method of library preparation to eliminate stutter noise
- Ability to quantitate STR repeat motifs and associated variants in phase with the STR

This method can generate reads which encompass the entire STR locus for thousands of STRs, thereby allowing highly multiplexed STR genotyping with next generation sequencing.

Stage of research

To validate the technology the inventors compared it with traditional capillary electrophoresis and found the STR-Seq method provided significantly improved accuracy for heterozygous samples. In addition, with this method the inventors were

able to simultaneously assay 2,500 STR loci.

Related technology
This method leverages another technology developed by researchers in Dr. Hanlee Ji's lab: Stanford Docket S10-233, an automated method to capture and directly sequence target DNA with next-generation sequencing.

Applications

- Next generation sequencing of entire short target sequences for:
  - Research
  - Forensic analysis

Advantages

- Allows multiplexed STR genotyping with next generation sequencing
- Informative allelotyping- can precisely determine STR allelotypes and also allelotypes having mutations
- Precise repeat counting
- Scalable
- Eliminates traditional sequence alignment

Publications

- GiWon Shin, Susan M. Grimes, Hojoon Lee, Billy T. Lau, Li Charlie Xia, Hanlee P. Ji, "CRISPR-Cas9-targeted fragmentation and selective sequencing enables massively parallel microsatellite analysis;" Nature Communications 8, Feb. 7, 2017; doi:10.1038/ncomms14291.
- US Patent Application No. 15/177,115 published on December 15, 2016.

Patents

- Published Application: 20160362751
- Issued: 10,465,241 (USA)

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