Shallow Whole Genome Sequencing Workflow - sWGS

Scientific Relevance

- Tumor-sequencing studies have demonstrated that most cancers are driven by either single-nucleotide variants (SNV) or structural variants (SV)[1]
- Shallow Whole Genome Sequencing (sWGS), also known as Low Coverage (LC) WGS, allows researchers to determine SV with 0.1 to 0.2X low sequencing coverage
- Low cost sWGS is emerging as a promising clinical sequencing strategy for SV-driven tumors[1]
- sWGS can be used for clinically relevant structural variants such as oncogenic amplification, tumor-suppressor deletion, and genomic instability[2]
- sWGS can be applied to DNA originating from Formalin-Fixed Paraffin-Embedded tissue (FFPE)[3], blood, or cfDNA[4]

Challenges

- Protocol requires library construction from DNA of different qualities and origins[5]
- Uniform coverage of the genome is challenging to obtain due to bias in sequencing technology[5]

Workflow

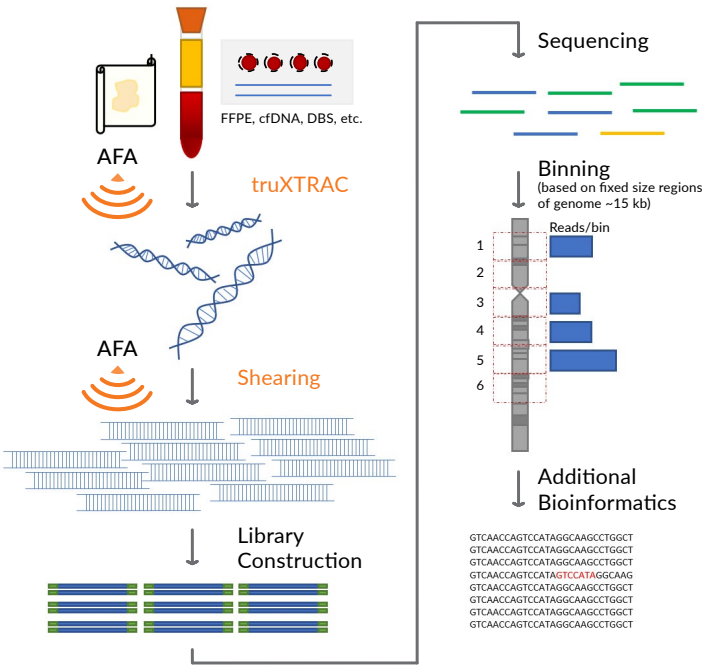

Fig 1: sWGS workflow enabled by AFA energetics from extraction to data analysis. AFA-Energetics are used for extraction of multiple sample types such as FFPE, cfDNA, and DBS. Post-extraction, samples are sheared with a Focused-ultrasonicator before library construction. After sequencing, reads are binned to genomic regions then additional bioinformatics is performed.

Advantages of Adaptive Focused Acoustics® (AFA®)

AFA technology is the gold standard for mechanical DNA shearing.

- Highly reproducible results
- Unbiased fragmentation regardless of GC content
- Compatible with all DNA inputs, quality, and origin, including FFPE samples
- Automation friendly options (LE220R-plus paired with oneTUBE-10™ consumables)

Suggested Covaris Products

- Covaris Focused-ultrasonicator (M-Series, S-Series, E-Series, or LE-Series)
- 96 oneTUBE-10 AFA Plate (PN 520249)
- 8 oneTUBE-10 Strip AFA Strip (PN 520225)
- truXTRAC FFPE
- truXTRAC cfDNA (PN 520221)

Citations

1. Macintyre G, Ylstra B, Brenton JD. Sequencing Structural Variants in Cancer for Precision Therapeutics. Trends Genet. 2016;32(9):530-542.
2. Deleye L, Dheedene A, De coninck D, et al. Shallow whole genome sequencing is well suited for the detection of chromosomal aberrations in human blastocysts. Fertil Steril. 2015;104(5):1276-85.e1.
3. Kader T, Goode DL, Wong SQ, et al. Copy number analysis by low coverage whole genome sequencing using ultra low-input DNA from formalin-fixed paraffin embedded tumor tissue. Genome Med. 2016;8(1):121.
4. Van roy N, Van der linden M, Menten B, et al. Shallow Whole Genome Sequencing on Circulating Cell-Free DNA Allows Reliable Noninvasive Copy-Number Profiling in Neuroblastoma Patients. Clin Cancer Res. 2017;23(20):6305-6314.
5. Scheinin I, Sie D, Bengtsson H, et al. DNA copy number analysis of fresh and formalin-fixed specimens by shallow whole-genome sequencing with identification and exclusion of problematic regions in the genome assembly. Genome Res. 2014;24(12):2022-32.

USA: Covaris, Inc. | Tel: +1 781.932.3959 | Fax: +1 781.932.8705 | Email: customerservice@covaris.com
Europe: Covaris Ltd. | Tel: +44 (0)845 872 0100 | Fax: +44 (0)845 384 9160 | Email: emeacustomerservice@covaris.com
Web: www.covaris.com | Applications: applicationsupport@covaris.com | Service and Support: techsupport@covaris.com
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