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upSPLAT a method for cost-effective, large-scale pooled sequencing library preparation applicable to diverse sample types

Background

While the cost for short-read sequencing continues to decrease, the cost of library preparation before sequencing remains constant. For smaller genomes we are already at the point where the cost for library preparation exceeds the sequencing cost. Consequently, for research projects comprising large numbers of samples, library preparation becomes very expensive.

Aim

At the Genomics Platform we see a major need for improved cost-efficient, scalable library preparation. To this end we are developing ultra-pooled SPLAT (**upSPLAT**) a flexible, low-cost library preparation workflow for pooled sequencing of large numbers of barcoded samples. The method is an adaptation of the *in house* developed ‘Splinted Ligation Adapter Tagging’ library prep technique.

upSPLAT method:

- ✓ Barcoding & Pooling
- ✓ In house developed library prep (SPLAT)
- ✓ Miniaturization
- ✓ Automation

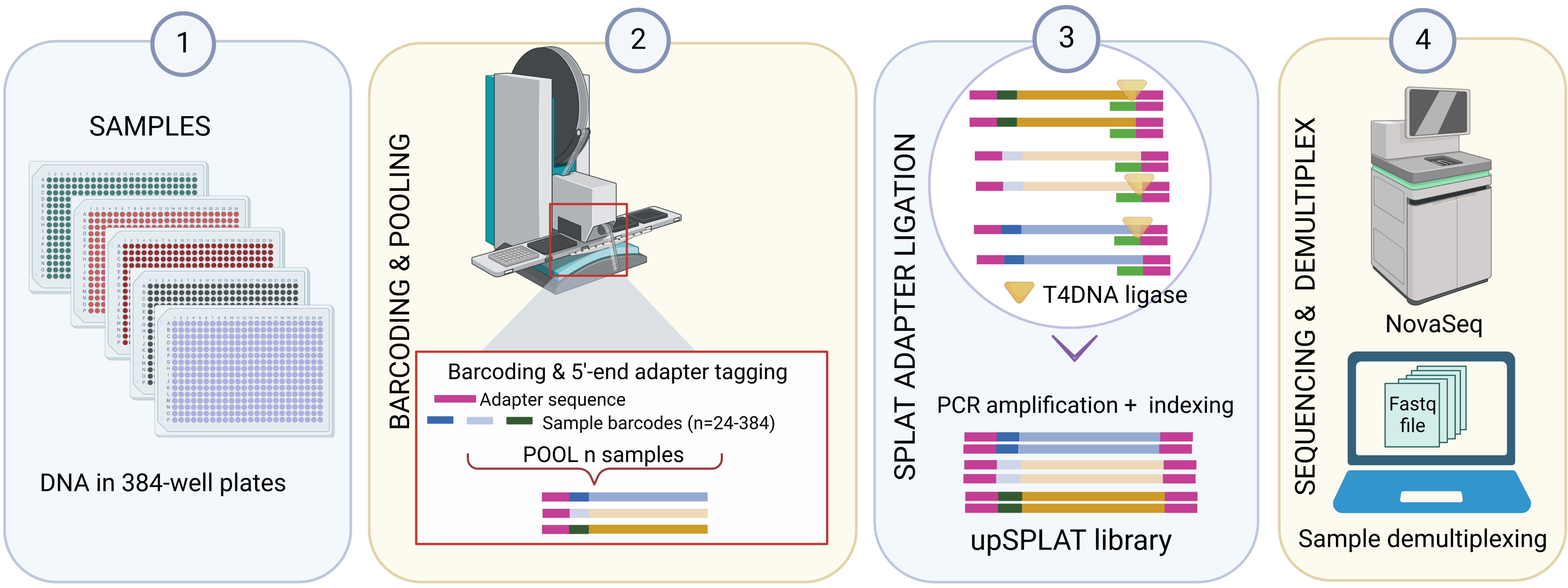

Figure 1 *Graphical outline of the upSPLAT workflow. 1) DNA in 384-well plates is subjected to enzymatic fragmentation. 2.) A sample barcode and a P5 adapter sequence is introduced for every sample. 3) Samples are pooled and (P7) adapter ligation and PCR is carried out in a bulk reaction. 4) Sample de-multiplexing is performed prior to delivering data to the platform user.*

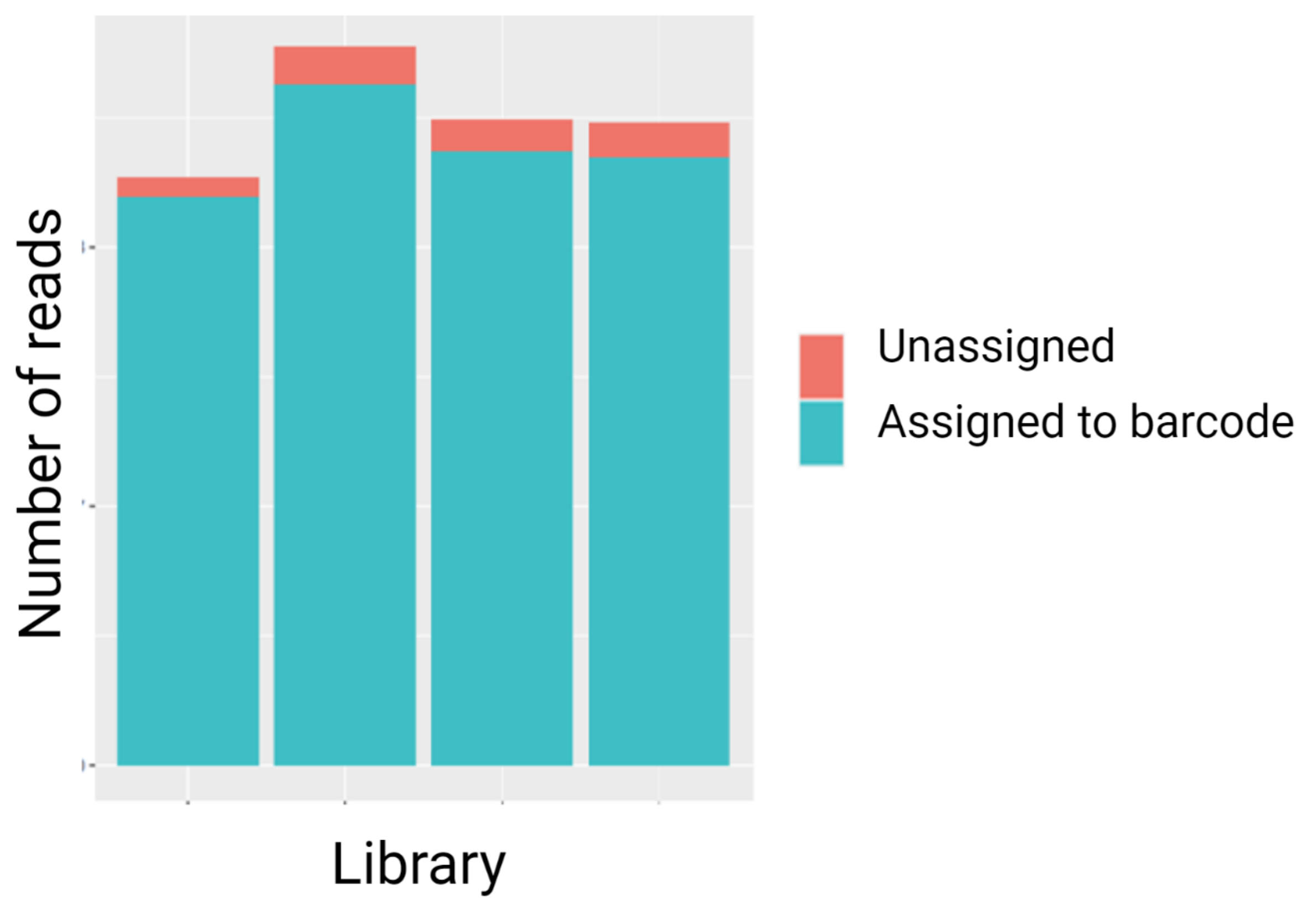

Figure 2*. Number of barcode-assigned reads in upSPLAT test-libraries (24-plex)*

Application areas

Cost effective scalable library prep is useful for a variety of applications, for example:

- Whole genome sequencing (WGS) of small genomes
- Low input WGS and methylome sequencing
- Low pass sequencing
- Metagenomics
- Single-cell sequencing

References:

1. Raine et al, *SPLAT method paper*, Nucleic Acids Research 2017
2. Raine et al, *scSPLAT a scalable plate-based method for single cell WGBS library prep*, Scientific Reports 2022
3. Raine and Nordlund, US patents US11198865B2 & US20220127598A1

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