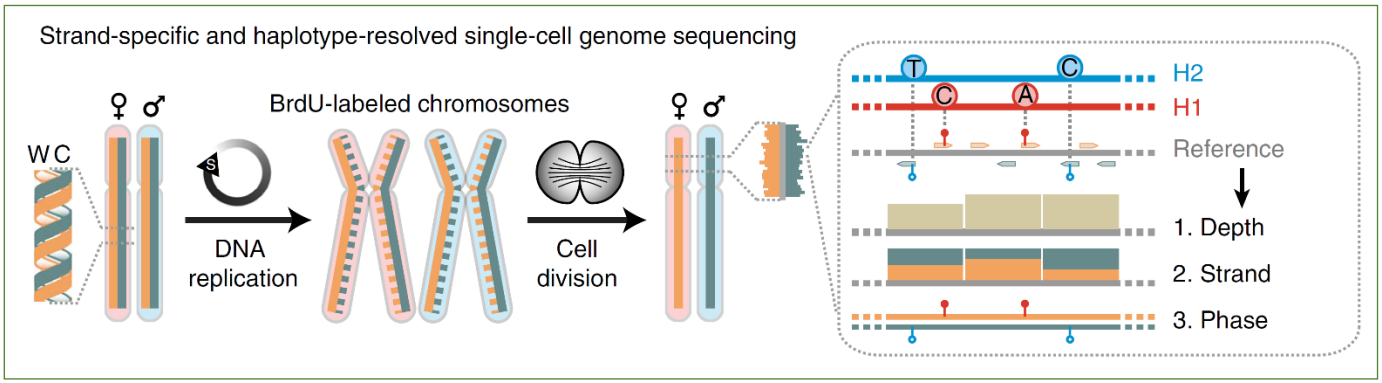
Single Cell Tri-Channel Processing (scTRIP)

Challenge

- Structural variation (SV), such as deletions, duplications, inversions or translocations in the DNA, is a major source of genetic variation and plays a role in numerous diseases.
- The discovery of SVs can help to better understand disease, enable precision medicine approaches, and allow for quality control in gene and cell therapy approaches.
- However, studying SVs is limited by high costs for sequencing coverage, challenges to discover SVs in repetitive regions and lacking approaches for single cell SV tracking.

Technology

Strand-specific single cell sequencing data are analyzed by a computational, bayesian framework to integrate three layers of information (depth of coverage, read orientation and haplotype phase) for calling SVs and to derive a specific 'diagnostic footprint'.



Haplotype-aware discovery of SVs in single cells by scTRIP: Overview of the Strand-seq protocol used to preserve strand orientation and homolog (haplotype) identity (for details see Sanders et al., 2019). Right: Haplotagging approach assigning individual Strand-seq reads to either haplotype (H)1 or H2. Red lollipops mark reads assigned to H1 based on overlapping SNPs; blue lollipops mark H2 reads. From this, three data layers are considered: (1) the total number of reads in a binned region are measured to calculate the 'depth' layer; (2) the relative proportion of W and C reads are measured to calculate the 'strand' layer; and (3) the number of W and C reads assigned to H1 or H2 are used to calculate the 'phase' layer.

Internal EMBLEM Reference

2018-007

Key Inventors

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Single Cell Tri-Channel Processing (scTRIP)

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Advantages

- Systematic, detailed and accurate
- Includes all known forms of karyotypic abnormalities
- Strand-specific single cell sequencing
- Integration of multiple information layers
- Less required sequencing depth than other methods
- More reliable than current standard
- cost-effective

Applications

- Disease classification for precision medicine
- Patient stratification for clinical studies
- Assessment of genome integrity in cell and gene therapy applications
- Therapeutic CRISPR-Cas9 editing
- Rare disease genetics.

Intellectual Property

A patent application has been filed.

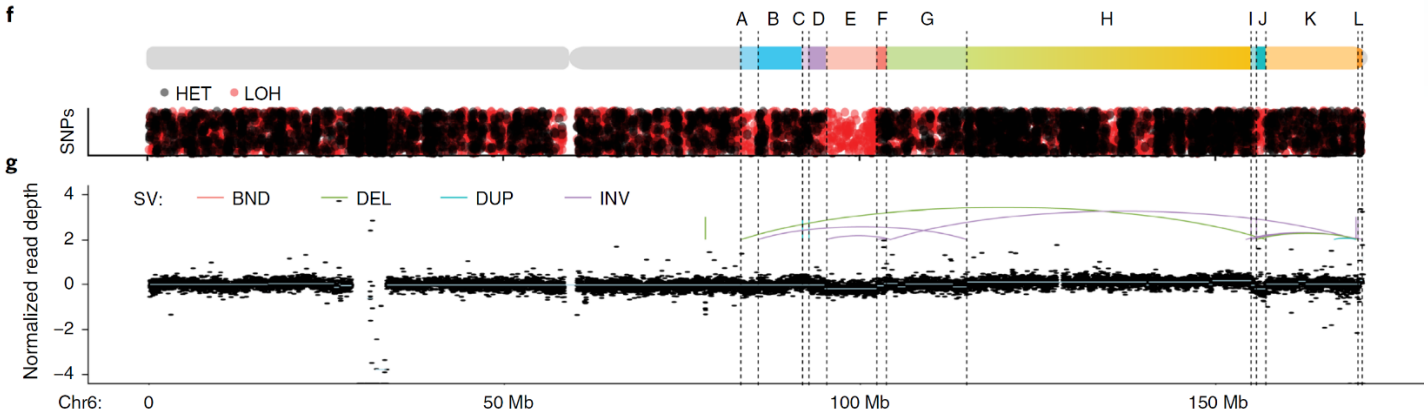
Commercial Opportunity

The technology is ready to use.
We offer a technology evaluation program as well as a licensing or collaboration/co-development opportunity.

Further Reading

EMBL News

Sanders et al., 2019



Application example: Locating previously unrecognized SVs in a T-cell acute lymphoblastic leukemia (T-ALL) relapse sample (for details see Sanders et al., 2019).

f, Detection of interspersed losses and retention of LOH in conjunction with the clustered SVs, indicative for a DNA rearrangement burst[43]. Regions with normal density of reference heterozygous SNPs (red), but with decreased density of heterozygous SNPs detected in P33 (black), are indicative for LOH (see Methods).
g, Verification of subclonal clustered rearrangement burst at 6q. Breakpoints inferred by scTRIP are shown as dotted lines and scTRIP-inferred segments are denoted using the letters A to L. Colored breakpoint-connecting lines depict the paired-end-mapping-based rearrangement graph (BND: translocation-type, DEL: deletion-type, DUP: tandem-duplication-type and INV: inversion-type paired-end SV pr-edictions). Using bulk whole-exome and mate-pair sequencing, read-depth shifts at these breakpoints were subtle and thus, this subclonal complex rearrangement escaped previous de novo SV detection efforts in bulk.