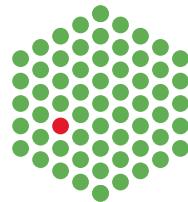
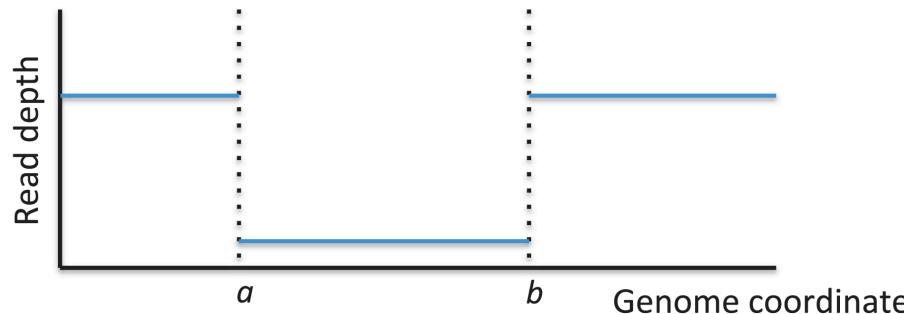
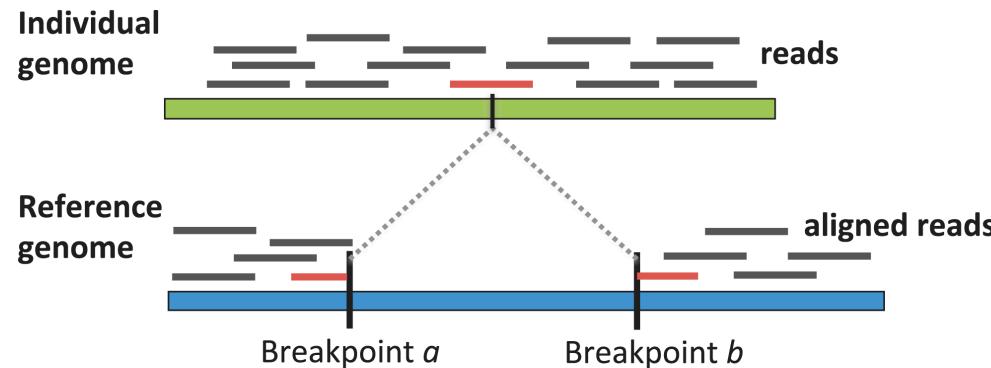


# Detection of SV breakpoint using BreakpointR

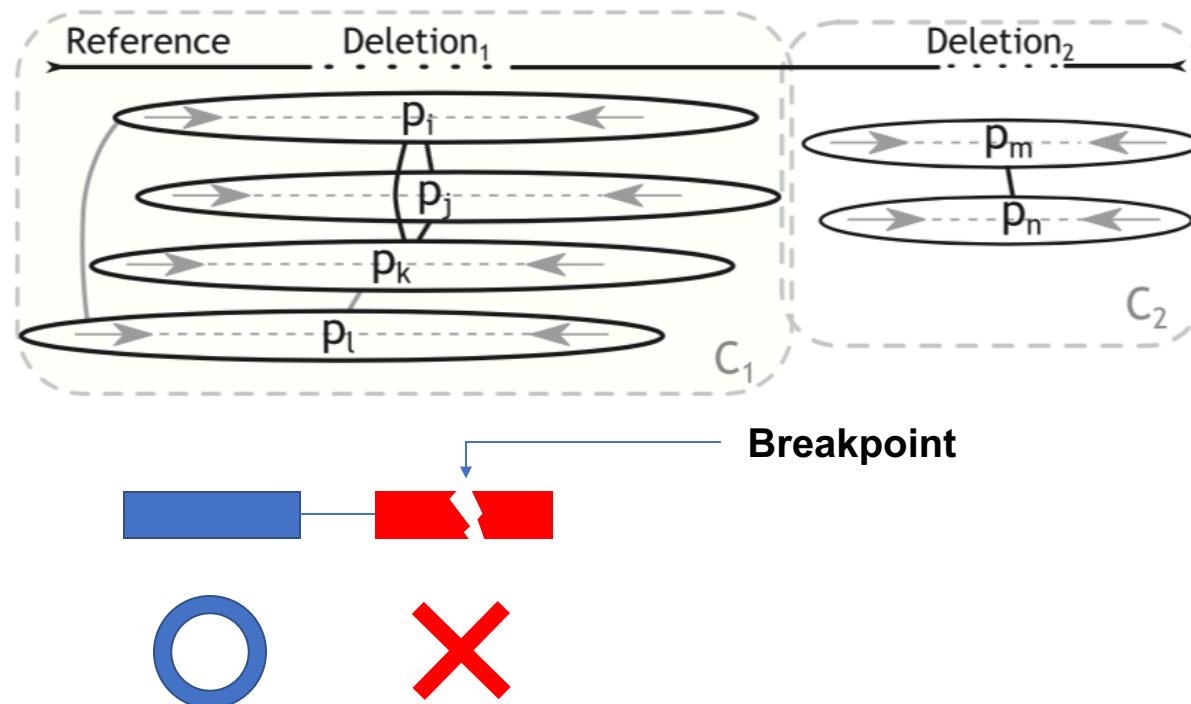


# Breakpoints are the start and end position of the structural variation



# Recapitulation of Breakpoint calling in Delly

A single-anchored paired-end is a read pair where one read maps to the reference and the other read is unmapped



*How do we detect breakpoint from the Strand-seq data?*

# Breakpoint calling from Strand-seq data

Bioinformatics, 2019, 1–2

doi: 10.1093/bioinformatics/btz681

Advance Access Publication Date: 30 August 2019

Applications Note



Genome analysis

## breakpointR: an R/Bioconductor package to localize strand state changes in Strand-seq data

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Maria Colomé-Tatché<sup>1,5</sup>, Peter M. Lansdorp<sup>1,3,6,‡</sup> and Victor Guryev<sup>1,‡</sup>

<sup>1</sup>European Research Institute for the Biology of Ageing, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, <sup>2</sup>Department of Genome Sciences, University of Washington School of Medicine, Seattle, WA, USA, <sup>3</sup>Terry Fox Laboratory, BC Cancer Agency, Vancouver, BC, Canada, <sup>4</sup>European Molecular Biology Laboratory (EMBL), Genome Biology Unit, Heidelberg, Germany, <sup>5</sup>Institute of Computational Biology, Helmholtz Zentrum München, Neuherberg, Germany and <sup>6</sup>Department of Medical Genetics, University of British Columbia, Vancouver, BC, Canada



David Porubsky

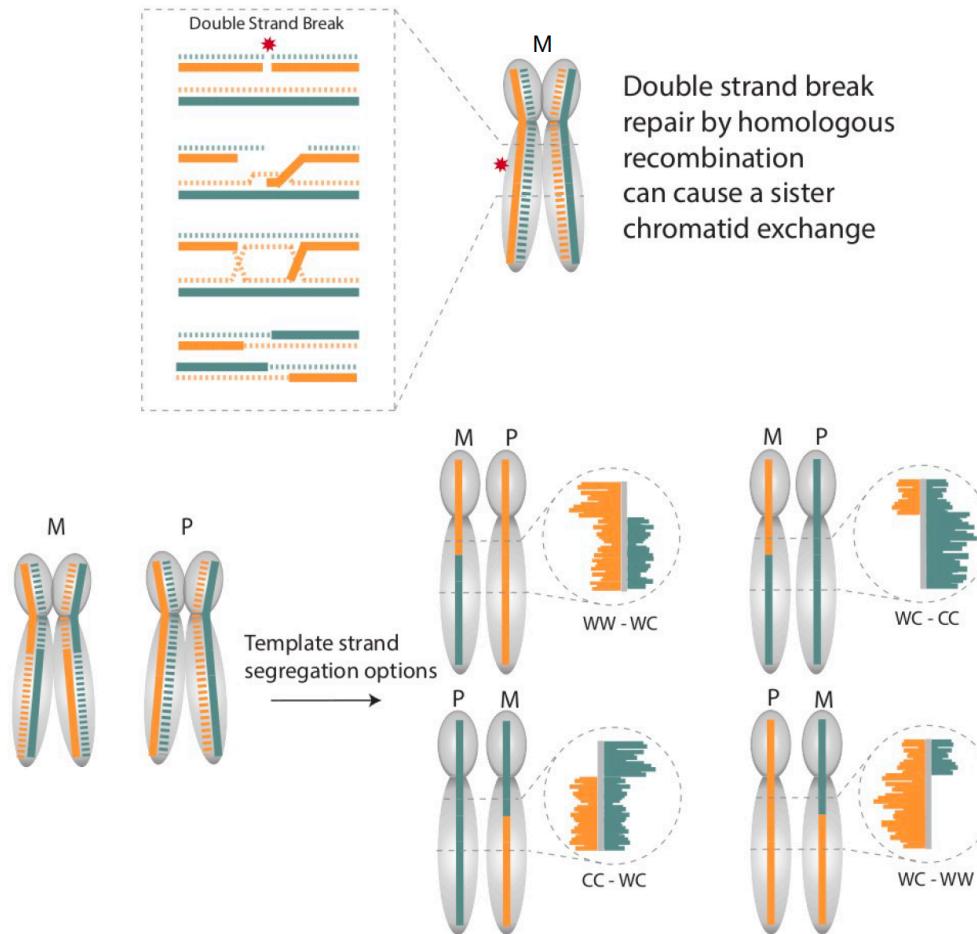
Ashley Sanders



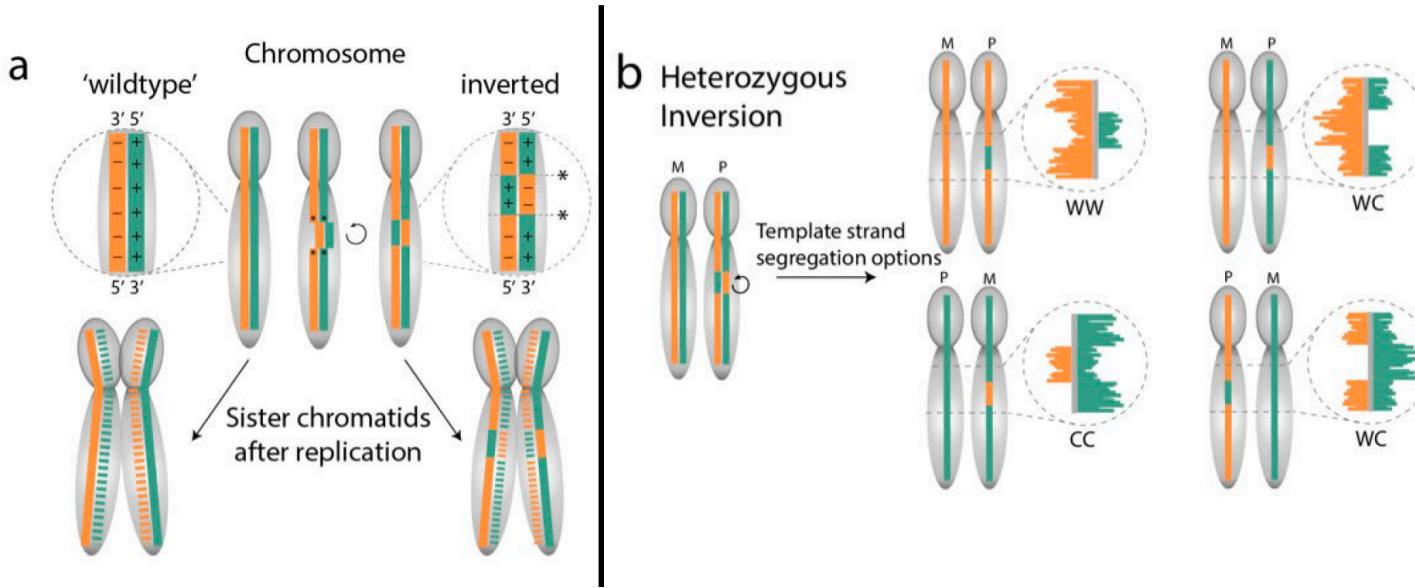
- BreakpointR detects local changes in strand directionality of aligned Strand-seq data, to enable fine-mapping of sister chromatid exchanges, inversions and to support global haplotype assembly.

*What is the local changes in strand directionality?*

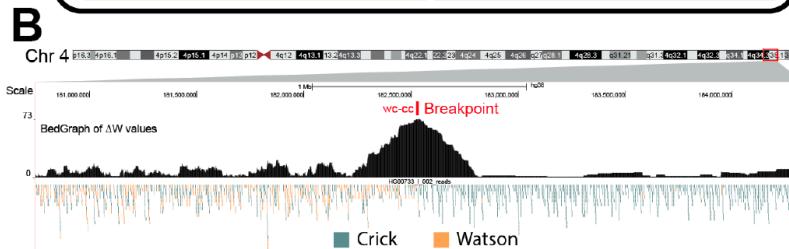
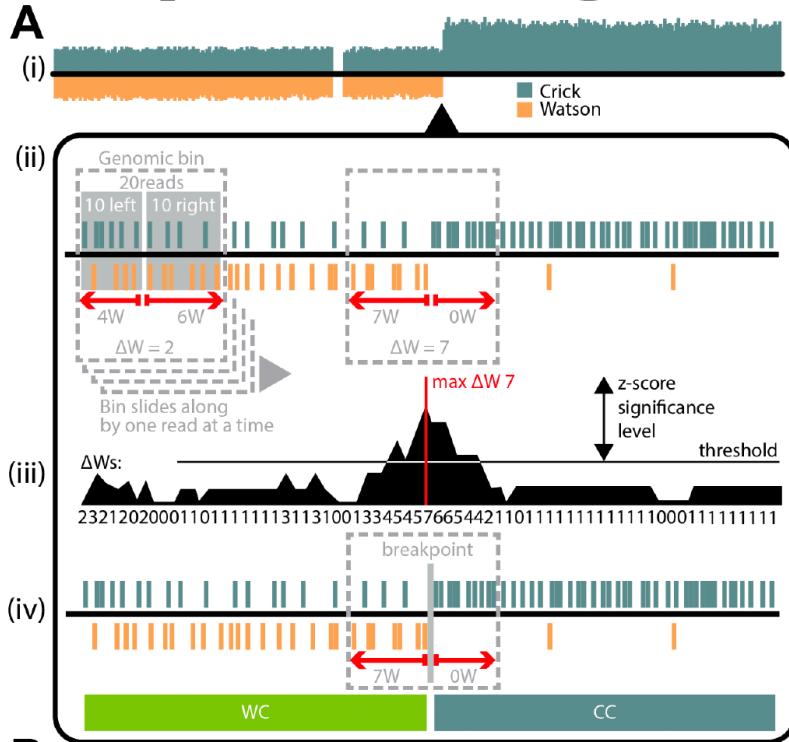
# Sister chromatid exchanges in Strand-seq data



# Mapping germline inversions in Strand-seq data



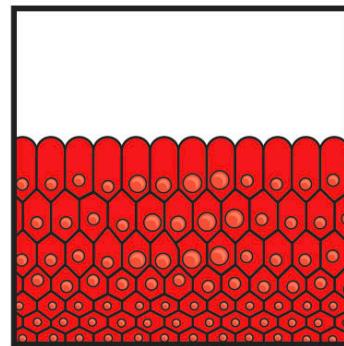
# **breakpointR algorithm**



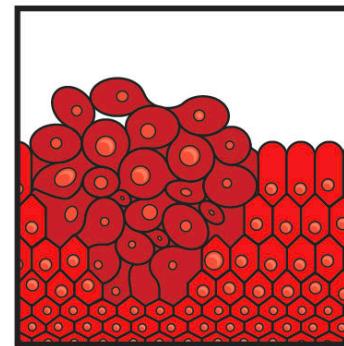
Porubsky et al. 2019

# Which data do we analyze today?

Real  
world



Normal cells



Cells forming a tumour

Model  
system

*RPE1-WT*



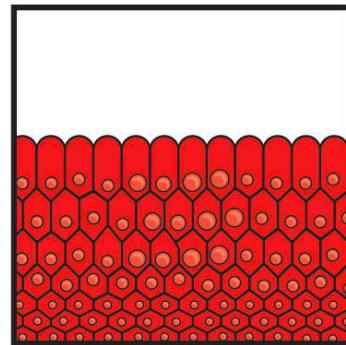
vs

*RPE1-BM510*



# Subclonal SVs revisited!! (WT BM510 mixture VAF 20% vs WT)

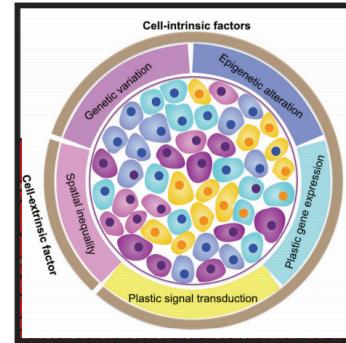
Real world



Normal cells

Model system

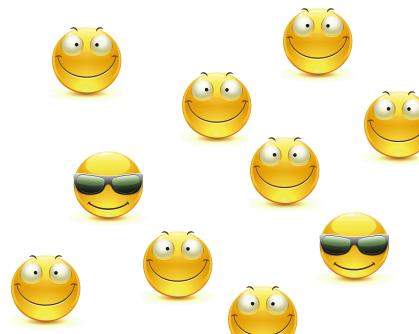
WT



Cells forming a tumour

VAF20% BM510

vs



*Can we detect subclonal translocation using Strand-seq?*

# Challenge: Find subclonal recurrent breakpoint in chr22!!

- STEP1 : Run breakpointR using following input folder and chr22
  - inputfolder = “/scratch/jeong/pipeline\_20190625\_RPE\_mixture/bam/RPE/selected/”
  - outputfolder = “BreakpointR\_results\_100cells”
  - chromosomes = ‘chr22’
- STEP2: Compare breakpoint with the Delly based breakpoint from WGS data (hint: /breakpoints/breakPointSummary.txt )
- STEP3: Upload bedgraph file to the UCSC browser track and see which gene is there around translocation breakpoint
- STEP4: Open question: Using overview plot and breakpointR result of 100 cells (mixture), can you guess which cells are come from BM510 (20 cells) and WT (80 cells)?

# Comparison of Delly and BreakpointR based translocation breakpoint in chr22!!

- CHROM, POS : [chr22, 37934425], [chr13, 20412250]
- MAPQ : mapping quality [60]
- GT : genotype [0/1] [0/0]
- GL : log10-scaled genotype likelihoods for RR, RA, AA genotypes [-23.6655,0,-90.8635] [0,-7.5218,-88.7961]
- GQ : Genotype Quality [10000] [75]
- FT : Per-sample genotype filter [PASS] [PASS]
- RC : Raw high-quality read counts for the SV [0] [0]
- RCL : Raw high-quality read counts for the left control region [0] [0]
- RCR : Raw high-quality read counts for the right control region [0] [0]
- CN : Read-depth based copy-number estimate for autosomal sites [-1] [-1]
- DR : # high-quality reference pairs [25] [23]
- DV : # high-quality variant pairs [5] [0]
- RR : # high-quality reference junction reads [27] [25]
- RV : # high-quality variant junction reads [9] [0]
- PRECISE/IMPRECISE : SVs refined using split-reads [PRECISE]
- PASS/LowQual : genotype quality [PASS]



```
seqnames start end CI.start CI.end genoT filenames
chr22 17553352 17567000 12693467 17642952 wc-cc Cell001.sort.mdur
chr22 37925136 37935646 37899037 37944092 cc-wc Cell001.sort.mdur
chr22 17876897 17876936 11974156 17949682 wc-cc Cell003.sort.mdur
chr22 38043988 38071100 38010266 38159426 cc-wc Cell003.sort.mdur
chr22 17544084 17554974 12293238 17583405 wc-ww Cell004.sort.mdur
chr22 17579347 17580826 12341586 17604242 wc-ww Cell006.sort.mdur
chr22 37934301 37938044 37901540 37952181 ww-wc Cell006.sort.mdur
chr22 17690760 17696506 12176341 17738540 wc-ww Cell008.sort.mdur
chr22 17524264 17525992 12402384 17564272 wc-ww Cell009.sort.mdur
chr22 37931913 37937498 37862362 37940415 ww-wc Cell009.sort.mdur
chr22 17523641 17532812 12411496 17567615 wc-ww Cell010.sort.mdur
chr22 37927507 37941108 37897587 37950947 ww-wc Cell010.sort.mdur
chr22 17068018 17104535 11975700 17278662 wc-cc Cell015.sort.mdur
chr22 18046125 18057965 12331299 18091681 wc-cc Cell018.sort.mdur
chr22 37910696 37941561 37837157 37943494 cc-wc Cell018.sort.mdur
chr22 17594004 17652660 12040556 17721340 wc-ww Cell020.sort.mdur
chr22 37855356 37907122 37814089 37985502 ww-wc Cell020.sort.mdur
chr22 17724174 17742638 11855691 17788145 wc-cc Cell021.sort.mdur
chr22 17286594 17295368 12363227 17315410 wc-ww Cell024.sort.mdur
chr22 17455607 17497839 12195010 17541676 wc-ww Cell026.sort.mdur
chr22 17169240 17172328 16037693 17192657 wc-cc Cell027.sort.mdur
chr22 48286474 48305477 48268423 48337762 wc-ww Cell028.sort.mdur
chr22 17281370 17293218 12526318 17310363 wc-ww Cell030.sort.mdur
chr22 17380219 17390168 12422319 17403606 wc-cc Cell035.sort.mdur
chr22 17429749 17442063 12404868 17506324 wc-cc Cell043.sort.mdur
chr22 17351297 17380332 12523128 17443444 wc-cc Cell044.sort.mdur
```

# Preparation for Day4

- Open tmux screen
  - tmux
  - tmux a
  - tmux ls
  - tmux kill-session –t 0
  - tmux switch –t 0
- Copy Mosaicatcher program and unzip
- Copy bam files and unzip
- It will take time, don't worry, you can close the screen and let it do the job, and check it tomorrow using tmux session!!

*Thank you for  
listening*

**COMING SOON**



**Day4**

**MOSAIC  
CATCHER**

