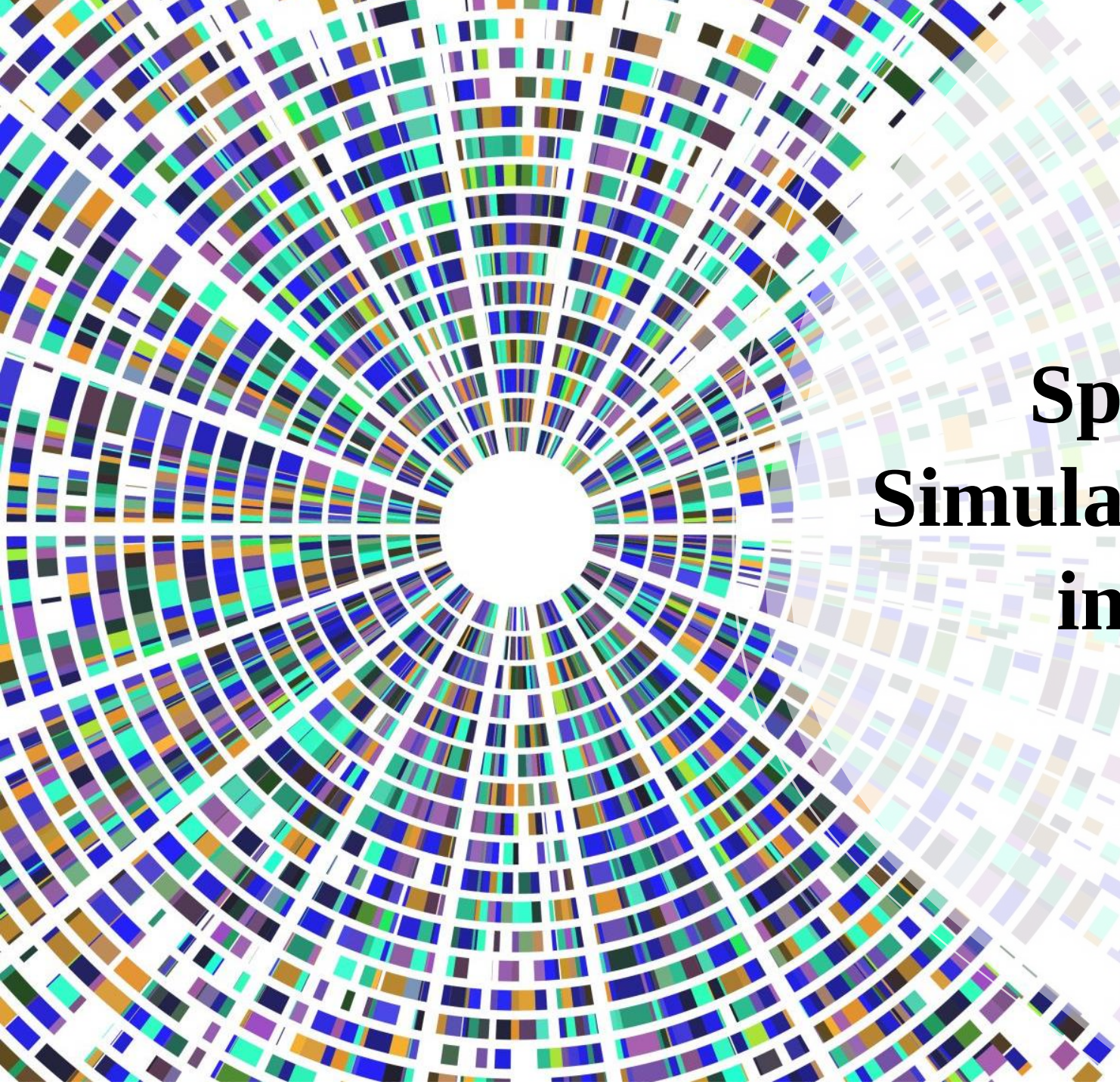


Group 2 :
SpikeVar & TykeVar
Simulation of Mosaic Variants
in Sequencing Data

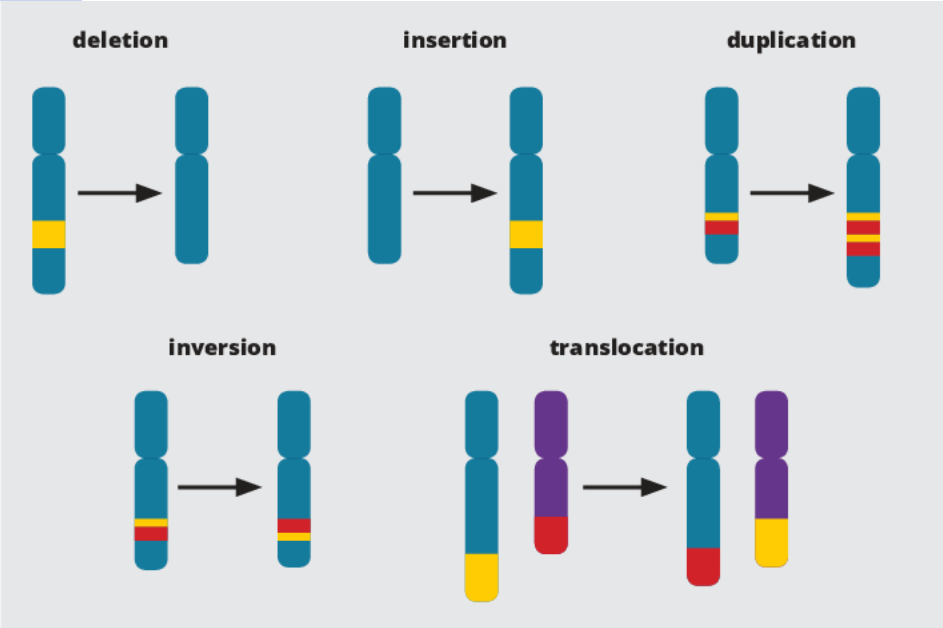
Farhang Jaryani,

Fritz Sedlazeck, Lab

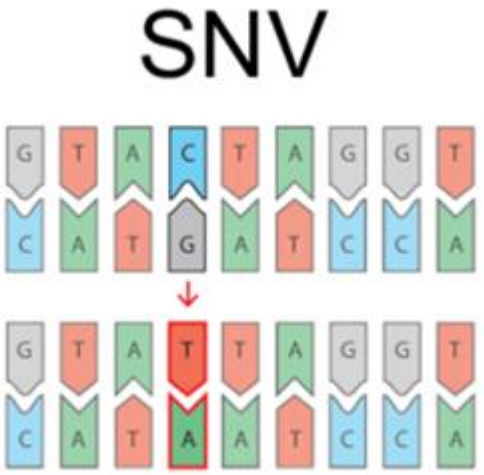
Human Genome Sequencing Center

Baylor college of Medicine

Structural Variants

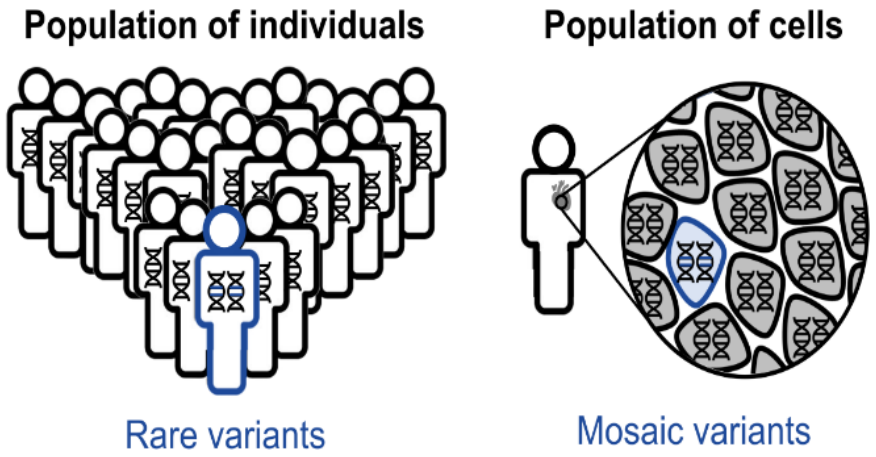


Reference	1 2 3
Insertion	1 2 5 3
Deletion	1 3
Inversion	1 3 2
Copy Number Variation	1 1 1 1 2 3
Tandem Duplication	1 1 2 3
Dispersed Duplication	1 2 1 3
Mobile Element Insertion	1 2 Mobile Element 3
Translocation	1 / 10 11 12 2 3



HUNTING STRUCTURAL VARIANTS , Luke Hickey
https://api.semanticscholar.org/CorpusID:204805198

Mosaic Variants



Mosaic Variants:

- ✓ **Potentially associated with disease**
- ✓ **Mixed in sequence data**
- ✓ **Requires mosaic variant callers to detect**

THE OHIO STATE UNIVERSITY
COLLEGE OF MEDICINE

Home Profiles Research units **Research output** Projects

Disease-associated mosaic variation in clinical exome sequencing: a two-year pediatric tertiary care experience

Cecelia R. Miller, Kristy Lee, Ruthann B. Pfau, Shalini C. Reshmi, Donald J. Corsmeier, Sayaka Hashimoto, Ashita Dave-Wala, Vijayakumar Jayaraman, Daniel Koboldt, Theodora Matthews, Danielle Mouhlas, Maggie Stein, Aimee McKinney, Tom Grossman, Benjamin J. Kelly, Peter White, Vincent Magrini, Richard K. Wilson, Elaine R. Mardis, Catherine E. Cottrell

Comprehensive Cancer Center, Comprehensive Cancer Center - Innate Immunity, Pathology, Pediatrics, Center for Clinical and Translational Science, Comprehensive Cancer Center - Molecular Biology and Cancer Genetics, Comprehensive Cancer Center - Experimental Therapeutics

Research output: Contribution to journal › Article › peer-review

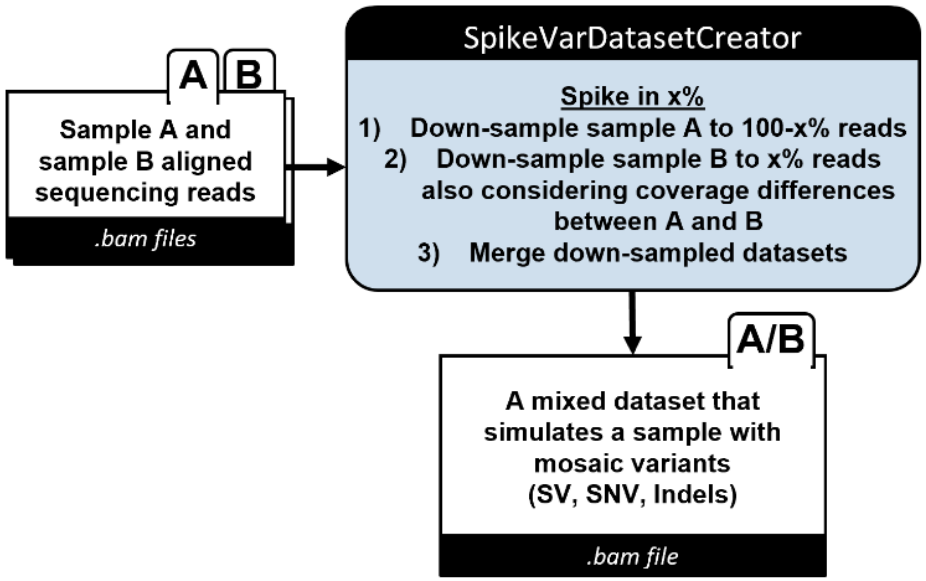
Disease-associated mosaic variation in clinical exome sequencing: a two-year pediatric tertiary care experience. Cold Spring Harb Mol Case Stud. 2020;6(3). Epub 20200612. doi: 10.1101/mcs.a005231. PubMed PMID: 32371413; PMCID: PMC7304353.

Spike in Known Exogenous Variants

❖ *Introducing User-Defined Spiking in Sequencing Data*

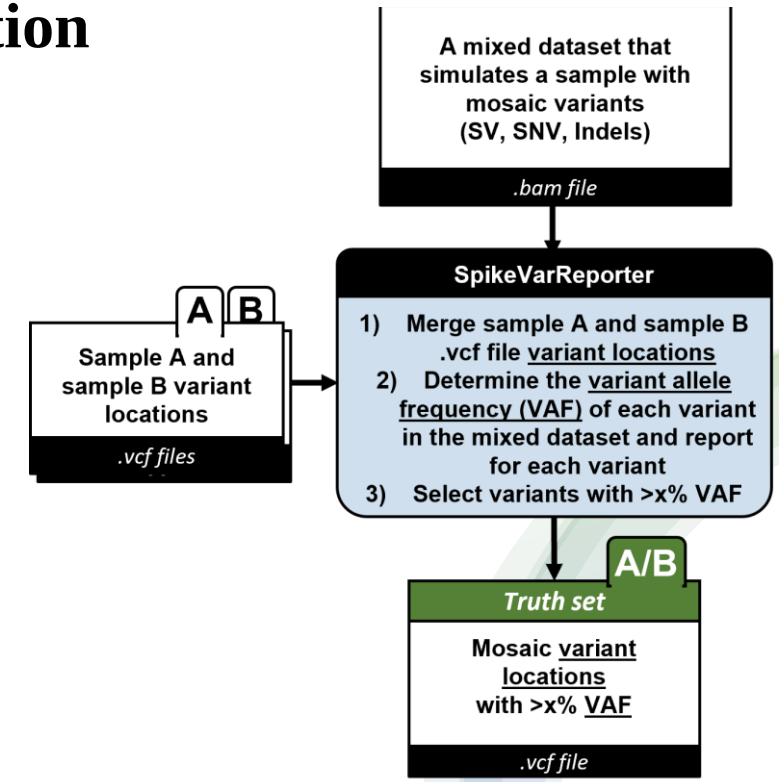
1) SpikeVar DatabaseCreator –

Generate Spiked-in Dataset

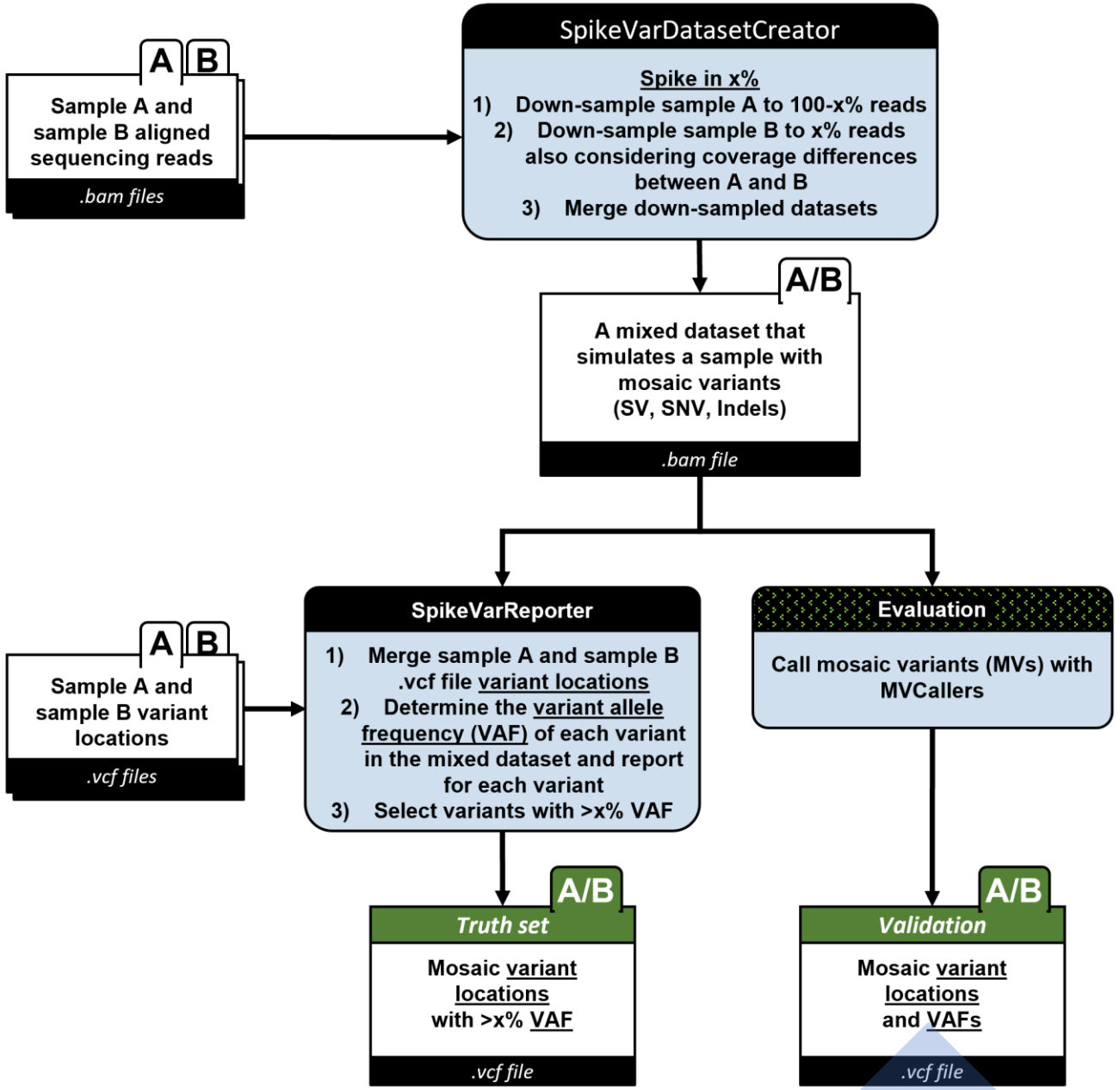


2) SpikeVarReporter –

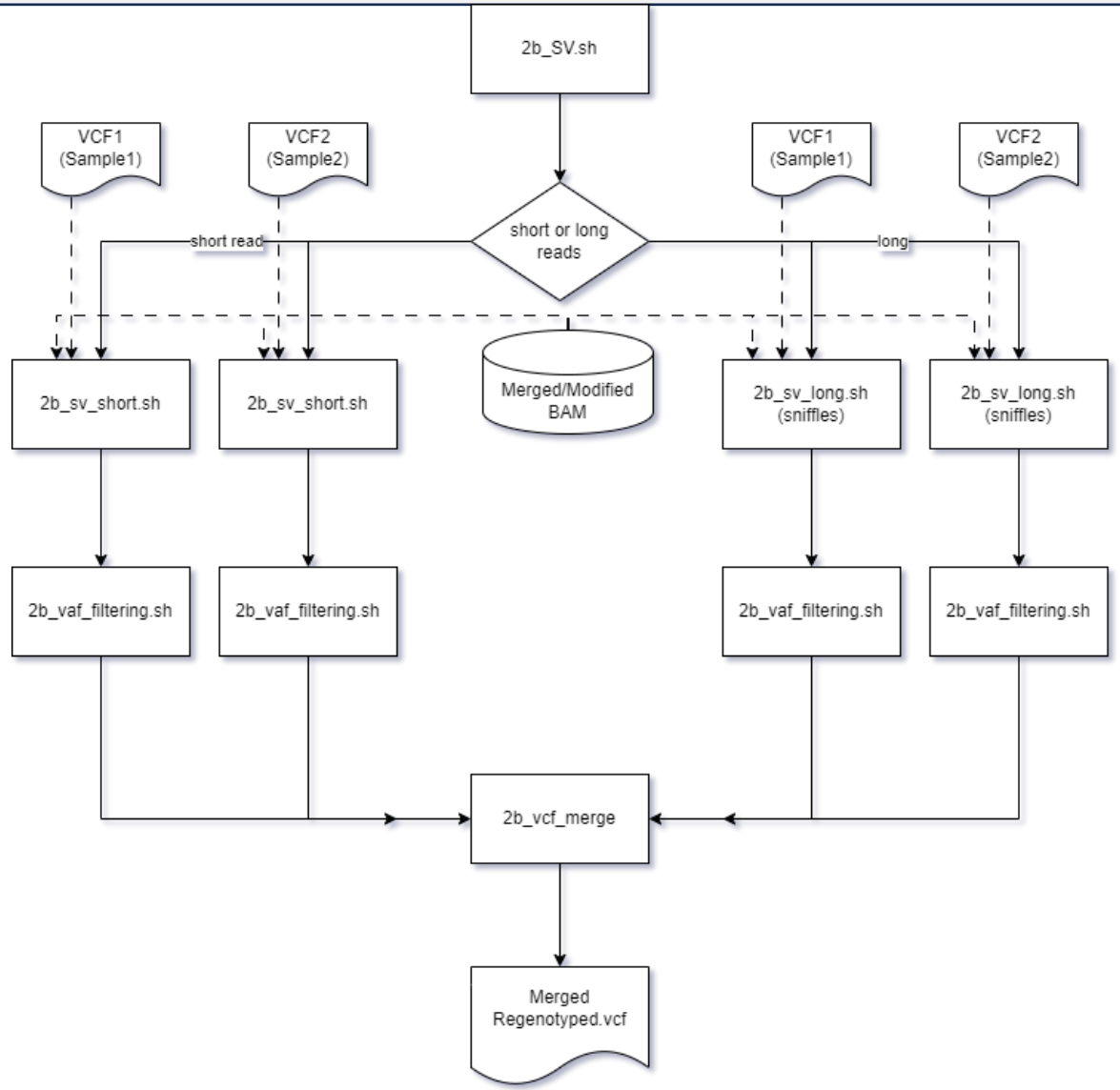
Filter Reads After Variant Allele Frequency Recalculation



*Sp*ike *i*n *K*nown *E*xogenous *Var*iants

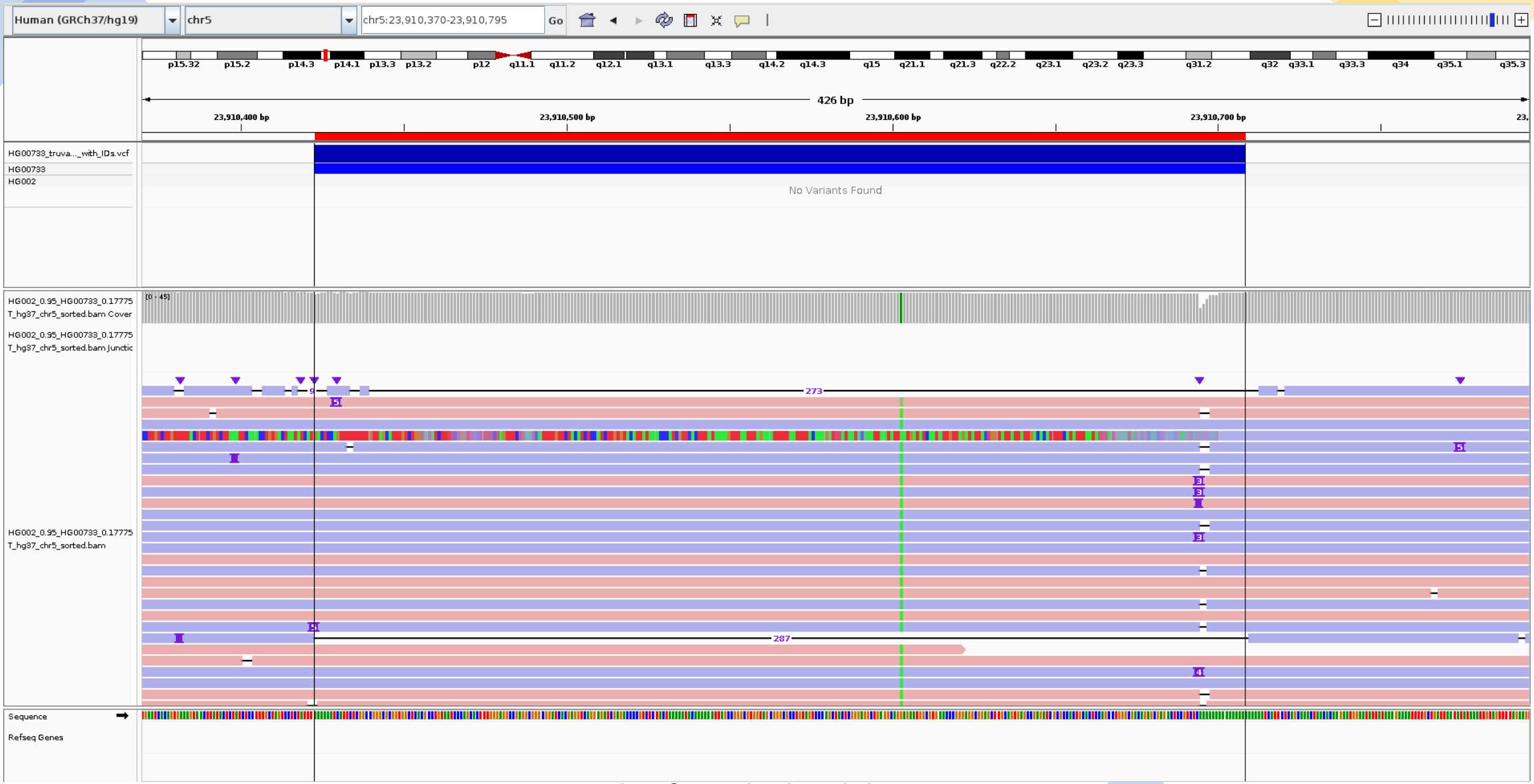


*Sp*ike *i*n *K*nown *E*xogenous *Var*iants



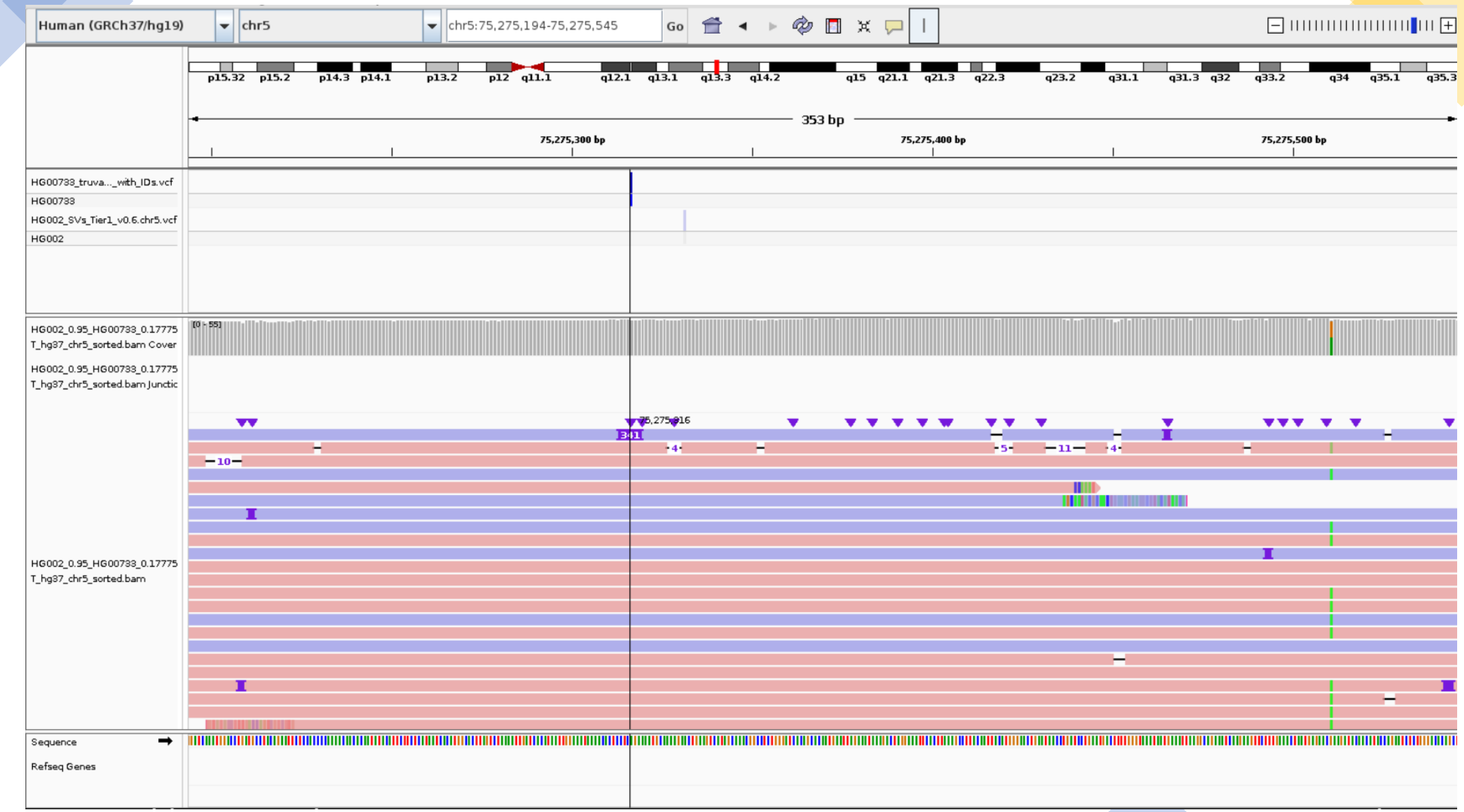
Flowchart of re-genotototyping both short and long reads SVs based on the modified generated bam file

Spike in Known Exogenous Variants



Example of a spiked in deletion.

*Sp*ike *i*n *K*nown *E*xogenous *Var*iants

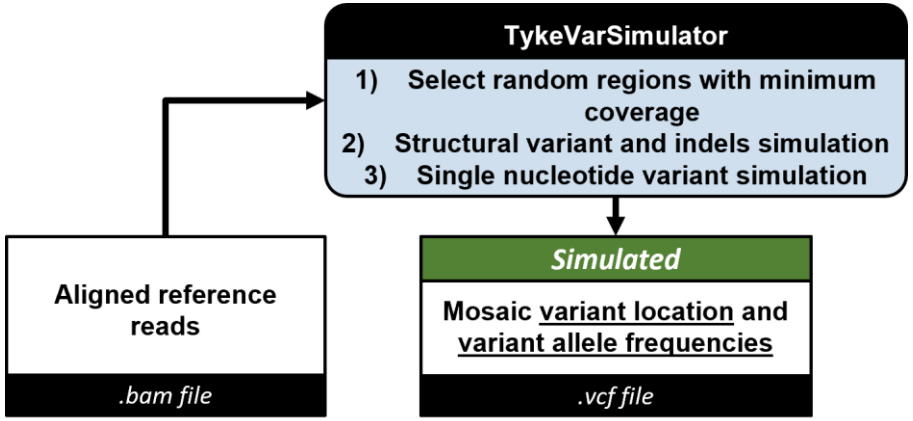


Example of a spiked in insertion.

*T*rack in *Y*our *K*ey *E*ndogenous *Var*iants

- creates a list of random mutations
- modifies a fraction of existing reads to match the user-defined MV frequency

1) TykeVarSimulator – Generate Simulated VCF



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chr22 32562272 HackIns1 N
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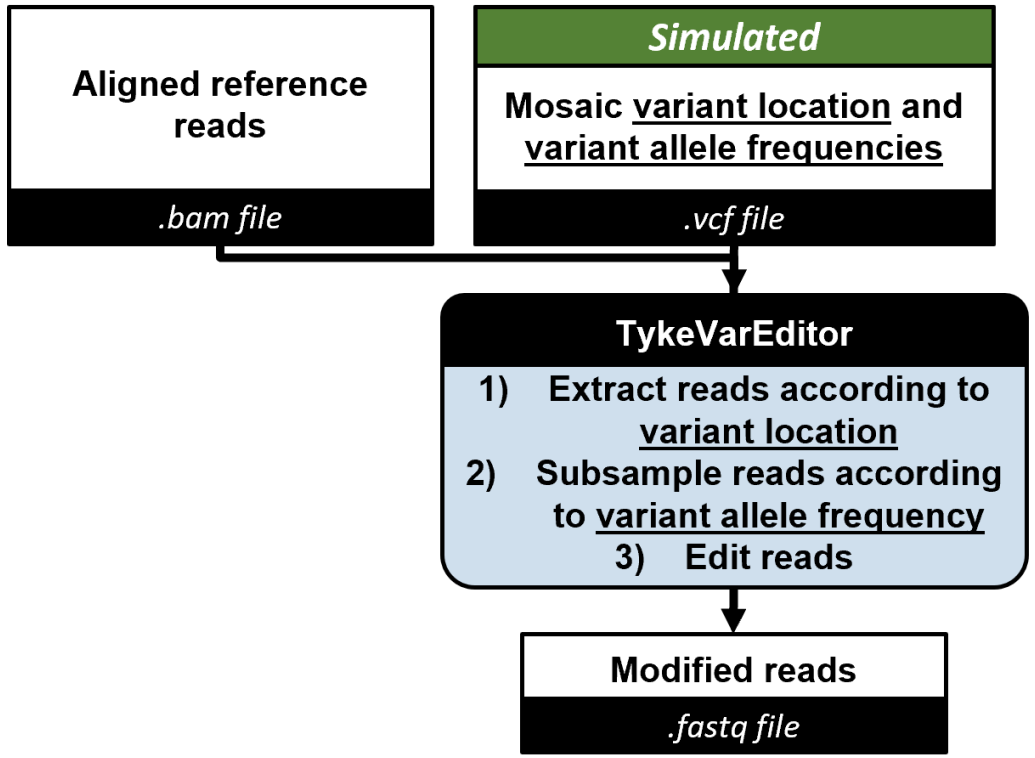
chr22 42134824 HackIns2 N
CCCCAGTGCTCAATCCATTCTCGTTTTTTGGTGGACCTCGGCGTTCGAGTAGGCTTTGATGTACGGTCTTCTCAGTTATAGATGCCTCGTGAGGCCCGCCGTTT>

chr22 43938337 HackIns3 N
CTCTAGAGAGTCGGGACCCGGTCGTGCTATTATCTAAACGCGTAATGCTTACACTGCAATGTACGTGGCTTAGGCATTTCGCGATACTTGAGTACCTAGACCTA>

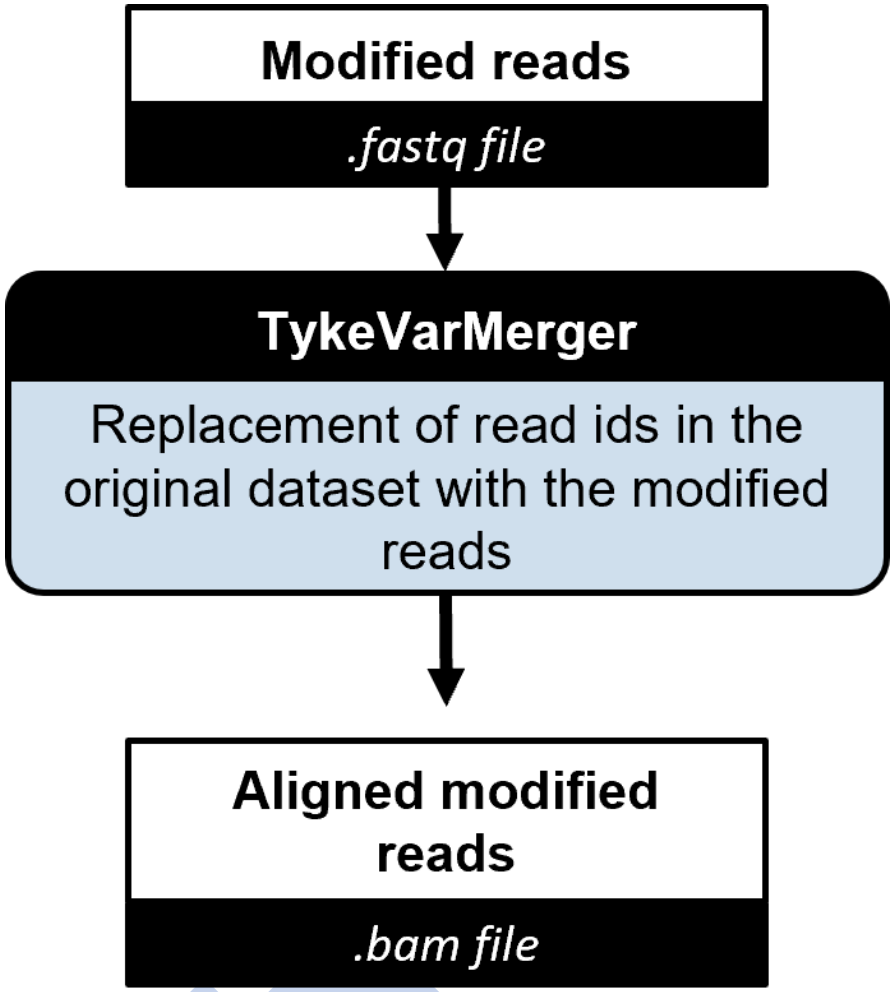
chr22 43366574 HackDel2 N <DEL> 60 PASS AF=0.07;END=43375935;PRECISE;SVLEN=-9361;SVTYPE=DEL GT:GQ 0/0:60

*T*rack in *Y*our *K*ey *E*ndogenous *Var*iants

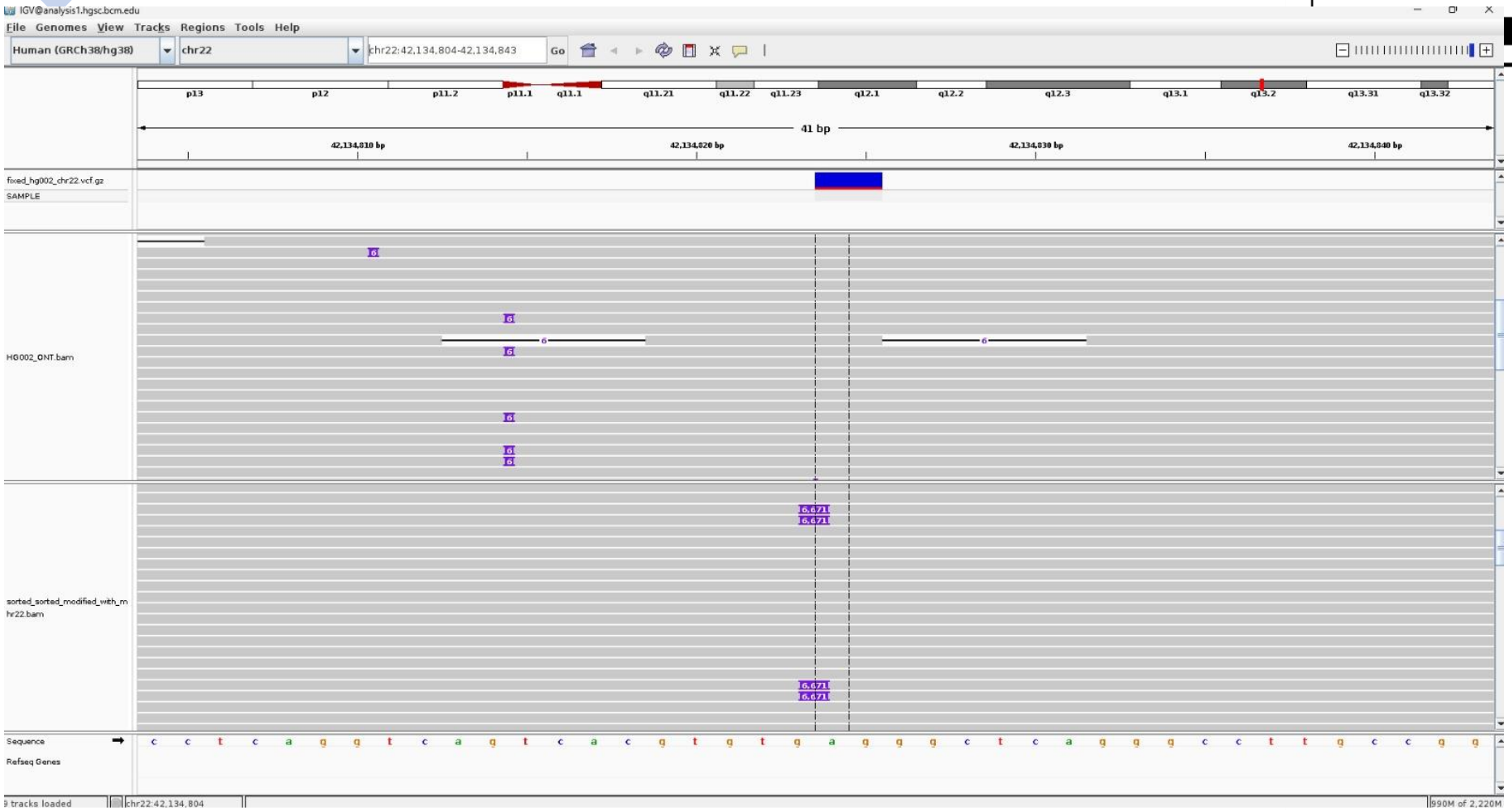
2) TykeVarEditor – Generate Edited Reads Based on Simulated VCF



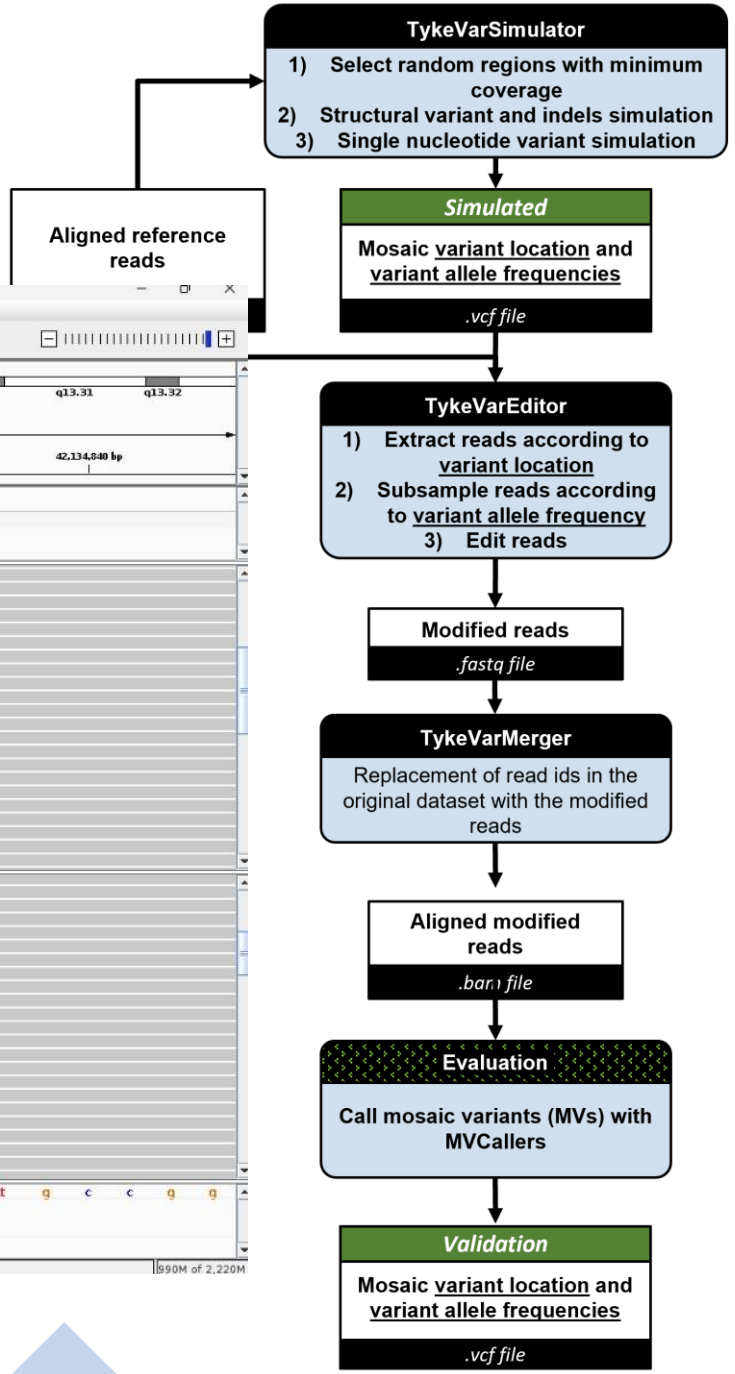
3) TykeVarMerger – Re-Align Modified Reads and Merge Them



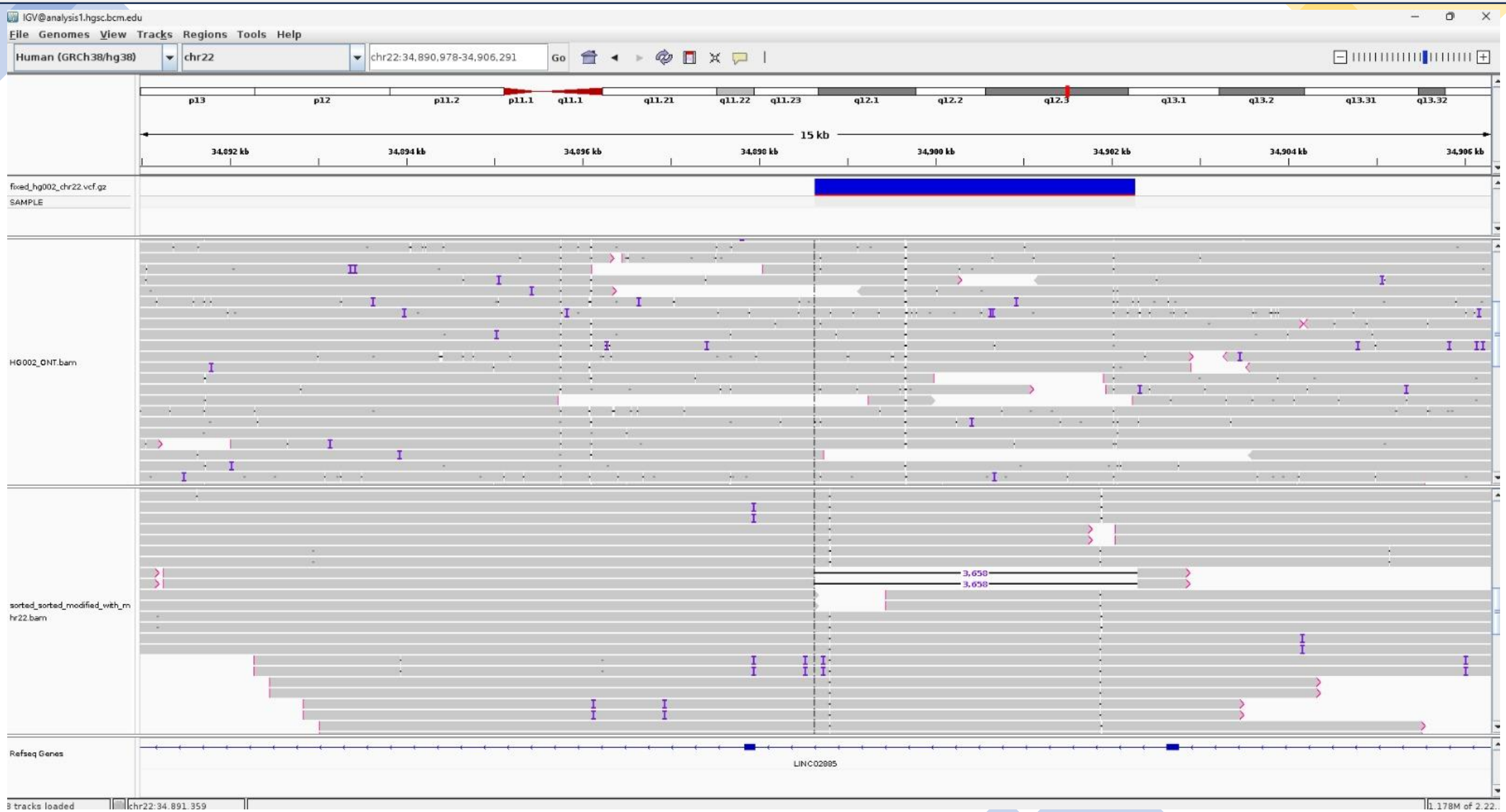
TykeVar – Creation of Sequencing Data With a Subset of Modified Reads



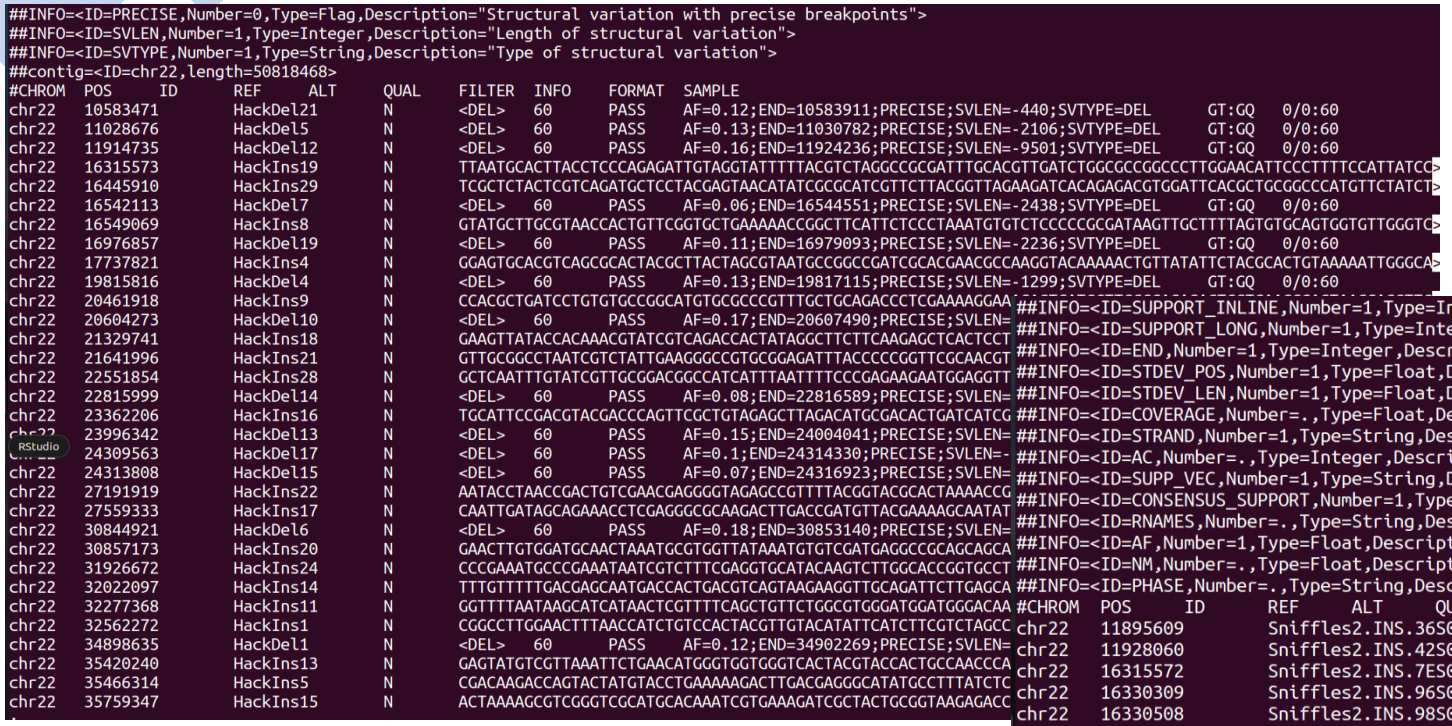
A mosaic SV insertion.



*T*rack in *Y*our *K*ey *E*ndogenous *Var*iants



*T*rack in *Y*our *K*ey *E*ndogenous *Var*iants



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chr22   16445910        HackIns29       N       TCGCTCTACTCGTCAGATGCTCCTACGAGTAACATATCGCGCATCGTTCTTACGGTTAGAAGATCACAGAGACGTGGATTCACGCTGCGGCCCATGTTCTATCT>
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chr22   27191919        HackIns22       N       AATACCTAACCGACTGTCGAACGAGGGGTAGAGCCGTTTTACGGTACGCACTAAAACCG
chr22   27559333        HackIns17       N       CAATTGATAGCAGAAACCTCGAGGGCGCAAGACTTGACCGATGTTACGAAAAGCAATAT
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chr22   32022097        HackIns14       N       TTTGTTTTTGACGAGCAATGACCACTGACGTCAGTAAGAAGGTTGCAGATTCTTGAGCA
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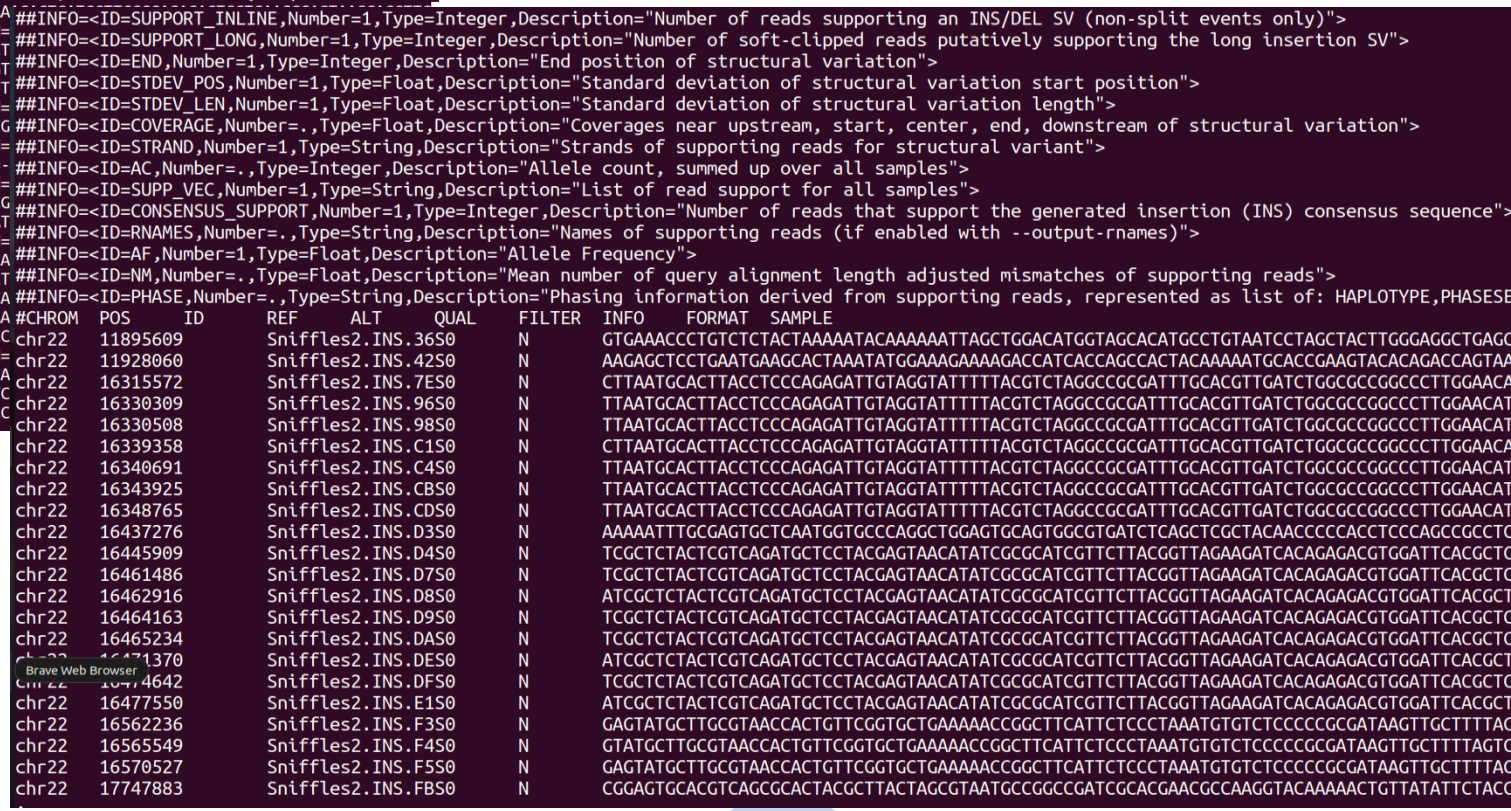
Ground Truth VCF



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chr22   16330508        Sniffles2.INS.98S0      N       TTAATGCACTTACCTCCCAGAGATTGTAGGTATTTTTACGTCTAGGCCGCGATTTGCACGTTGATCTGGCGCCCGGCCCTTGGAACAT
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chr22   16471370        Sniffles2.INS.DES0      N       ATCGCTCTACTCGTCAGATGCTCCTACGAGTAACATATCGCGCATCGTTCTTACGGTTAGAAGATCACAGAGACGTGGATTCACGCT
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chr22   16477550        Sniffles2.INS.E1S0      N       ATCGCTCTACTCGTCAGATGCTCCTACGAGTAACATATCGCGCATCGTTCTTACGGTTAGAAGATCACAGAGACGTGGATTCACGCT
chr22   16562236        Sniffles2.INS.F3S0      N       GAGTATGCTTGCGTAACCACTGTTCGGTGCTGAAAAACCGGCTTCATTCTCCCTAAATGTGTCTCCCCCGCGATAAGTTGCTTTTAC
chr22   16565549        Sniffles2.INS.F4S0      N       GTATGCTTGCGTAACCACTGTTCGGTGCTGAAAAACCGGCTTCATTCTCCCTAAATGTGTCTCCCCCGCGATAAGTTGCTTTTAGTG
chr22   16570527        Sniffles2.INS.F5S0      N       GAGTATGCTTGCGTAACCACTGTTCGGTGCTGAAAAACCGGCTTCATTCTCCCTAAATGTGTCTCCCCCGCGATAAGTTGCTTTTAC
chr22   17747883        Sniffles2.INS.FBS0      N       CGGAGTGCACGTCAGCGCACTACGCTTACTAGCGTAATGCCGGCCGATCGCACGAACGCCAAGGTACAAAAACTGTTATATTCTACG
```

Sniffles Mosaic Results

Acknowledgement

Baylor College of Medicine

HGSC
HUMAN GENOME SEQUENCING CENTER

Sedlazeck lab

- Fritz J Sedlazeck
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- Farhang Jaryani