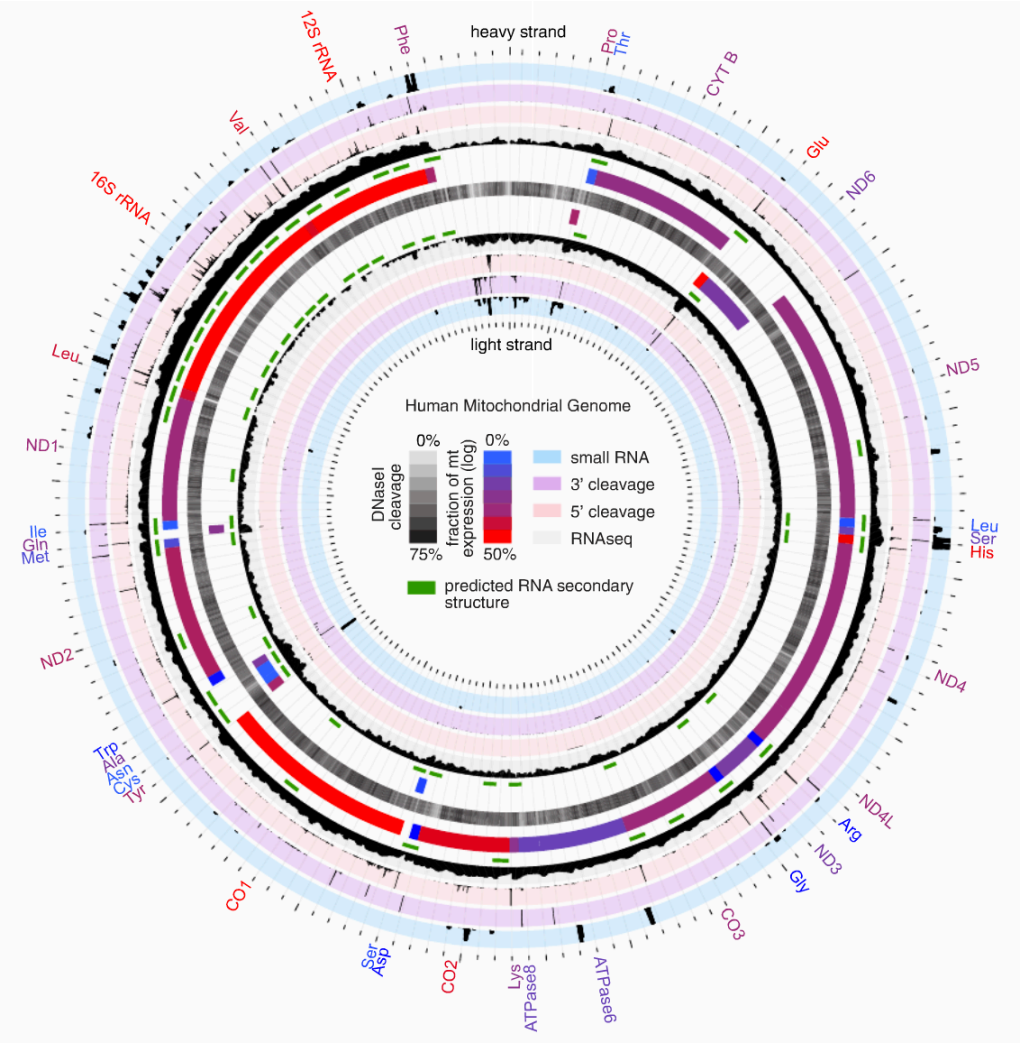
# PAWG-15: Mitochondria and HLA

- Leader
  - Han Liang
  - Hidewaki Nakagawa
- Members
  - Japan
    - Seiya Imoto, Shinichi Mizuno, Akihiro Fujimoto, Tatsuhiko Tsunoda, Rui Yamaguchi, Satoru Miyano,
  - Korea
    - Kwang-Sung Ahn, Hyun Sub Cheong, Jung Kyoon Choi, Yeun-Jun Chung, Jongsun Jung, Hyung-Lae Kim, Youngil Koh, Ji Wan Park, Keunchil Park, Sungsoo Yoon, Youngwook Kim
  - USA
    - Chad Creighton, Leng Han, Jun Li, Yuan Yuan, Li Zhang, Mike McLellan, Matt Bailey, John Weinstein, Cathy Wu , Sachet, Gad Getz

# Mitochondria and Cancer

- Motivation
  - Cells' powerhouse and suicidal weapon store
  - Dysregulated in cancer cells: Warburg effect



# Goals and planned analyses

- Somatic mutations in mitochondrial DNA (mtDNA)
- Copy number variations of mtDNAs
- Co-evolution and co-expression in mitochondrial genes with nuclear genes
- Clinical relevance of mtDNA variations
- Energy metabolism of mtDNA variations

# Mutation Callers

- MuTect: SNV
- VarScan: SNV and indel
- GATK Unified Genotyper: SNV and indel

# Running time

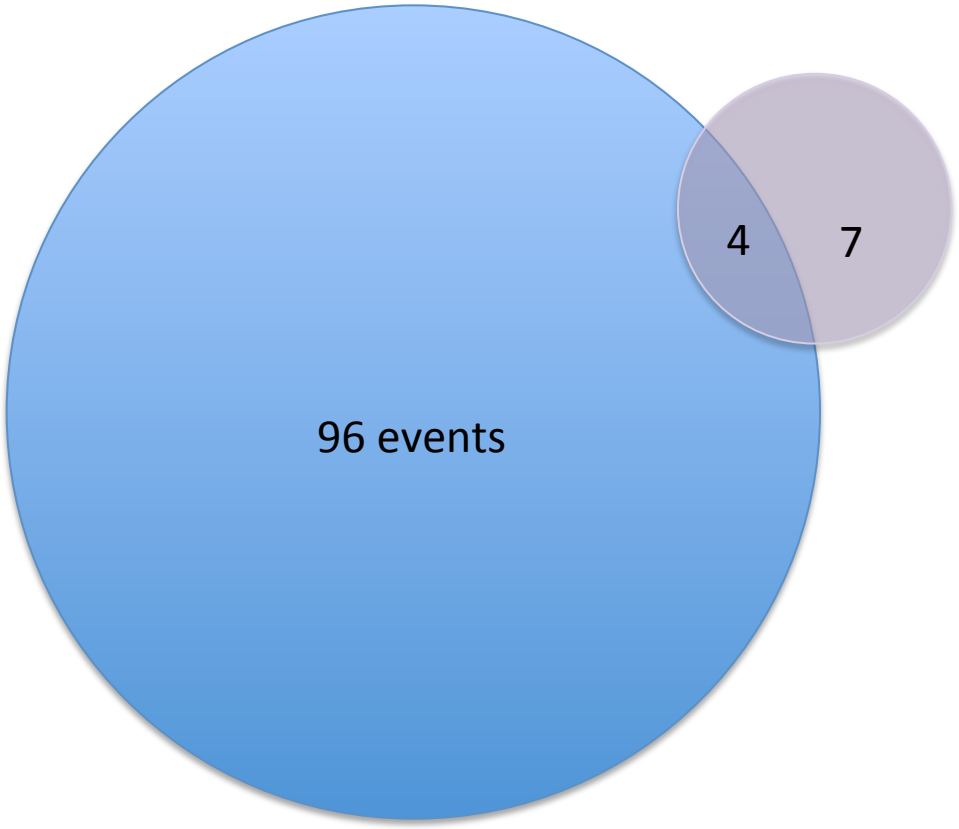
- MuTect: ~10 mins
- VarScan: ~ 1 hour
- GATK: > 6 hours

# mtDNA benchmark dataset

- Somatic mtDNA calls made on the TCGA KICH (chrCC) cases
  - 53 samples verified by long-range PCR (LR-PCR)
- 37 Samples shared between ICGC Train2 and benchmark dataset
  - 96 events by LR-PCR: 70 SNVs, 26 indels

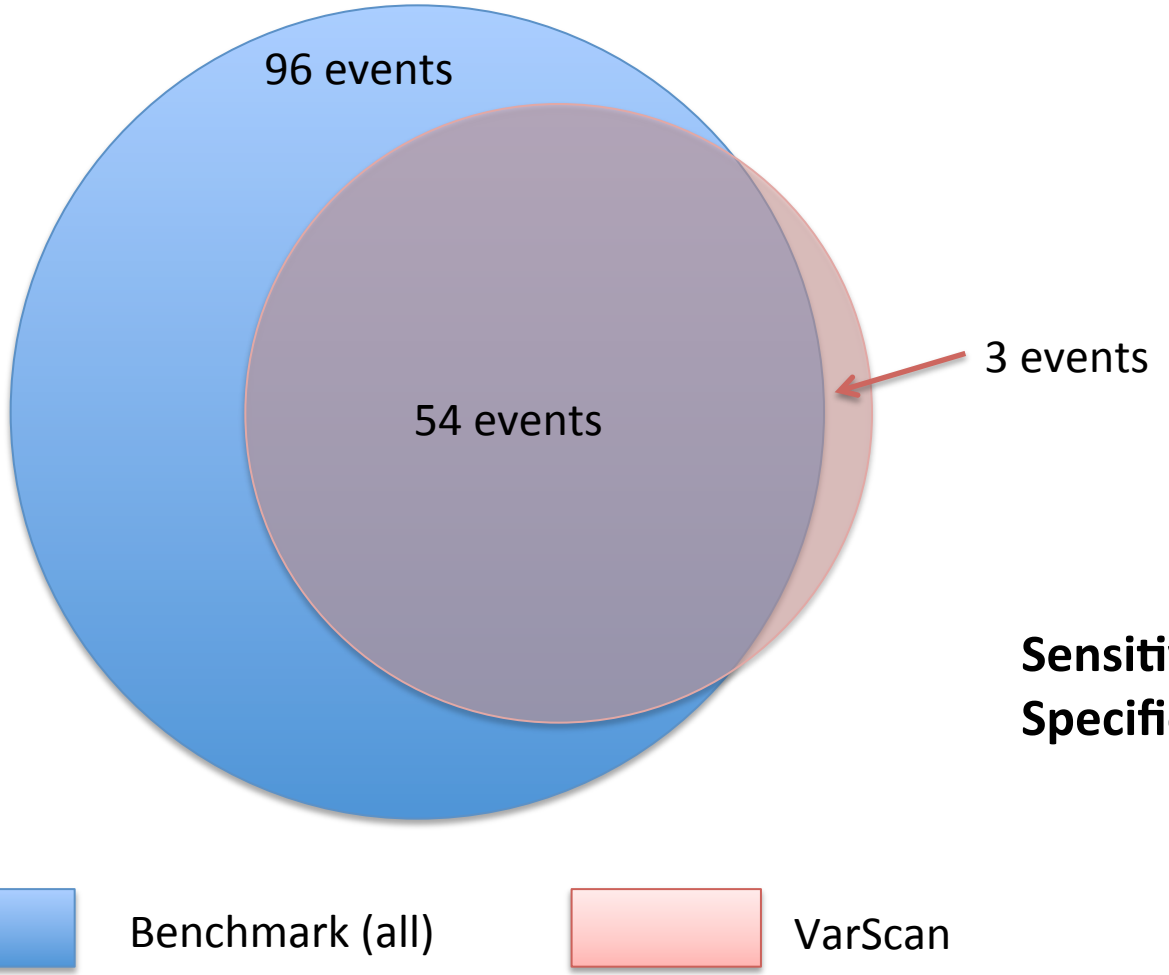
Davis et al, Cancer Cell (2014)

# Events detected by Mutect



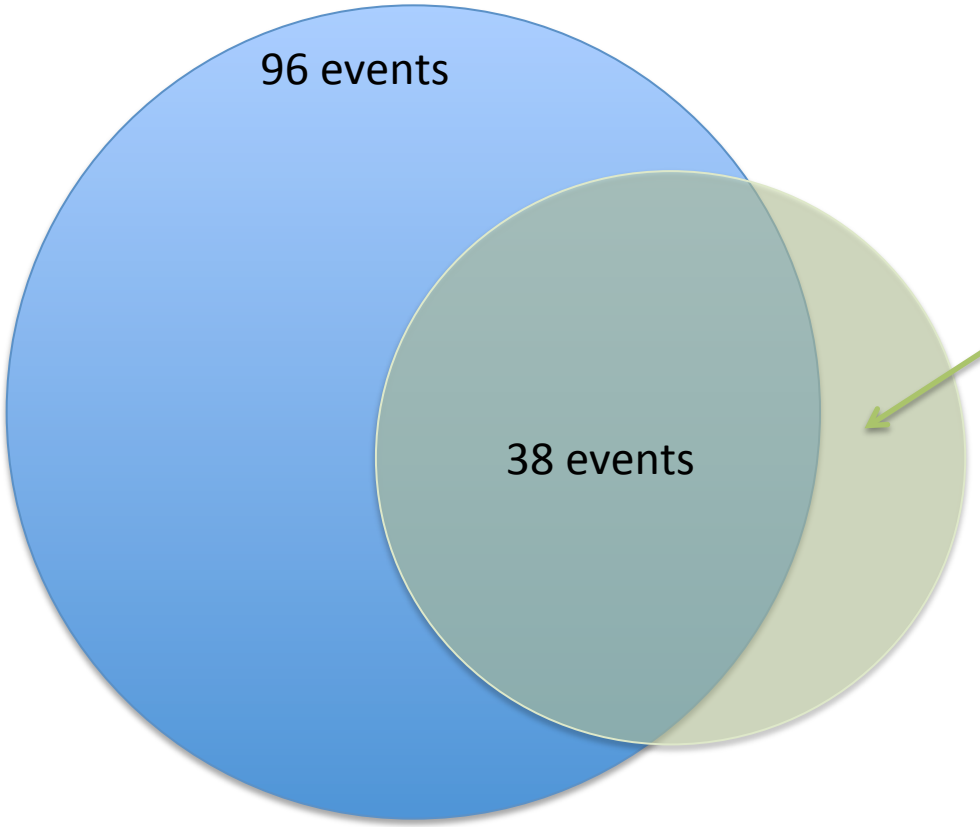

**Sensitivity= 4/96= 4%**
**Specificity= 4/11= 36%**

# Events detected by VarScan




**Sensitivity= 54/96= 56%**
**Specificity= 54/57= 95%**

# Events detected by GATK




**Sensitivity= 38/96= 40%**
**Specificity= 54/57= 78%**

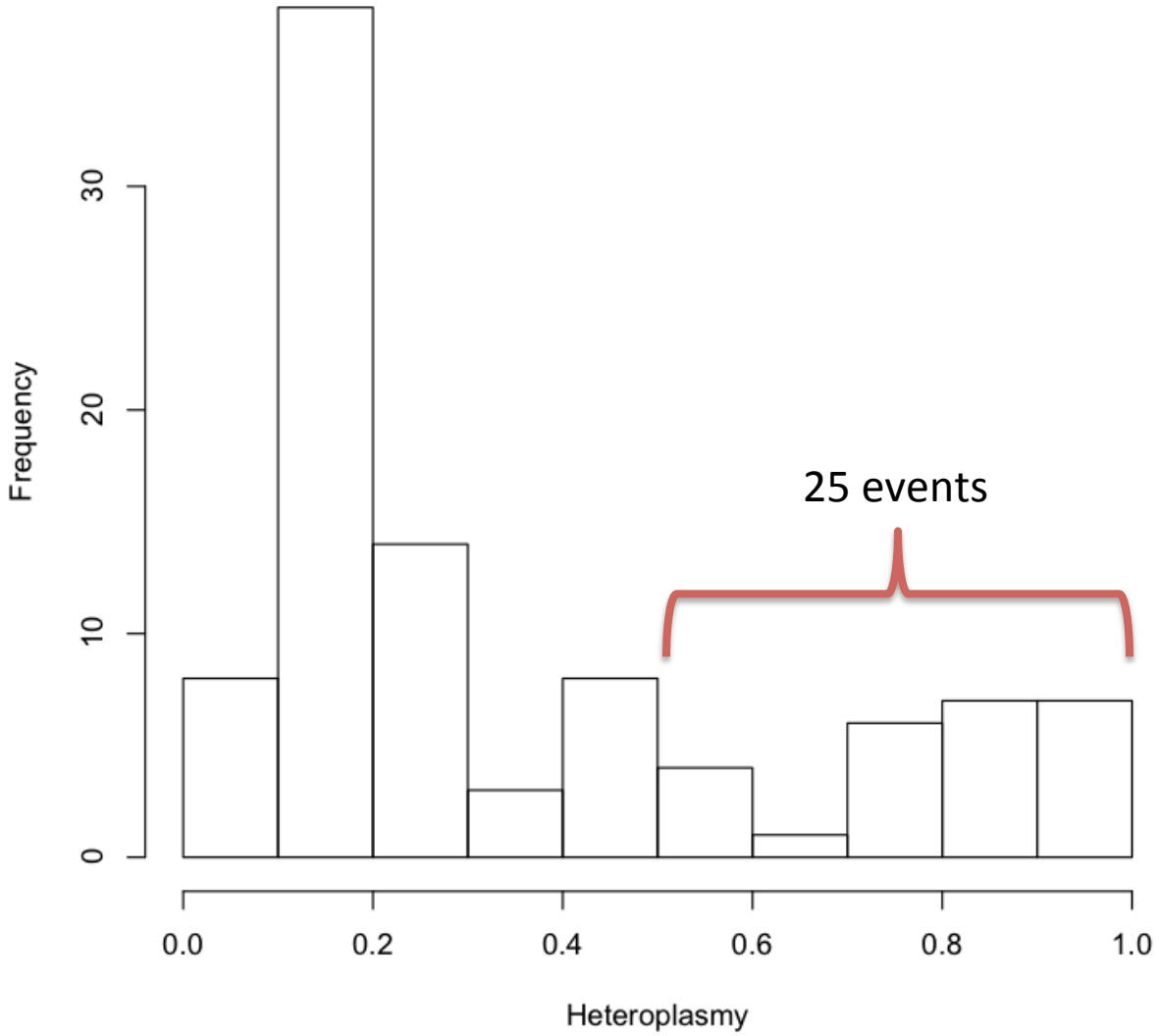
Benchmark (all)

GATK

# Varscan shows the highest sensitivity and precision

| Tool | Total events | True positive | Sensitivity (Total events = 96) | Precision |
|---|---|---|---|---|
| MuTect | 11 | 4 | 4% | 36% |
| VarScan | 57 | 54 | 56% | 95% |
| GATK | 49 | 38 | 40% | 78% |

# Most of the 96 events have low heteroplasmy



# VarScan was able to capture most (22/25) of the **top events**

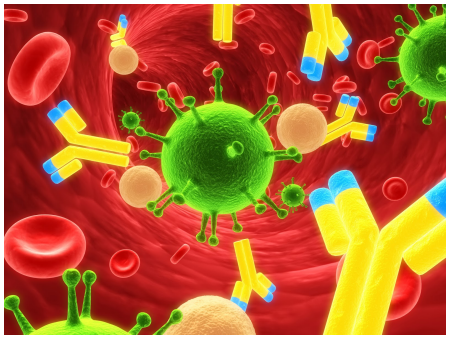
| SNV/indel | POS | REF | ALT | Sample | heteroplasmy | Region | Mutect | GATK | VarScan |
|---|---|---|---|---|---|---|---|---|---|
| indel | 11866 | A | AC | TCGA-KL-8326 | 0.82 | ND4 | | | Yes |
| indel | 65 | T | TG | TCGA-KL-8327 | 0.59 | D-Loop | | | Yes |
| SNV | 16426 | C | A | TCGA-KL-8331 | 0.50 | D-Loop | | | |
| SNV | 5767 | C | T | TCGA-KL-8333 | 0.73 | C | | Yes | Yes |
| SNV | 14159 | C | A | TCGA-KL-8341 | 0.81 | ND6 | | Yes | Yes |
| indel | 3565 | A | AC | TCGA-KL-8343 | 0.79 | ND1 | | | Yes |
| indel | 13127 | AC | A | TCGA-KL-8344 | 0.86 | ND5 | | Yes | Yes |
| SNV | 4569 | G | A | TCGA-KM-8438 | 0.82 | ND2 | | | Yes |
| SNV | 5738 | G | C | TCGA-KM-8438 | 0.86 | OLR | | | Yes |
| indel | 65 | T | TG | TCGA-KM-8438 | 0.93 | D-Loop | | | Yes |
| indel | 13230 | CA | C | TCGA-KM-8441 | 0.90 | ND5 | | Yes | Yes |
| indel | 3105 | AC | A | TCGA-KM-8442 | 0.93 | 16s rRNA | | | |
| SNV | 16426 | C | A | TCGA-KM-8476 | 0.51 | D-Loop | | | |
| indel | 12384 | TC | T | TCGA-KM-8477 | 0.76 | ND5 | | Yes | Yes |
| SNV | 10806 | G | A | TCGA-KM-8477 | 0.98 | ND4 | | Yes | Yes |
| SNV | 4429 | G | A | TCGA-KM-8477 | 0.99 | M | | | Yes |
| SNV | 4969 | G | C | TCGA-KM-8477 | 0.99 | ND2 | | Yes | Yes |
| indel | 12417 | C | CA | TCGA-KN-8419 | 0.72 | ND5 | | | Yes |
| indel | 65 | T | TG | TCGA-KN-8422 | 0.71 | D-Loop | | | Yes |
| SNV | 1900 | A | G | TCGA-KN-8428 | 0.93 | 16s rRNA | | | Yes |
| SNV | 6490 | T | C | TCGA-KN-8432 | 0.95 | COI | Yes | Yes | Yes |
| SNV | 3922 | G | A | TCGA-KN-8434 | 0.67 | ND1 | | Yes | Yes |
| SNV | 9651 | C | T | TCGA-KN-8434 | 0.76 | COIII | | | Yes |
| SNV | 16156 | G | A | TCGA-KN-8435 | 0.51 | D-Loop | | Yes | Yes |
| indel | 13230 | CA | C | TCGA-KN-8437 | 0.89 | ND5 | | Yes | Yes |

# Summary

- Focused on shared samples between the benchmark dataset and ICGC Train2
- Compared performance of three popular mutation callers
- VarScan showed the best performance

# Future directions

- Apply the best performing tool (VarScan) to all Train2 samples



# Cancer ImmunoGenomics

- ✓ Immunological surveillance in carcinogenesis and immunological response to cancer treatment are now an important issue in cancer research and clinics.

- ✓ Hematological tumors are inflammation-related cancers are involved with genetic alterations of many immunology-related genes

HLA/KIR genotyping and mutation
Mutations and expression of immunology-related genes
Neo-antigens

# HLA and Immunogenomics

- ✓ They are located at Chr *6p21* and most polymorphic regions
- ✓ Their variants are related with immune response and immune diseases
- ✓ The IMGT/HLA Database is a central repository for sequences of HLA

- ◆ Genomic approach to cancer immuno-editing in human through pan-cancer analysis (Imoto Seiya, Shin-ichi Mizuno, Satoru Miyano, University of Tokyo)
- ◆ Defining genomic alterations underlying “immunologic tumor” using whole genome sequencing data of various tumor types (Jongsun Jung, Youngil Koh, Sung-Soo Yoon, Seoul National University)
- ◆ Characterization of DNA copy number variation in HLA region in the human genome (Li Zhang, MDACC)
- ◆ Sachet, Cathy Wu , Gad Getz

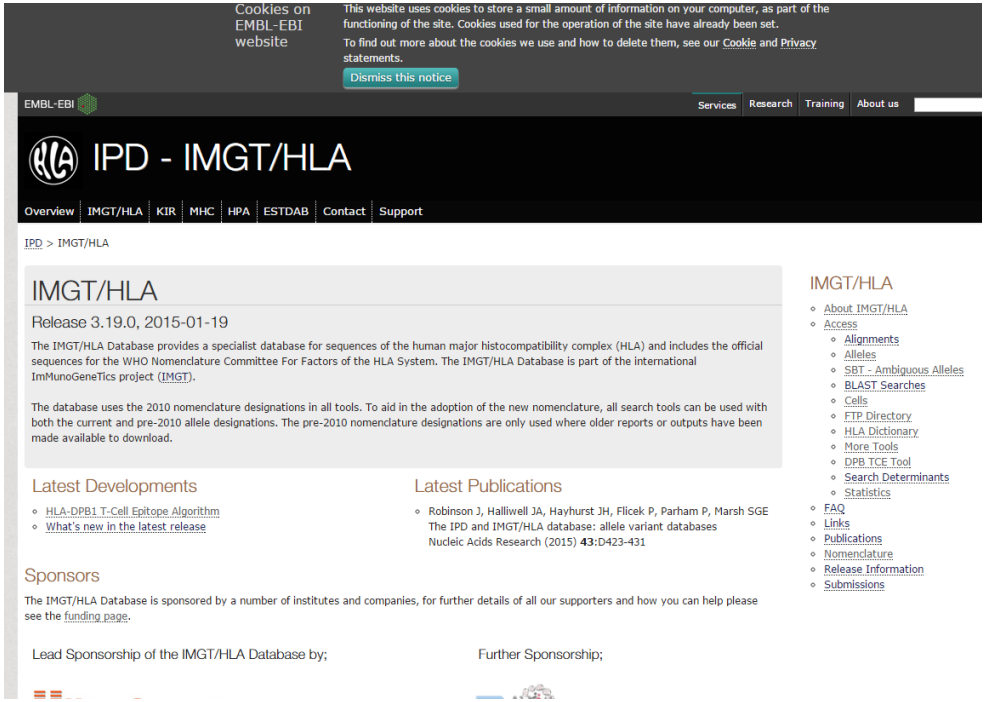
# datasets

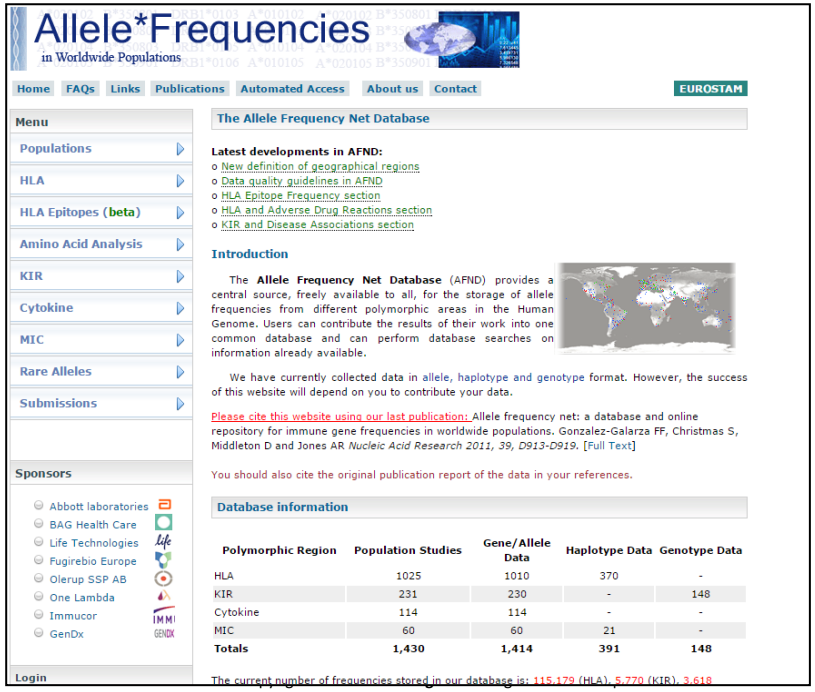
IMGT from EBI

Allele Frequency Net Database

- IPD IMGT/HLA – 12,672 alleles from Class I, Class II, and Class II–DRB genes

- IPD KIR – 753 alleles from 17 KIR genes (15 protein genes, 2 pseudo genes) – 27 fully sequenced KIR haplotypes



# HLA Pilot: 10 WGS data (x30) of RIKEN liver cancers

Plan A

BWAmem alignment to hg19

Unaligned reads

Aligned to HLA regions

BWAmem,
Novoalgn

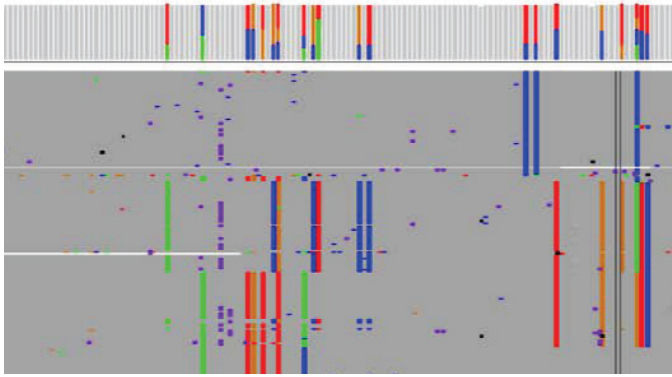
RE-alignment to IMGT/HLA Database

Plan B

BWAmem alignment to hg19 + IMGT/HLADatabase

Plan C

BWAmem alignment to (modified) IMGT/HLA Database



**BAM file for HLA regions**

Variant call by
- Tokyo・Korea new methods
- ATHLATES
- HLAminer
- GATK UnifiedGenotype

HLA genotype by SBT

| ID | HLA-A | | HLA-B | |
|---|---|---|---|---|
| RK014_B | A*26:03:01 | A*31:01:02 | B*35:01:01:01 | B*35:01:01:01 |
| RK032_B | A*02:01:02 | A*24:02:58 | B*40:06:01:01 | B*54:01:01 |
| RK041_B | A*24:02:01:01 | A*24:02:01:01 | B*52:01:01:01 | B*54:01:01 |
| RK053_B | A*24:02:01:01 | A*24:02:01:01 | B*15:18:01 | B*35:01:01:01 |
| RK092_B | A*24:02:01:01 | A*31:01:02 | B*35:01:01:01 | B*54:01:01 |
| RK135_B | A*02:07:01 | A*24:02:01:01 | B*46:01:01 | B*52:01:01:01 |
| RK139_B | A*02:01:01:01 | A*24:02:01:01 | B*44:03:01 | B*48:01:01 |
| RK153_B | A*24:02:01:01 | A*31:01:02 | B*40:02:01 | B*51:01:01 |
| RK167_B | A*24:02:01:01 | A*24:20 | B*40:01:01 | B*52:01:01:01 |
| RK287_B | A*11:01:01 | A*24:02:01:01 | B*15:01:01:01 | B*35:01:01:01 |
| RK303_B | A*11:01:01 | A*31:01:02 | B*15:01:01:01 | B*39:01:01:01 |

# HLA Genotyping from WGS Data

**Shuto Hayashi**[1], Rui Yamaguchi[1], Shinichi Mizuno[2], Mitsuhiro Konuma[1], Hidewaki Nakagawa[3], Satoru Miyano[1], **Seiya Imoto**[1]

[1]Human Genome Center, The Institute of Medical Sciences, The University of Tokyo

[2]Division of Cancer Research, Center for Advanced Medical Innovation, Kyushu University

[3]Laboratory for Genome Sequencing Analysis, Center for Integrative Medical Sciences, Riken

# Accuracy Rate for HLA Typing

We have evaluated our newly developed HLA typing method (**a Bayesian model and MCMC procedure for selecting HLA** using 20 pilot samples of Japanese liver cancer.

Table 1. The rate at which true HLA types are matched to the best output candidates.

| Resolution | HLA-A | HLA-B | HLA-C |
|---|---|---|---|
| 2-digit | 1.000 (40/40) | 0.975 (39/40) | 1.000 (40/40) |
| 4-digit | 1.000 (40/40) | 0.900 (36/40) | 0.825 (33/40) |
| (6-digit) | (0.975 (39/40)) | (0.875 (35/40)) | (0.825 (33/40)) |

Note: the HLA typing kit is guaranteed to 4-digit and the results of 6-digit is just for reference.

Table 2. The rate at which true HLA types are included in the output candidates.

| Resolution | HLA-A | HLA-B | HLA-C |
|---|---|---|---|
| 2-digit | 1.000 (40/40) | 1.000 (40/40) | 1.000 (40/40) |
| 4-digit | 1.000 (40/40) | 0.975 (39/40) | 0.975 (39/40) |
| (6-digit) | (0.975 (39/40)) | (0.950 (38/40)) | (0.975 (39/40)) |

Note: the HLA typing kit is guaranteed to 4-digit and the results of 6-digit is just for reference.

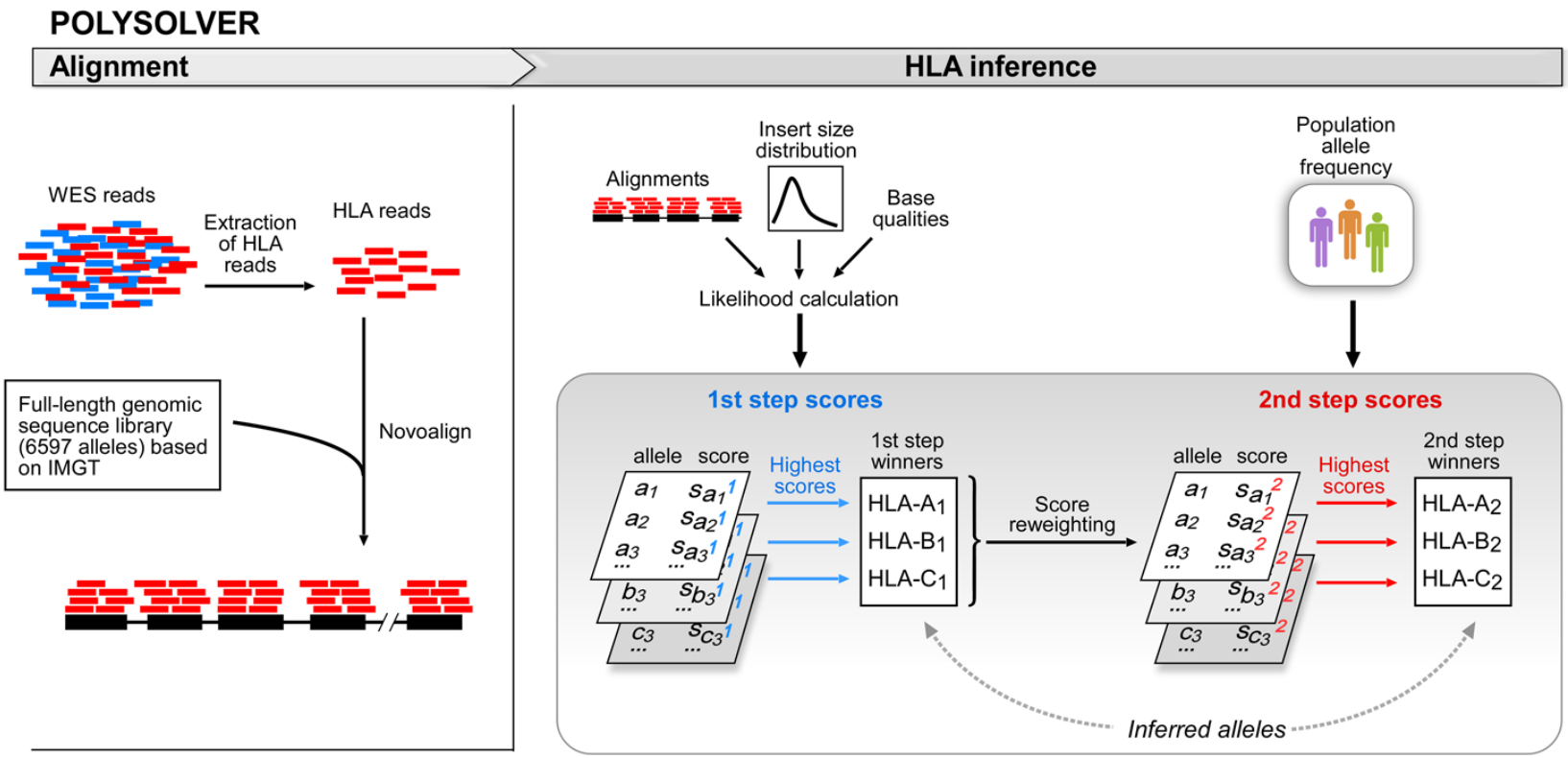
# A Key Task: Collecting HLA Reads

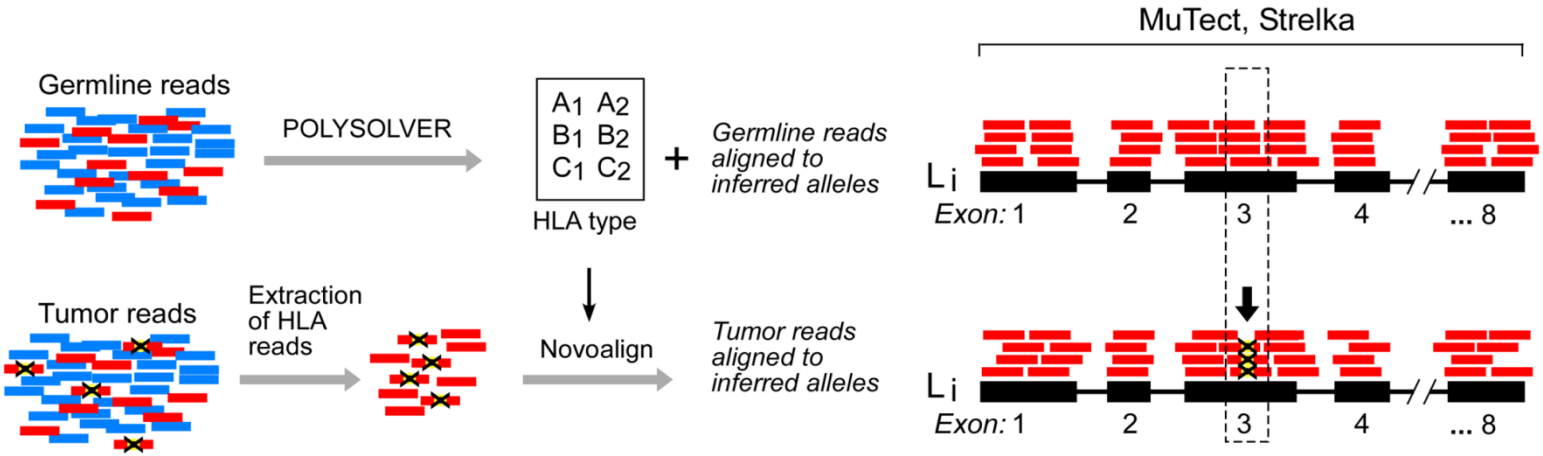
I. A "Plan-A BAM file" is converted to FASTQ files.
II. The reads in the FASTQ files are aligned to the IMGT/HLA Database using BWA-MEM.
III. The mapped reads are filtered based on the following information:
   ① The number of mismatches and indels
   ② Base qualities
   ③ Paired reads or single reads

Criteria for collecting reads are carefully tuned:

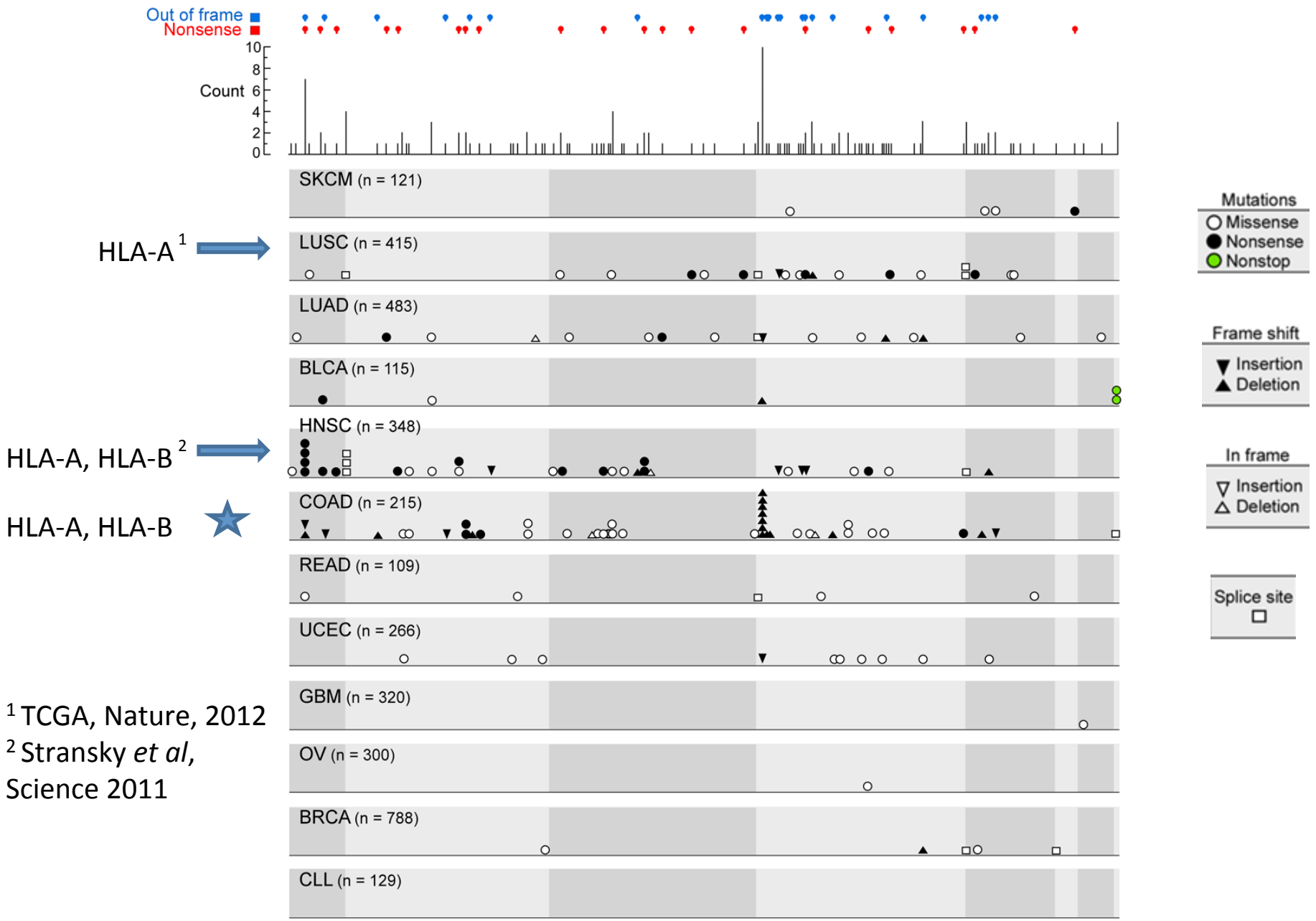
- If the criteria are too strict, the collected reads would be insufficient to determine the target HLA types. (low coverage)
- If the criteria are too loose, the collected reads would include a lot of reads produced by homologous non-target HLA genes and pseudogenes, which would lead to mistyping. (many false positives)

# HLA typing and mutation detection



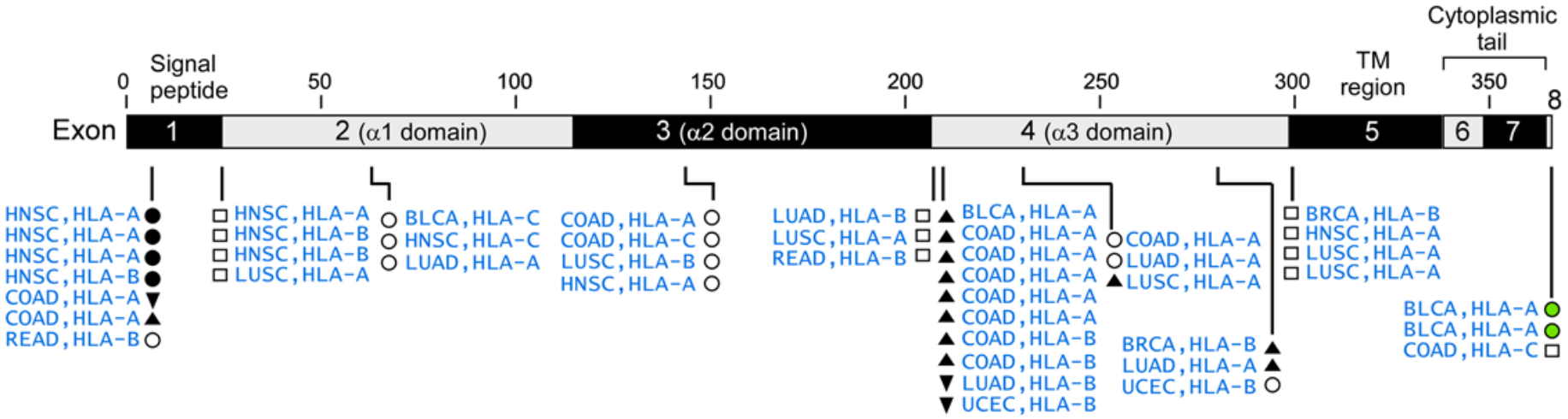



# Pan-cancer HLA mutational spectrum

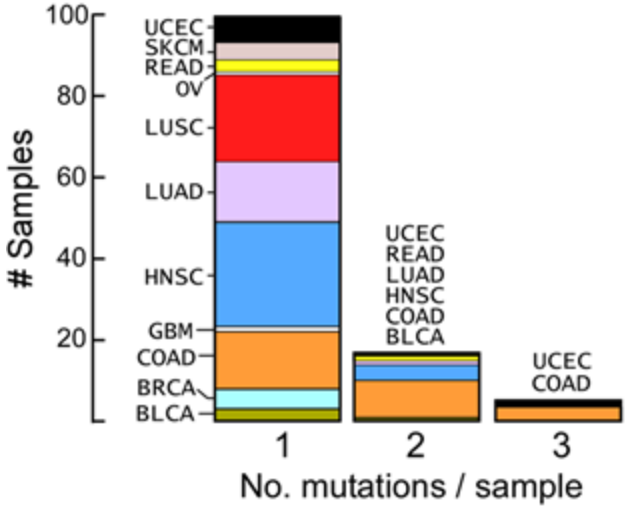



[1] TCGA, Nature, 2012
[2] Stransky *et al*, Science 2011

# Recurrent mutation sites indicate positive selection

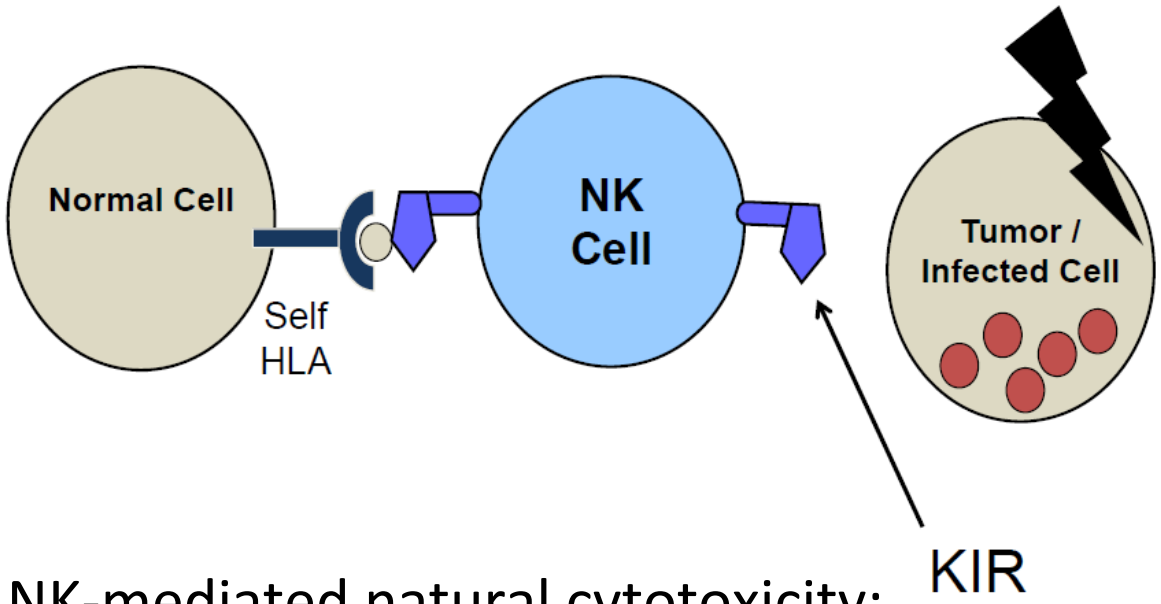



| Mutations | Frame shift | In frame | |
|---|---|---|---|
| ○ Missense<br>● Nonsense<br>● Nonstop | ▼ Insertion<br>▲ Deletion | ▽ Insertion<br>△ Deletion | Splice site □ |



# Killer Immunoglobulin-Like Receptors (KIR) Detect "Missing Self"

- test

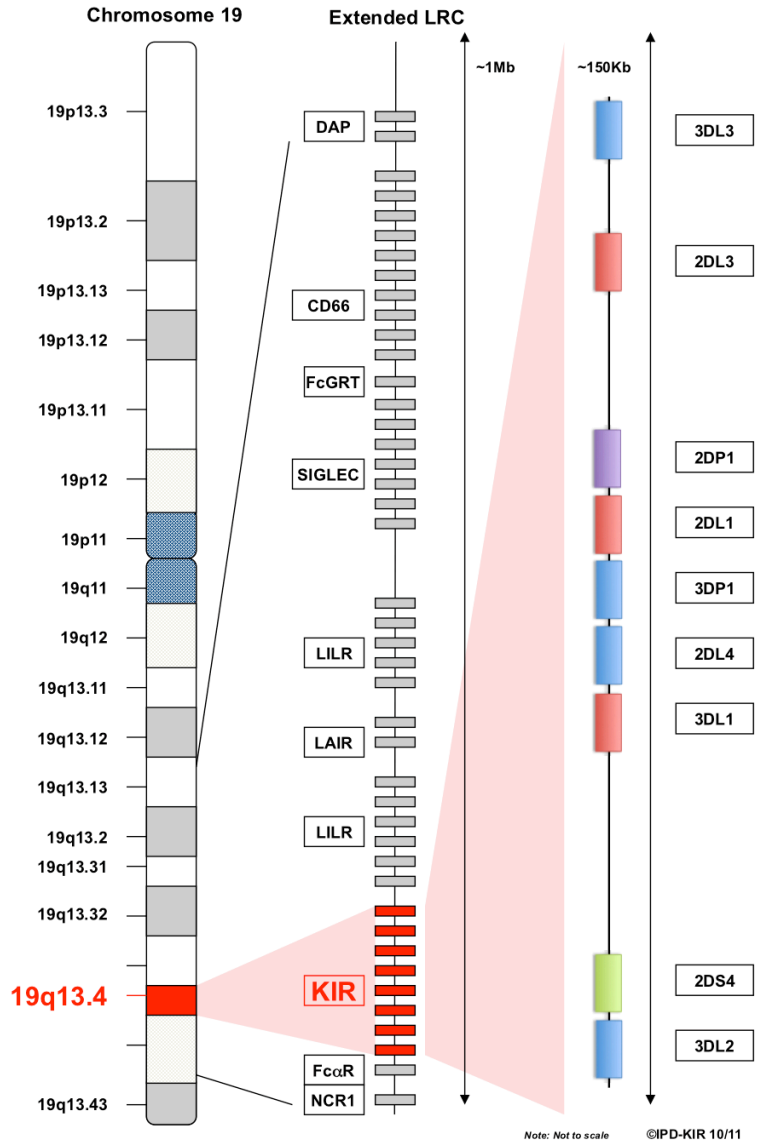



Triggering NK-mediated natural cytotoxicity:

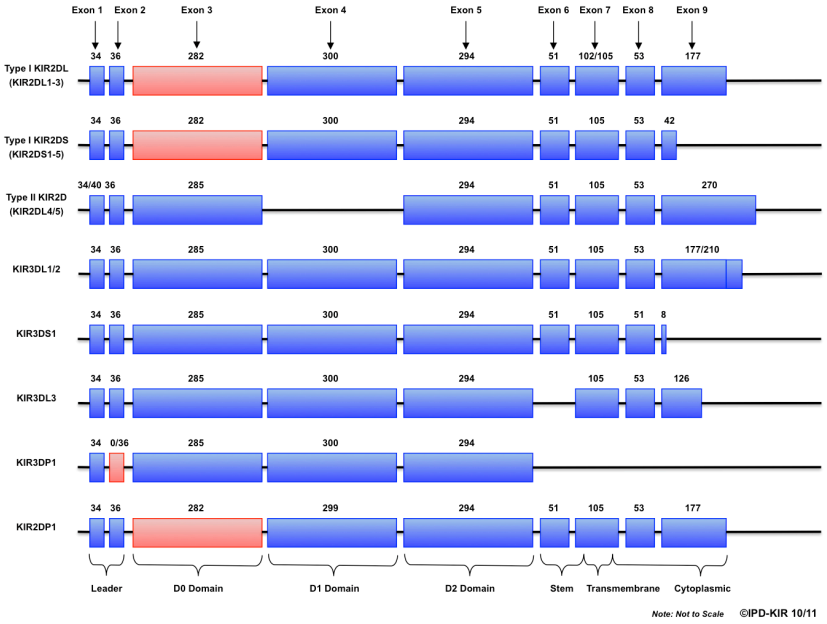
- KARs (meaning: Killer Activation Receptors)
- KIRs (meaning: Killer Inhibitory Receptors).

It is the balance between these competing signals that determines whether or not the cytotoxic activity of the NK cell should get started.

# KIR genes (1)



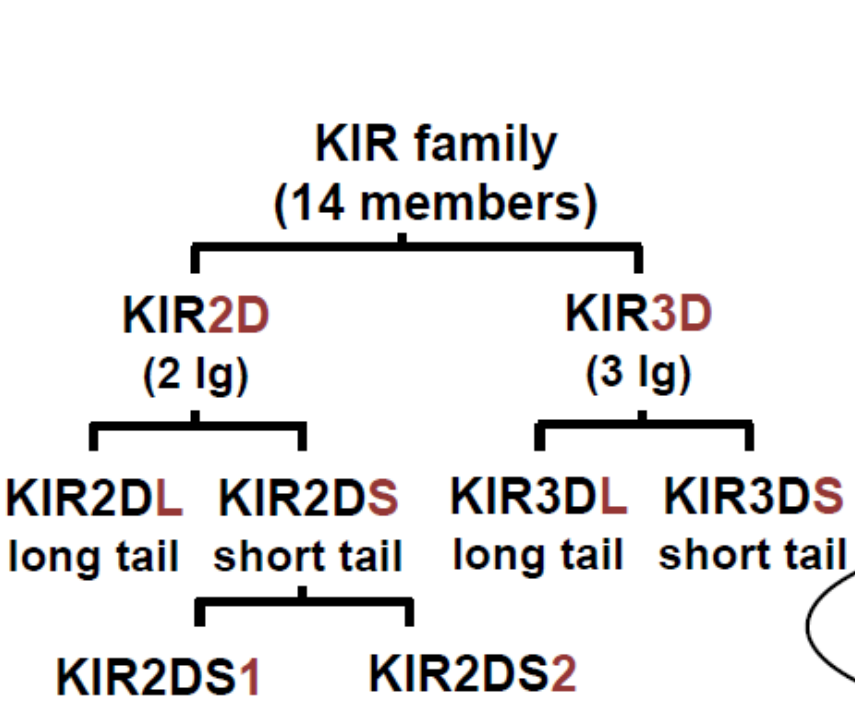

- KIR genes vary in length from 4 to 16 Kb
- three groups according to their structural feature
  - Type I KIR2D genes
  - Type II KIR2D genes
  - KIR3D genes

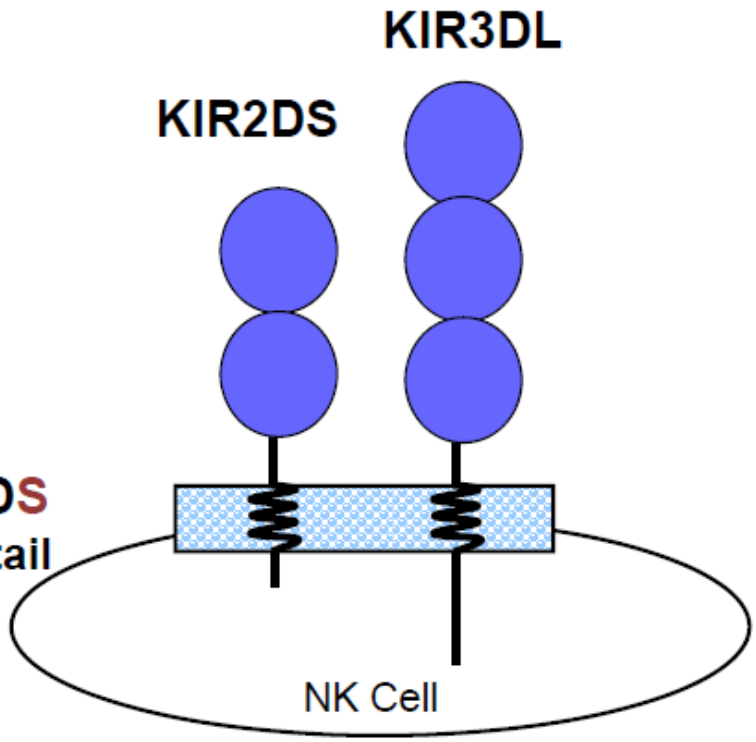


# KIR Genes (2)

14 KIR Based on Structure

- Family of 14 different receptors on surface of NK cells



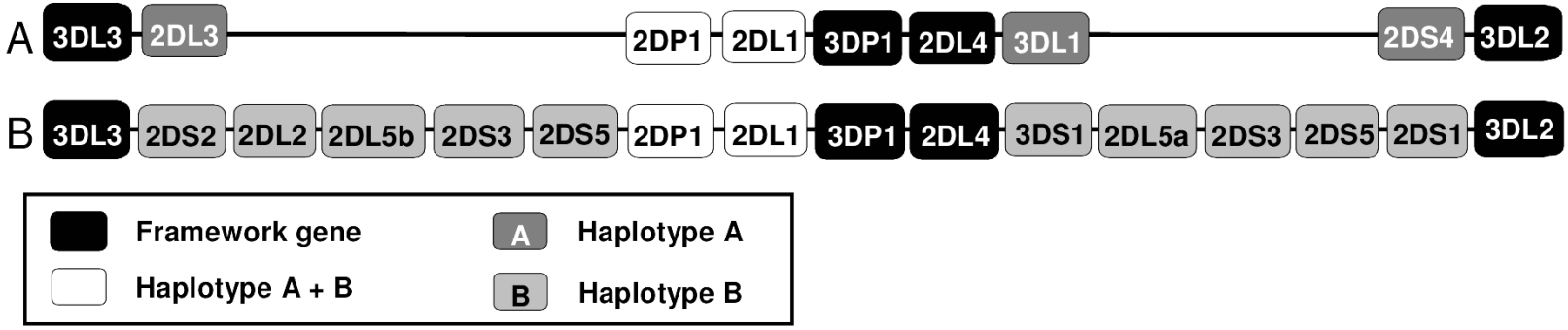



# KIR Genes (common)

These 5 Are most common in European Americans

- Centromeric
  - cA01 3DL3~2DL3~2DL1
  - cB01 3DL3~2DS2~2DL2~2DL5~2DS3~2DL1
  - cB02 3DL3~2DS2~2DL2

  Telomeric
  - tA01 2DL4~3DL1~2DS4~3DL2
  - tB01 2DL4~3DS1~2DL5~2DS5~2DS1~3DL2



# KIR genes Statistics for Release 2.6.0 (October 2014)

KIR Alleles : 753

| Gene | 2DL1 | 2DL2 | 2DL3 | 2DL4 | 2DL5 | 2DS1 | 2DS2 | 2DS3 | 2DS4 | 2DS5 | 3DL1 | 3DS1 | 3DL2 | 3DL3 | 2DP1 | 3DP1 | # of total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alleles | 48 | 30 | 55 | 52 | 48 | 16 | 22 | 15 | 31 | 18 | 110 | 30 | 112 | 111 | 28 | 27 | 753 |
| Proteins | 28 | 13 | 31 | 28 | 20 | 8 | 8 | 6 | 14 | 12 | 66 | 17 | 82 | 57 | 0 | 0 | 390 |
| Nulls | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 1 | 0 | 0 | 0 | 7 |

ully Sequenced KIR Haplotypes

he graphic below illustrates the gene compostion of a number of fully sequenced KIR haplotypes. Where possible the alleles sequenced at the genes are also listed. The allele designations will be displayed if you hover the mouse over the gene of nterest. Clicking on the gene of interest will also take you to the entry page for the allele listed. Some genes are only partially sequenced and for these an allele designation is not provided. Clicking on the Source name will take you to the Cell Directory ntry for the Haplotype source. The nomenclature for KIR haplotypes has not yet been implemented and the entry in the Hap. column uses a local designation for describing the haplotypes listed.

| ource | Haplotype | 3DL3 | 2DS2 | 2DL2/3 | 2DL5B | 2DS3/5 | 2DP1 | 2DL1 | 3DP1 | 2DL4 | 3DL1/S1 | 2DL5A | 2DS3/5 | 2DS1 | 2DS4 | 3DL2 | Sequence |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BC08 | A | | | 3 | | | | | | | L1 | | | | | | View |
| 085 | A | | | 3 | | | | | | | L1 | | | | | | View |
| SH | A | | | 3 | | | | | | | L1 | | | | | | View |
| H06 | A | | | 3 | | | | | | | L1 | | | | | | View |
| V5HL9-5B | A | | | 3 | | | | | | | L1 | | | | | | View |
| UCE | A | | | 3 | | | | | | | L1 | | | | | | View |
| H13 | A | | | 3 | | | | | | | L1 | | | | | | View |
| 248 | A | | | 3 | | | | | | | L1 | | | | | | View |
| 7526 | A | | | 3 | | | | | | | L1 | | | | | | View |
| H05 | A | | | 3 | | | | | | | L1 | | | | | | View |
| H15 | A | | | 3 | | | | | | | L1 | | | | | | View |
| H08 | A | | | 3 | | | | | | | L1 | | | | | | View |
| BC08 | AB | | | 3 | | | | | | | S1 | | | | | | View |
| RC212 | AB | | | 3 | | | | | | | S1 | | 3 | | | | View |

# Approach

**Reads Filtering**

- Reads mapped to HLA genes locus (6q21.1-21.3)
- Reads mapped to KIR regions (19q13.4)
- Unmapped reads

**Join Reads if possible**

- Overlapping Paired End Reads

**Alignment**

- Align each reads against all the allele sequences from IGMT/HLA and KIR databases

**Reads to Gene Mapping**

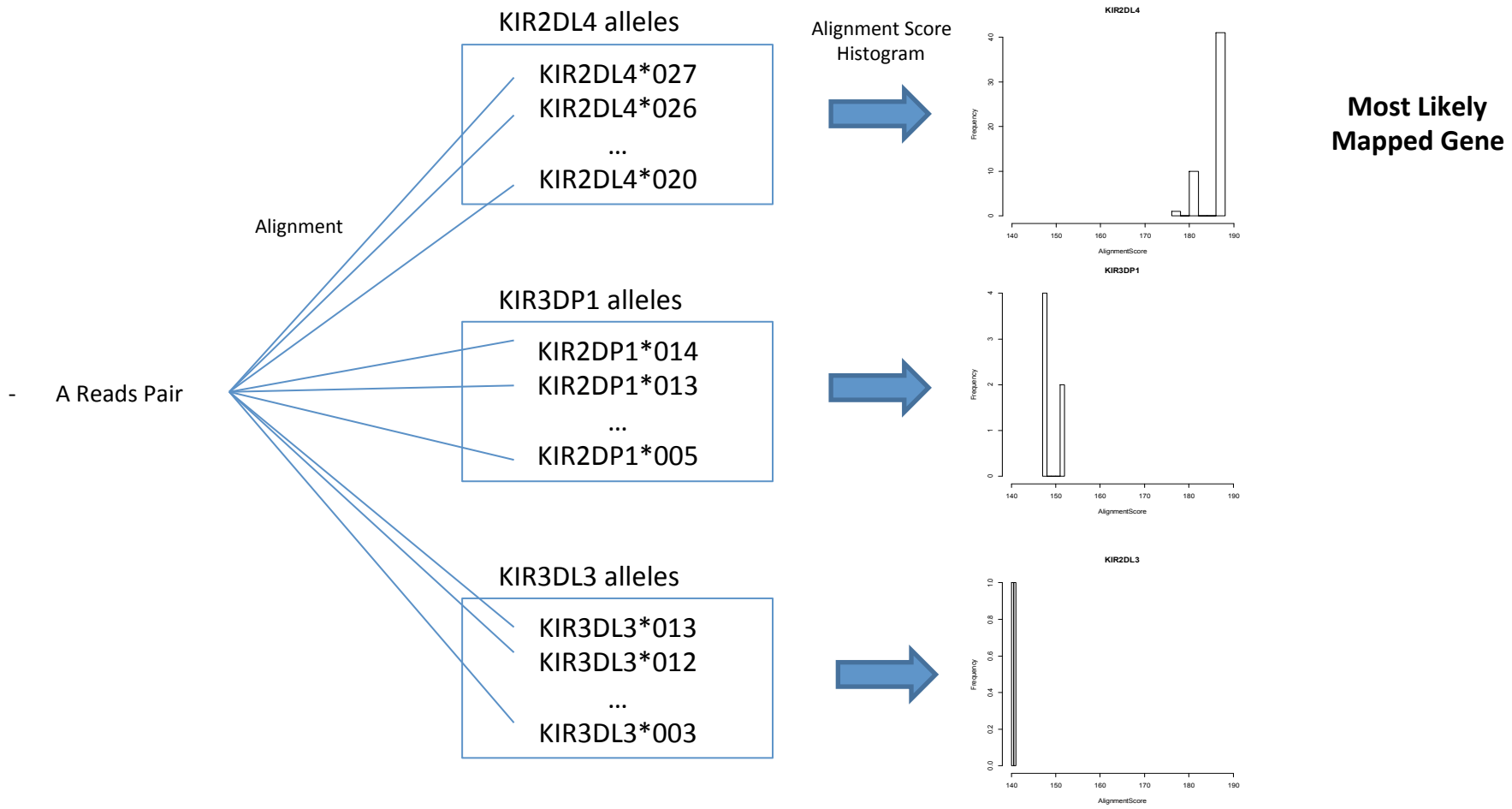
- How well aligned are the alleles of a gene with a read?

**Allele Inference**

- Which allele is the most well explained with the reads assigned to the gene?

By In Ho Park (SDS)

# Gene Mapping of Reads




By In Ho Park (SDS)

# Allele Inference with Alignment Score Matrix

KIR2DL4 gene alleles

Reads

| | KIR2DL4*027 | KIR2DL4*026 | … | KIR2DL4*021 | KIR2DL4*020 |
|---|---|---|---|---|---|
| $R_1$ | 187 (1) | 187 (1) | 187 (1) | 182 (4) | 176 (5) |
| $R_2$ | 180 (2) | 190 (1) | 180 (2) | 170 (4) | 170 (4) |
| $R_3$ | … (2) | … (1) | … (2) | … (4) | … (5) |
| $R_4$ | … (1) | … (1) | … (3) | … (4) | … (4) |
| $R_5$ | … (2) | … (1) | … (3) | … (4) | … (4) |
| $R_6$ | … (2) | … (1) | … (3) | … (4) | … (5) |
| RankSum | 10 | 6 | 14 | 24 | 27 |

**Most Possible Allele**

Each cell is filled with the alignment score and the rank within a row.

# SNU 04 examples

## Mapping at KIR coding regions

| SNU 04 example | Paired end (PE1) | Paired end (PE2) |
|---|---|---|
| Total # of reads | 2,096,062 | 2,096,062 |
| Initial Reads (Unmapped or Mapped at KIR region) | 8,356 | 8,238 |
| - PE1 and PE2 at the same time | 6,250 | |
| - uniquely mapping at a specific KIR gene | 1,567 | |
| - mapping at two KIR genes | 128 | |
| - mapping at three KIR genes | 29 | |
| - unmapped (all blast score is below than cutoff) | 4,526 | |

# of reads

# Read mapping

KIR genes

reads

| PE1 | _read_r | PE2 | _read_r | 2DL1 | 2DL2 | 2DL3 | 2DL4 | 2DL5A | 2DL5B | 2DP1 | 2DS1 | 2DS2 | 2DS3 | 2DS4 | 2DS5 | 3DL1 | 3DL2 | 3DL3 | 3DP1 | 3DS1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7980 | 7853 | 2004105 | [illegible] | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 159.5 | 187 | 0 |
| 7984 | 7859 | 2005227 | 2005227 | 0 | 151 | 151 | 0 | 0 | 0 | 133.5 | 0 | 0 | 0 | 187 | 0 | 0 | 149.5 | 0 | 0 | 0 |
| 7986 | 7862 | 2005660 | 2005660 | 0 | 153.5 | 155.5 | 0 | 0 | 0 | 151 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7998 | 7876 | 2008566 | 2008566 | 147.5 | 0 | 142 | 0 | 0 | 0 | 0 | 144.5 | 0 | 0 | 148.5 | 147.5 | 0 | 187 | 0 | 0 | 0 |
| 8001 | 7878 | 2009709 | 2009709 | 148 | 154 | 156.5 | 0 | 0 | 0 | 154 | 157 | 154 | 0 | 154 | 151.5 | 149 | 139 | 130.5 | 187 | 146.5 |
| 8010 | 7888 | 2012343 | 2012343 | 0 | 154.5 | 157.5 | 0 | 0 | 0 | 154 | 0 | 154.5 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8030 | 7909 | 2016349 | 2016349 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 175.5 | 0 | 0 | 181.5 |
| 8041 | 7918 | 2018272 | 2018272 | 185 | 186 | 185 | 0 | 0 | 0 | 166 | 0 | 0 | 0 | 0 | 0 | 177 | 158.5 | 164 | 0 | 0 |
| 8061 | 7940 | 2022753 | 2022753 | 148 | 154 | 154 | 0 | 0 | 0 | 156.5 | 148.5 | 154 | 0 | 154 | 157 | 187 | 0 | 0 | 0 | 184.5 |
| 8067 | 7944 | 2025000 | 2025000 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8069 | 7948 | 2025697 | 2025697 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 186 | 0 | 0 |
| 8070 | 7949 | 2025709 | 2025709 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8072 | 7951 | 2025878 | 2025878 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 172.5 | 0 | 0 | 179 |
| 8091 | 7963 | 2029962 | 2029962 | 0 | 0 | 0 | 187 | 0 | 0 | 113 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8092 | 7964 | 2030142 | 2030142 | 158.5 | 0 | 149.5 | 0 | 0 | 0 | 0 | 148.5 | 0 | 0 | 142.5 | 162 | 0 | 187 | 0 | 0 | 0 |
| 8095 | 7967 | 2030605 | 2030605 | 119.5 | 125 | 127 | 0 | 0 | 0 | 120 | 0 | 128 | 0 | 0 | 0 | 153.5 | 187 | 0 | 127 | 151 |
| 8097 | 7970 | 2030843 | 2030843 | 156.5 | 145 | 150 | 0 | 0 | 0 | 142 | 151 | 145 | 0 | 187 | 156.5 | 146.5 | 146.5 | 0 | 0 | 145 |
| 8101 | 7975 | 2032139 | 2032139 | 0 | 151 | 154 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8106 | 7980 | 2033162 | 2033162 | 187 | 153.5 | 156.5 | 0 | 0 | 0 | 150 | 184.5 | 153.5 | 159 | 0 | 0 | 0 | 0 | 0 | 159 | 0 |
| 8112 | 7985 | 2034362 | 2034362 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 182 | 0 | 156.5 | 0 | 0 | 0 | 0 | 0 | 154 | 0 |
| 8114 | 7988 | 2034700 | 2034700 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 173.5 | 0 | 0 | 181.5 |
| 8125 | 7997 | 2036778 | 2036778 | 162 | 154 | 156.5 | 0 | 0 | 0 | 156.5 | 156.5 | 154 | 0 | 157 | 162 | 0 | 187 | 0 | 0 | 0 |
| 8130 | 8001 | 2038067 | 2038067 | 141.5 | 151 | 151 | 0 | 0 | 0 | 144.5 | 136.5 | 151 | 139 | 0 | 136.5 | 187 | 157 | 0 | 147.5 | 181.5 |
| 8141 | 8011 | 2040527 | 2040527 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 | 0 |
| 8149 | 8021 | 2042403 | 2042403 | 187 | 167 | 172.5 | 0 | 0 | 0 | 170 | 173.5 | 167 | 164 | 156.5 | 181.5 | 150.5 | 161 | 0 | 148.5 | 149 |
| 8165 | 8034 | 2044973 | 2044973 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 186 | 0 | 0 |
| 8168 | 8036 | 2045201 | 2045201 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 184.5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 162 | 0 |
| 8180 | 8052 | 2049606 | 2049606 | 154.5 | 184.5 | 187 | 0 | 0 | 0 | 172.5 | 155 | 179 | 154 | 0 | 154 | 0 | 117 | 118.5 | 154.5 | 0 |
| 8187 | 8057 | 2051226 | 2051226 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8196 | 8064 | 2052613 | 2052613 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8198 | 8068 | 2053614 | 2053614 | 155.5 | 153 | 158.5 | 0 | 0 | 0 | 153 | 153 | 153 | 0 | 187 | 155.5 | 149.5 | 147.5 | 0 | 0 | 149.5 |
| 8205 | 8079 | 2055257 | 2055257 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8213 | 8085 | 2056603 | 2056603 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 |
| 8221 | 8092 | 2058819 | 2058819 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 170.5 | 187 | 0 |
| 8225 | 8095 | 2059696 | 2059696 | 142.5 | 156.5 | 156.5 | 0 | 0 | 0 | 154 | 0 | 0 | 140 | 187 | 0 | 0 | 0 | 0 | 143 | 0 |
| 8229 | 8100 | 2061370 | 2061370 | 170.5 | 157 | 165 | 0 | 0 | 0 | 159.5 | 165 | 157 | 154 | 187 | 168 | 156 | 160 | 0 | 0 | 153 |
| 8232 | 8103 | 2061682 | 2061682 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 |
| 8242 | 8113 | 2063794 | 2063794 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 | 0 |
| 8243 | 8114 | 2064048 | 2064048 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 153.5 | 0 |
| 8245 | 8116 | 2064365 | 2064365 | 148.5 | 153.5 | 156.5 | 0 | 0 | 0 | 153.5 | 157 | 153.5 | 0 | 153 | 151 | 143 | 137 | 126 | 187 | 140 |
| 8247 | 8118 | 2064579 | 2064579 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8248 | 8119 | 2064724 | 2064724 | 171 | 184.5 | 184.5 | 0 | 127.5 | 127.5 | 187 | 159.5 | 184.5 | 179 | 145.5 | 165 | 0 | 145.5 | 0 | 142.5 | 0 |
| 8260 | 8127 | 2067785 | 2067785 | 153 | 0 | 147.5 | 0 | 0 | 0 | 0 | 145 | 0 | 0 | 136.5 | 156 | 0 | 187 | 0 | 0 | 0 |
| 8263 | 8129 | 2068305 | 2068305 | 187 | 165 | 173.5 | 0 | 0 | 0 | 171 | 173.5 | 161 | 159.5 | 164 | 181.5 | 144.5 | 156.5 | 0 | 147.5 | 145 |
| 8264 | 8130 | 2068448 | 2068448 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 160 | 0 |
| 8267 | 8135 | 2070242 | 2070242 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 173.5 | 0 | 0 | 181.5 |
| 8273 | 8141 | 2071555 | 2071555 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 156.5 | 0 | 0 | 181.5 |
| 8274 | 8142 | 2071954 | 2071954 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 | 0 |
| 8277 | 8145 | 2072299 | 2072299 | 162 | 158.5 | 161 | 0 | 0 | 0 | 150.5 | 155 | 158.5 | 157.5 | 149.5 | 151 | 0 | 124.5 | 0 | 187 | 0 |
| 8282 | 8150 | 2073711 | 2073711 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 |
| 8285 | 8153 | 2073973 | 2073973 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 0 | 0 |
| 8287 | 8156 | 2074190 | 2074190 | 0 | 167.5 | 176 | 0 | 0 | 0 | 187 | 0 | 162 | 0 | 146.5 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8292 | 8161 | 2074715 | 2074715 | 0 | 151 | 154 | 0 | 0 | 0 | 147.5 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8293 | 8164 | 2075342 | 2075342 | 158.5 | 158.5 | 161.5 | 0 | 0 | 0 | 164 | 0 | 0 | 0 | 0 | 0 | 182 | 187 | 0 | 0 | 0 |
| 8303 | 8173 | 2078716 | 2078716 | 143.5 | 0 | 152 | 0 | 141 | 141 | 0 | 149 | 0 | 0 | 156.5 | 149 | 187 | 138.5 | 118.5 | 148.5 | 184.5 |
| 8305 | 8176 | 2079836 | 2079836 | 0 | 0 | 0 | 187 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8315 | 8190 | 2084101 | 2084101 | 187 | 154 | 154 | 0 | 0 | 0 | 154 | 182 | 151 | 159.5 | 0 | 0 | 0 | 0 | 0 | 162 | 0 |
| 8333 | 8214 | 2089210 | 2089210 | 167.5 | 181.5 | 184.5 | 0 | 0 | 0 | 187 | 170.5 | 181.5 | 170.5 | 171 | 170.5 | 0 | 156.5 | 131.5 | 151 | 0 |
| 8335 | 8216 | 2089836 | 2089836 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 187 | 168 | 0 | 0 | 179 |
| 8343 | 8228 | 2092734 | 2092734 | 159.5 | 184.5 | 187 | 0 | 0 | 0 | 176 | 153.5 | 179 | 154 | 154 | 148 | 125 | 120 | 0 | 156.5 | 0 |
| 8346 | 8230 | 2093611 | 2093611 | 154 | 0 | 148.5 | 0 | 0 | 0 | 0 | 148.5 | 0 | 0 | 148 | 156.5 | 0 | 187 | 0 | 0 | 0 |
| | | | | 106 | 1 | 31 | 230 | 0 | 0 | 78 | 0 | 0 | 0 | 141 | 0 | 236 | 241 | 300 | 203 | 0 |

Row : uniquely mapping reads (PE1 & PE2)

Column : KIR genes

Value : blast scores

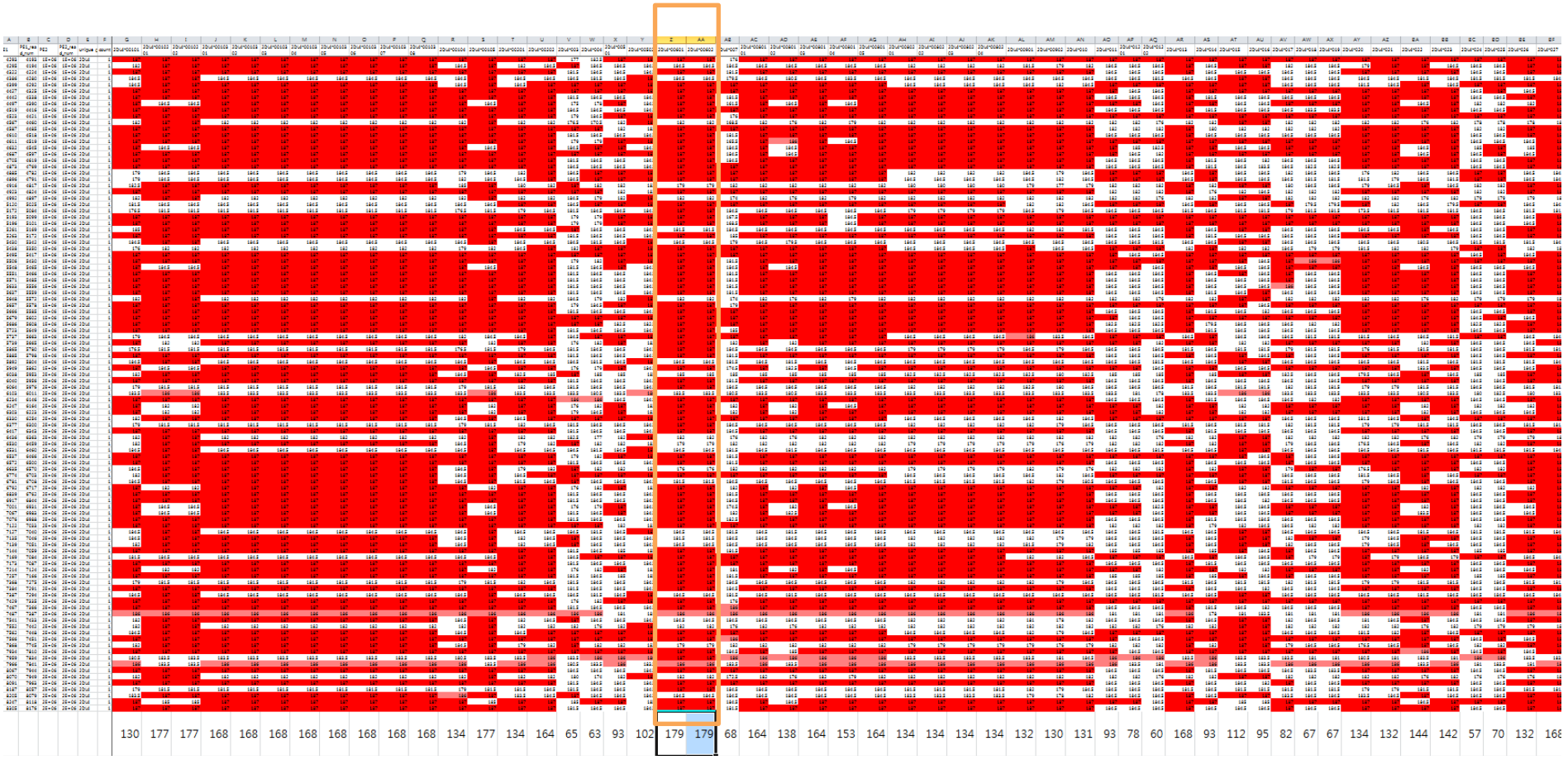
(red : perfect match)

# of reads

# Alleles (2DL4)

**Candidate alleles**

2DL4*00601,2DL4*00602



Copyright © 2014 **Samsung SDS** All rights reserved | Confidential