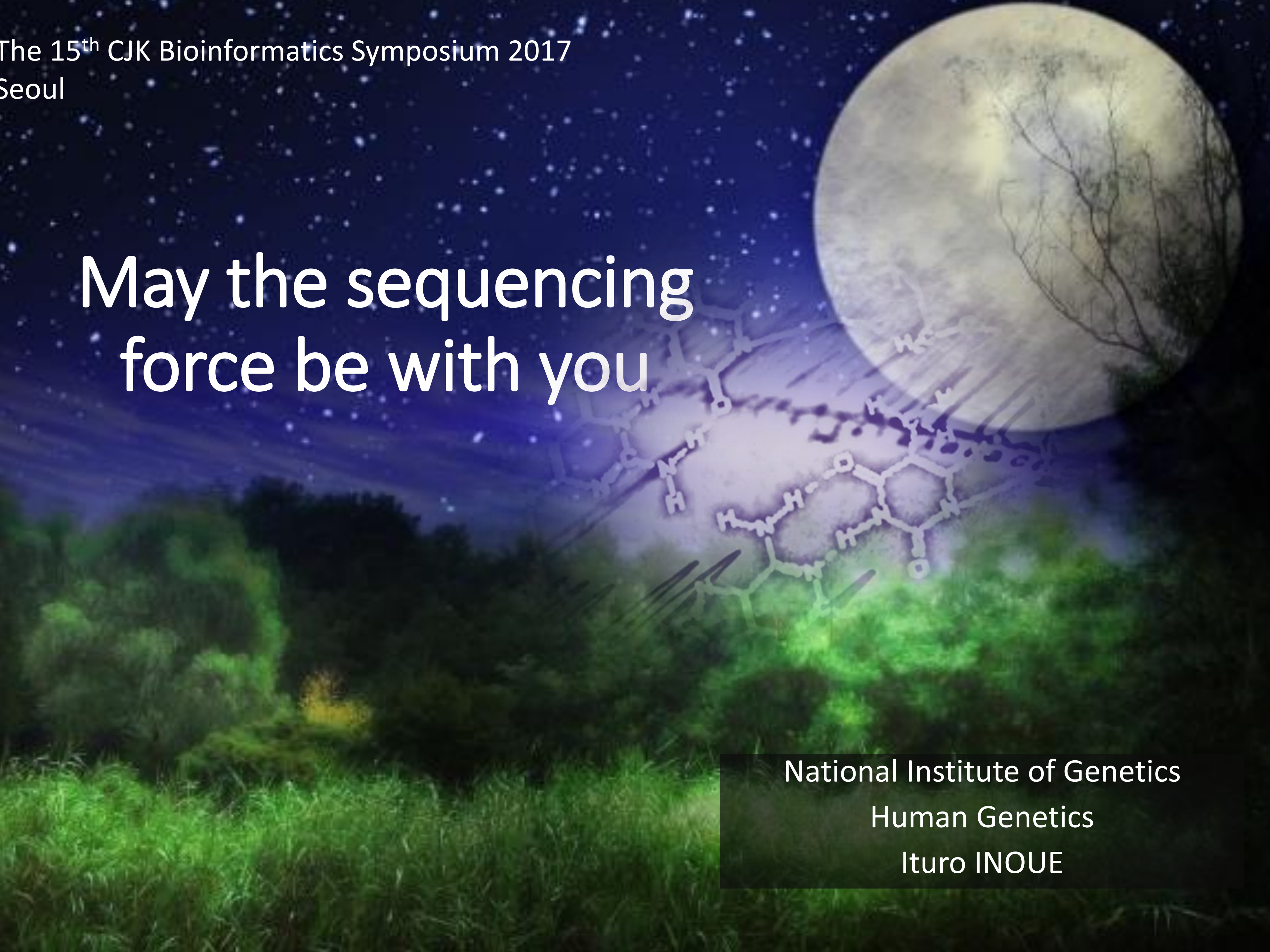
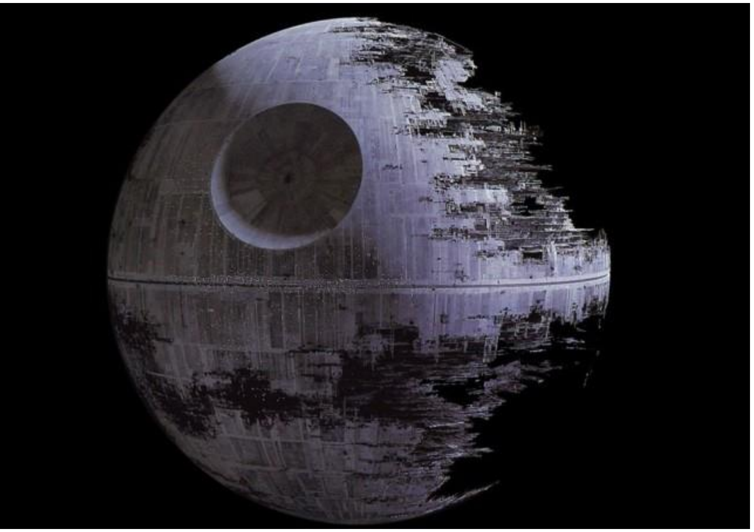
The 15th CJK Bioinformatics Symposium 2017
Seoul



May the sequencing force be with you

National Institute of Genetics
Human Genetics
Ituro INOUE



2013 January

Official White House Response to Secure resources and funding, and begin construction of a Death Star by 2016.

This Isn't the Petition Response You're Looking For

By Paul Shawcross

The Administration shares your desire for job creation and a strong national defense, but a Death Star isn't on the horizon. Here are a few reasons:

The construction of the Death Star has been estimated to cost more than $850,000,000,000,000,000. We're working hard to reduce the deficit, not expand it.

The Administration does not support blowing up planets.

Why would we spend countless taxpayer dollars on a Death Star with a fundamental flaw that can be exploited by a one-man starship?

“Don't be too proud of this technological terror you've constructed. The ability to destroy a planet is insignificant next to the power of the force.”

By Darth Vader (Episode IV)

Genealogy of Human Genome Project

1986 Renato Dulbecco

Essential to study genome structure to understand cancer biology

1991 International consortium with US, Europe, and Japan

1994 Completion of human genome map

Genetic mapping：

marker position was determined by genetic linkage analysis

Physical mapping：

with YAC, BAC, PAC clones, contig was completed

1996 1st Bermuda Conference

Sequencing:

Shotgun-sequencing of BAC, PAC clones,
High-throughput sequencing technology ABI3700; capillary sequencer

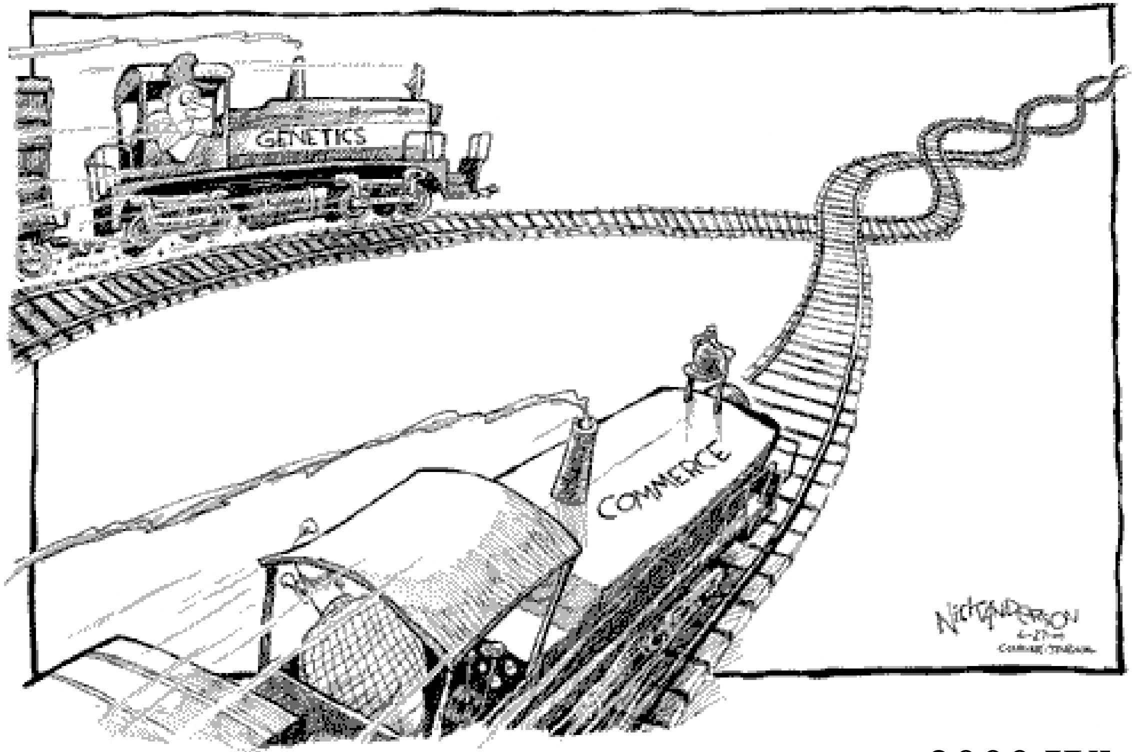
In silico analysis:

Gene identification with Bio-informatics

Data release and sharing policy

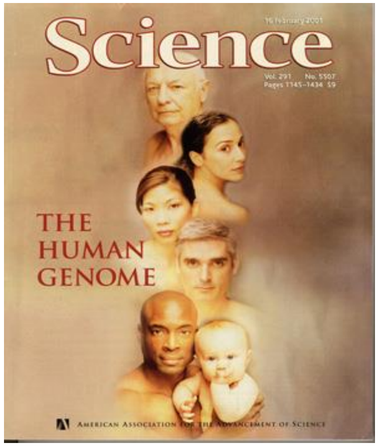
1998 NIH and DOE sign MOA for launching NHGRI

1998 Celera announced their own project

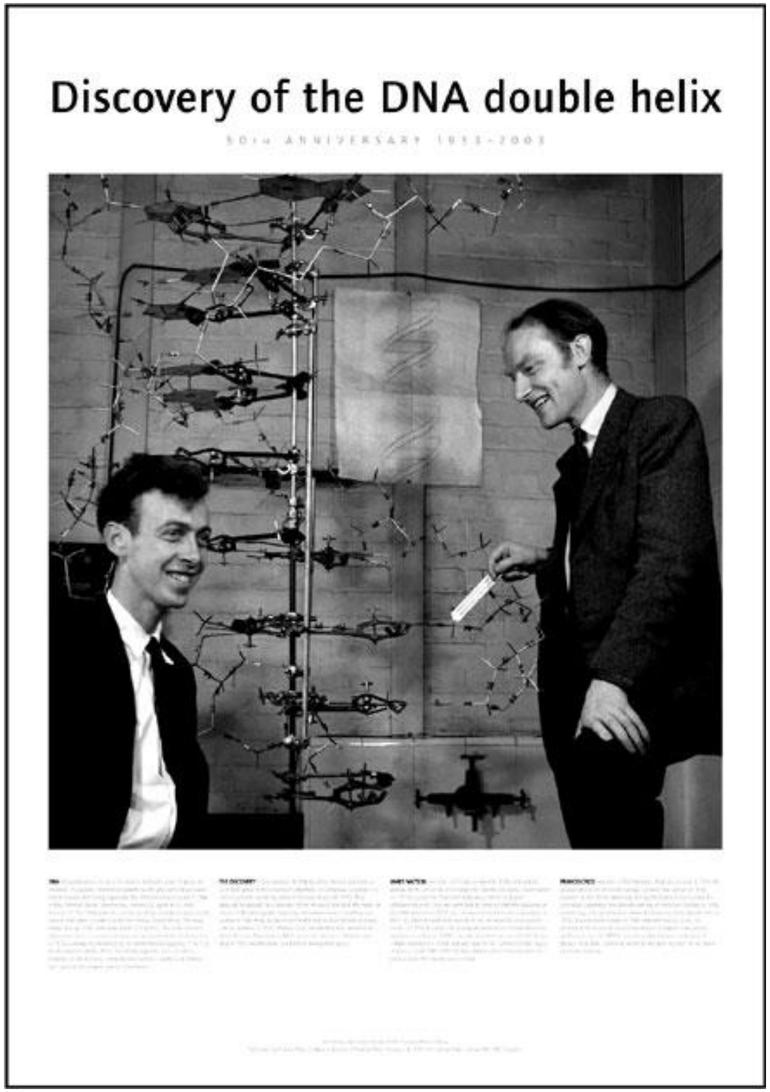


2001 February

Draft sequence of Human Genome



2000 White House with Bill Clinton



DNA Double Helix 1953

Complete Decoding of Human Genome

2003 April 14th

Ultimate Goals of Human Genome Project

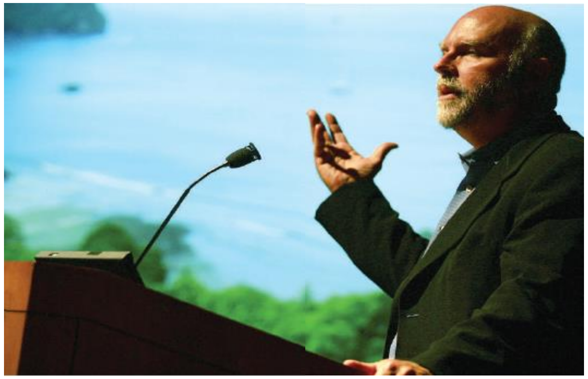
Biomarker Discovery

Target Therapy

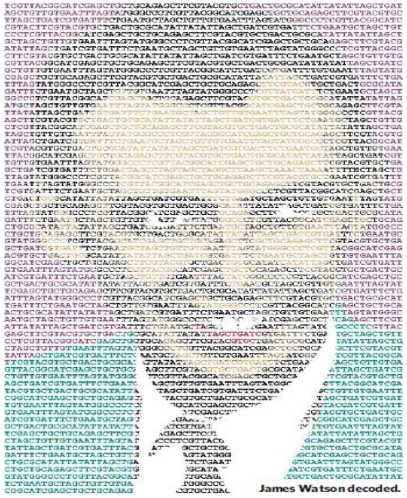
Personalized Medicine

Drug Development

Personal Genome of the Four



PLoS Biology Oct 2007



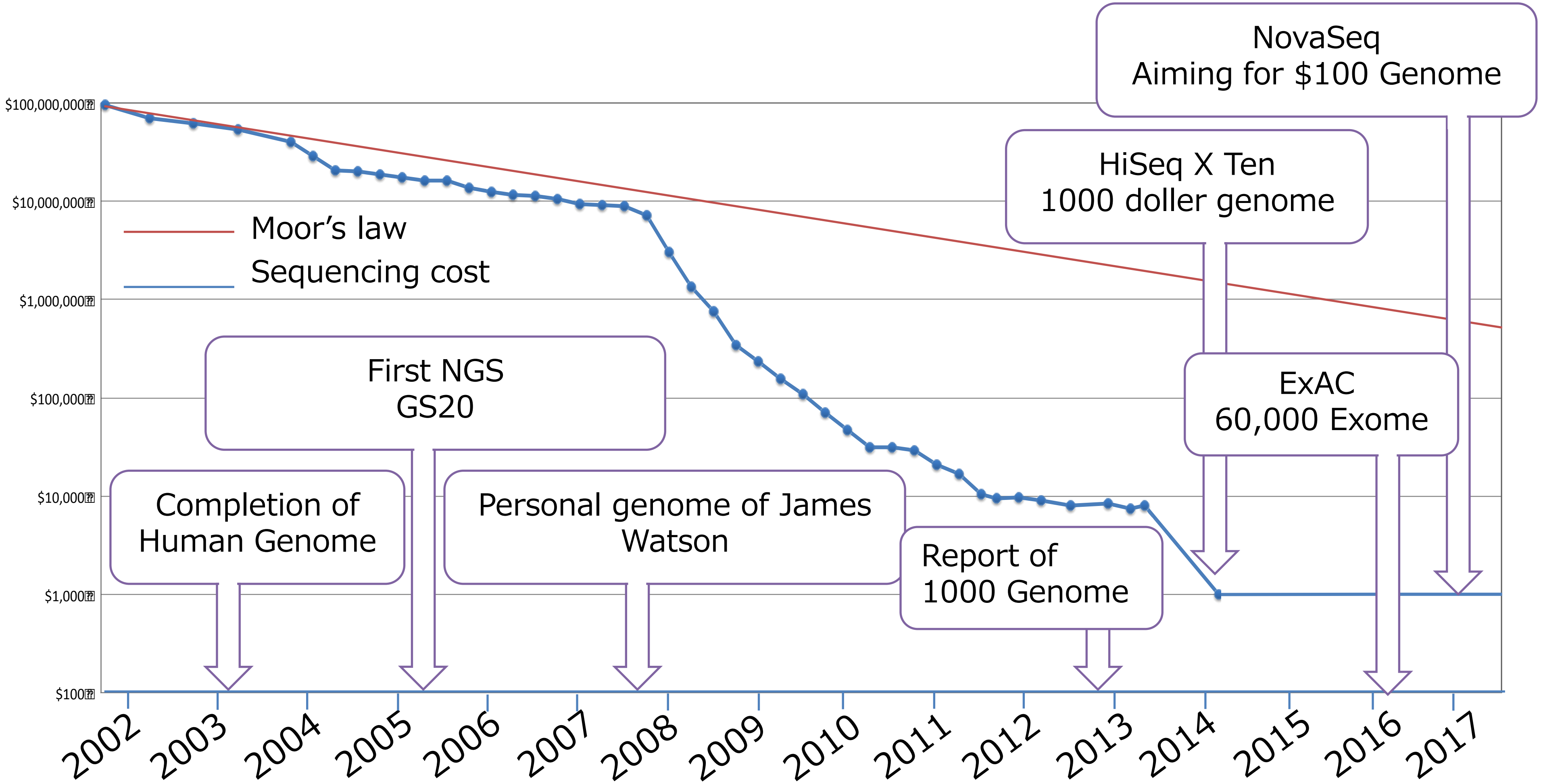
Nature April 2008

Nature
November, 2008

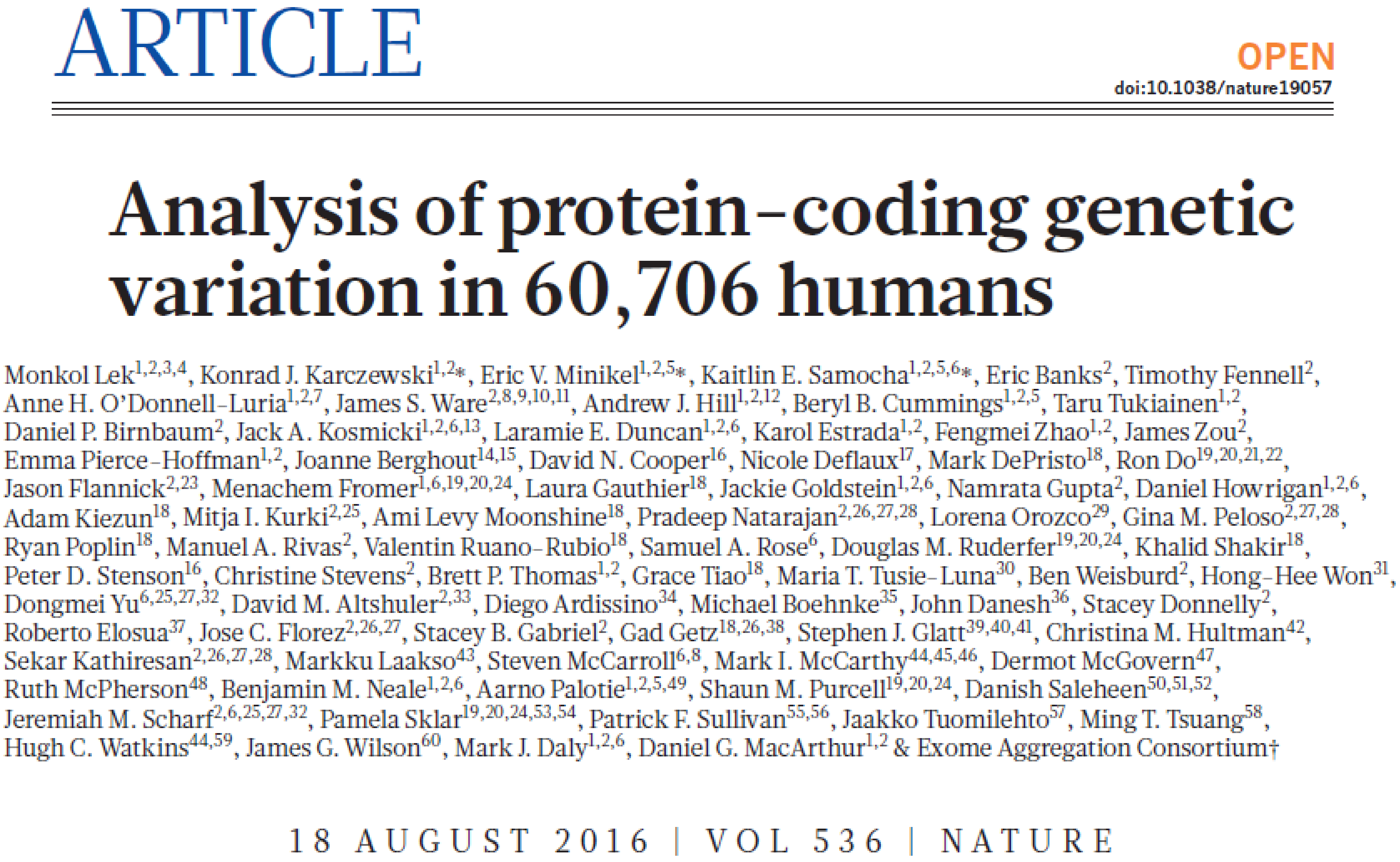
Yoruba man, Nigeria

YH, Han Chinese

Advent of NGS and cost for Human Genome



Costs for Human Genome	
2001	$3,700,000,000
2007	$350,000
2014	$1,000



ARTICLE

OPEN

doi:10.1038/nature19057

Analysis of protein-coding genetic variation in 60,706 humans

Monkol Lek[1,2,3,4], Konrad J. Karczewski[1,2]*, Eric V. Minikel[1,2,5]*, Kaitlin E. Samocha[1,2,5,6]*, Eric Banks[2], Timothy Fennell[2], Anne H. O'Donnell-Luria[1,2,7], James S. Ware[2,8,9,10,11], Andrew J. Hill[1,2,12], Beryl B. Cummings[1,2,5], Taru Tukiainen[1,2], Daniel P. Birnbaum[2], Jack A. Kosmicki[1,2,6,13], Laramie E. Duncan[1,2,6], Karol Estrada[1,2], Fengmei Zhao[1,2], James Zou[2], Emma Pierce-Hoffman[1,2], Joanne Berghout[14,15], David N. Cooper[16], Nicole Deflaux[17], Mark DePristo[18], Ron Do[19,20,21,22], Jason Flannick[2,23], Menachem Fromer[1,6,19,20,24], Laura Gauthier[18], Jackie Goldstein[1,2,6], Namrata Gupta[2], Daniel Howrigan[1,2,6], Adam Kiezun[18], Mitja I. Kurki[2,25], Ami Levy Moonshine[18], Pradeep Natarajan[2,26,27,28], Lorena Orozco[29], Gina M. Peloso[2,27,28], Ryan Poplin[18], Manuel A. Rivas[2], Valentin Ruano-Rubio[18], Samuel A. Rose[6], Douglas M. Ruderfer[19,20,24], Khalid Shakir[18], Peter D. Stenson[16], Christine Stevens[2], Brett P. Thomas[1,2], Grace Tiao[18], Maria T. Tusie-Luna[30], Ben Weisburd[2], Hong-Hee Won[31], Dongmei Yu[6,25,27,32], David M. Altshuler[2,33], Diego Ardissino[34], Michael Boehnke[35], John Danesh[36], Stacey Donnelly[2], Roberto Elosua[37], Jose C. Florez[2,26,27], Stacey B. Gabriel[2], Gad Getz[18,26,38], Stephen J. Glatt[39,40,41], Christina M. Hultman[42], Sekar Kathiresan[2,26,27,28], Markku Laakso[43], Steven McCarroll[6,8], Mark I. McCarthy[44,45,46], Dermot McGovern[47], Ruth McPherson[48], Benjamin M. Neale[1,2,6], Aarno Palotie[1,2,5,49], Shaun M. Purcell[19,20,24], Danish Saleheen[50,51,52], Jeremiah M. Scharf[2,6,25,27,32], Pamela Sklar[19,20,24,53,54], Patrick F. Sullivan[55,56], Jaakko Tuomilehto[57], Ming T. Tsuang[58], Hugh C. Watkins[44,59], James G. Wilson[60], Mark J. Daly[1,2,6], Daniel G. MacArthur[1,2] & Exome Aggregation Consortium†

18 AUGUST 2016 | VOL 536 | NATURE

Database ↔ **Data sharing**

Deep sequencing of 10,000 human genomes

Amalio Telenti[a,b,1], Levi C. T. Pierce[a,c,1], William H. Biggs[a,1], Julia di Iulio[a,b], Emily H. M. Wong[a], Martin M. Fabani[a], Ewen F. Kirkness[a], Ahmed Moustafa[a], Naisha Shah[a], Chao Xie[d], Suzanne C. Brewerton[d], Nadeem Bulsara[a], Chad Garner[a], Gary Metzker[a], Efren Sandoval[a], Brad A. Perkins[a], Franz J. Och[a,c], Yaron Turpaz[a,d], and J. Craig Venter[a,b,2]

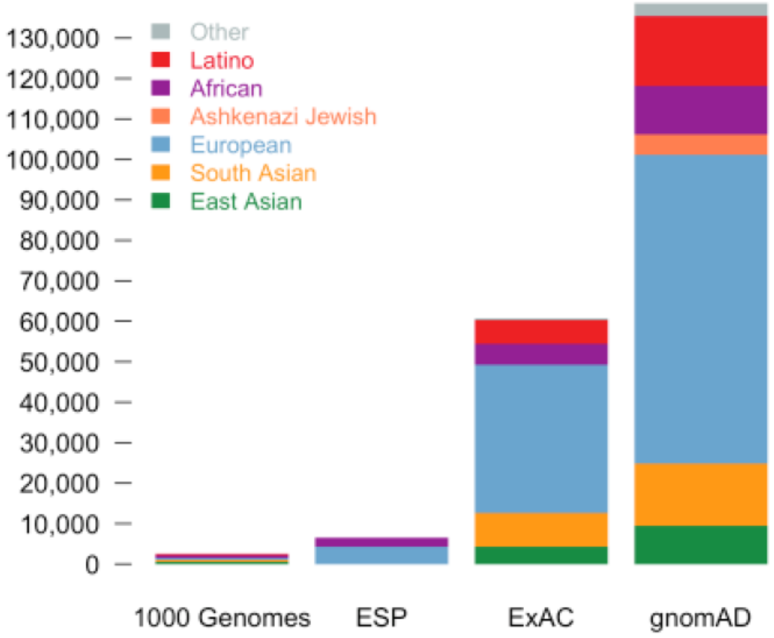
[a]Human Longevity Inc., San Diego, CA 92121; [b]J. Craig Venter Institute, La Jolla, CA 92037; [c]Human Longevity Inc., Mountain View, CA 94041; and [d]Human Longevity Singapore Pte. Ltd., Singapore 138542

Contributed by J. Craig Venter, August 18, 2016 (sent for review July 1, 2016; reviewed by David B. Goldstein and Stephen W. Scherer)

PNAS | October 18, 2016 | vol. 113 | no. 42 | 11901–11906

Genome Aggregation Database (gnomAD)

May 31st 2017



POPULATION	DESCRIPTION	GENOMES	EXOMES	TOTAL
AFR	African/African American	4,368	7,652	12,020
AMR	Admixed American	419	16,791	17,210
ASJ	Ashkenazi Jewish	151	4,925	5,076
EAS	East Asian	811	8,624	9,435
FIN	Finnish	1,747	11,150	12,897
NFE	Non-Finnish European	7,509	55,860	63,369
SAS	South Asian	0	15,391	15,391
OTH	Other (population not assigned)	491	2,743	3,234
	Total	15,496	123,136	138,632

Advanced Genomics Center at NIG

High-Throughput Sequencing System

ABI 3730xl

Illumina HiSeq2500

PacBio RSII / Sequel

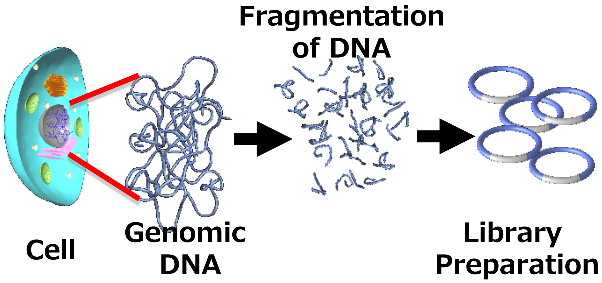
Irys

Chromium

MinION

close cooperation

Genome Resources



Fragmentation of DNA

Cell

Genomic DNA

Library Preparation

Pickers

DNA Prep Machines

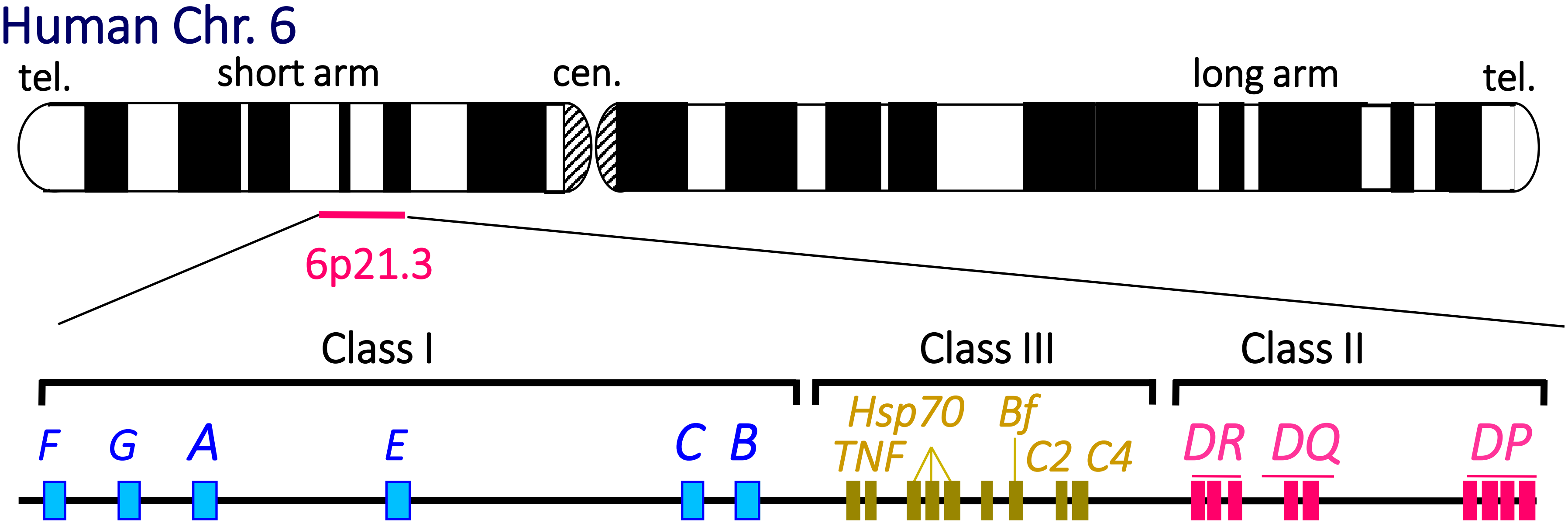
Ultra-Deep Freezers

PCR Machines

Informatics

DDBJ Supercomputer

Genomic features of the HLA region



HLA is

- **Critical for “self” and “non-self” discrimination.**
- **Involved in inflammation, the complement cascade, innate and adaptive immune responses.**
- **Observed from shark to human.**
- **Strongly associated with more than 100 diseases and adverse drug reactions.**

HLA associated diseases

Disease	Specified diseases	Susceptible genes
Myasthenia gravis (MG)	○	HLA-DRB1*0901
Aarcoidosis	○	HLA-DRB1*11/14/08
Diffuse panbronchiolitis (DPB)	○	DDR1?, MICA?
Ulcerative colitis (UC)	○	HLA-B*5201
Crohn's disease	○	HLA-DRB4*0103
Autoimmune hepatitis	○	HLA-DRB1*04/15
Primary biliary cirrhosis (PBC)	○	HLA-DRB1*0803
Behcet's disease	○	HLA-B*5101, -A*2601, TRIM10?
Malignant rheumatoid arthritis (MRA)	○	NFKBIL1
Systemic sclerosis (SSc)	○	HLA-DQB1*0501
Pustular psoriasis	○	HLA-DQB1*0303
Pemphigus vulgaris	○	HLA-DRB1*0406/1406
Mixed connective tissue disease (MCTD)	○	HLA-DRB1*0401
Juvenile-onset type diabetes mellitus		HLA-DRB1*0405/-DQB*0401
Rheumatoid arthritis (RA)		HLA-DRB1*0405, NFKBIL1
Psoriasis vulgaris		HLA-Cw*0602, SEEK1?
Vogt-Koyanagi-Harada syndrome (VKH)		HLA-DQB1*0401/0402
Lung cancer		HLA-DQA1*03

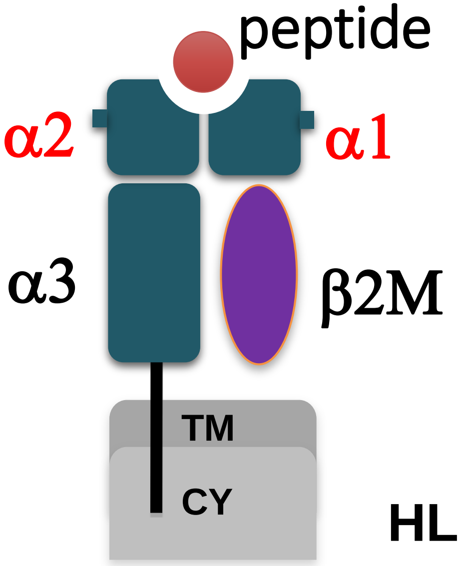
Drug adverse reaction associated with HLA allele

Drug adverse reaction	HLA allele	Positive rate	OR
Tiopronin and intrahepatic cholestasis	*HLA-A*33:03*	100%	41.5
Carbamazepine and Stevens-Johnson syndrome	*HLA-B*15:02*	100%	895.5
Abacavir and hypersensitivity syndrome	*HLA-B*57:01*	78%	117.5
Allopurinol and severe cutaneous adverse reactions	*HLA-B*58:01*	100%	393.5
Ticlopidine and hepatotoxicity	*HLA-A*33:03*	86%	36.5
Amoxicillin-clavulanate potassium and hepatotoxicity	*HLA-DRB1*15:01*	78%	35.6
Flucloxacillin and hepatotoxicity	*HLA-B*57:01*	84%	80.6

Amino acid sequence alignment of the HLA class I α1- and α2-domains

```
                                                    5 amino acids                      3
B52:01 AGSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRTEPRAPWIEQEGPEYWDRETQISKTNTQTYRENLRIALRYYNQSEAG
B44:03 AGSHSMRYFYTAMSRPGRGEPRFITVGYVDDTLFVRFDSDATSPRKEPRAPWIEQEGPEYWDRETQISKTNTQTYRENLRTALRYYNQSEAG
B07:02 AGSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYWDRNTQIYKAQAQTDRESLRNLRGYYNQSEAG
B54:01 AGSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRGEPRAPWVEQEGPEYWDRNTQIYKAQAQTDRESLRNLRGYYNQSEAG
B46:01 AGSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRMAPRAPWIEQEGPEYWDRETQKYKRQAQTDRVSLRNLRGYYNQSEAG
       ***********..***********.*******.********.*** .*****.**********.**..* ..**.*..**....********

B52:01 SHTWQTMYGCDVGPDGRLLRGHNQYAYDGKDYIALNEDLSSWTAADTAAQITQRKWEAAREAEQLRAYLEGLCVEWLRRHLENGKETLQRAD
B44:03 SHIIQRMYGCDVGPDGRLLRGYDQDAYDGKDYIALNEDLSSWTAADTAAQITQRKWEAARVAEQLRAYLEGLCVESLRRYLENGKETLQRAD
B07:02 SHTLQSMYGCDVGPDGRLLRGHDQYAYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKLERAD
B54:01 SHTWQTMYGCDLGPDGRLLRGHNQLAYDGKDYIALNEDLSSWTAADTAAQITQRKWEAARVAEQLRAYLEGTCVEWLRRYLENGKETLQRAD
B46:01 SHTLQRMYGCDVGPDGRLLRGHDQSAYDGKDYIALNEDLSSWTAADTAAQITQRKWEAAREAEQWRAYLEGLCVEWLRRYLENGKETLQRAD
       **. * *****.*********..* **************.********************.***.******.***.***.*****..*.***
          3 3                  4                                       3      3
```



HLA class I

Most common 5 *HLA-B* alleles in Japanese

amino acid identity : **88.9%**

nucleotide identity : **93.9%**

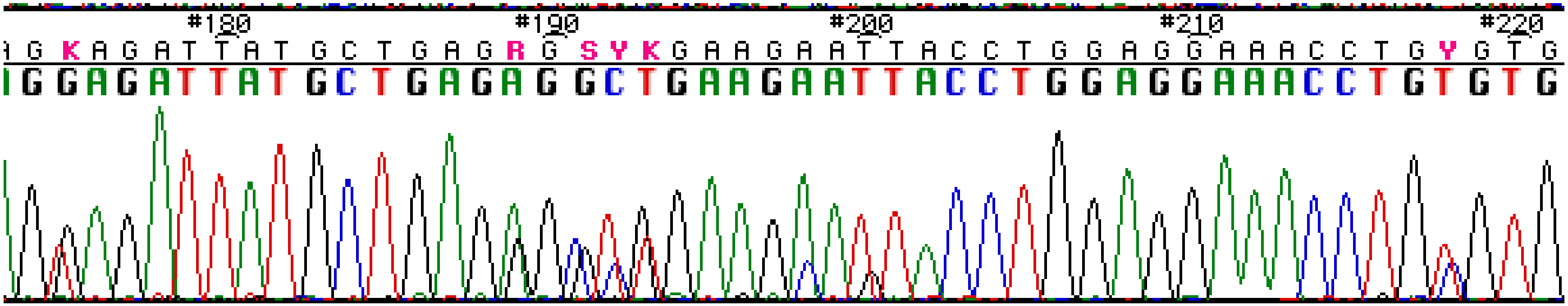
Current and past HLA typing method

PCR-RFLP	restriction fragment length polymorphism
PCR-SSCP	single strand conformational polymorphism
PCR-SSO	sequence specific oligonucleotide
PCR-SSP	sequence specific primers
PCR-SBT	sequencing based typing

In order to obtain reliable information on HLA types, DNA typing with SBT or SSO/SBT typing sets is increasingly performed.

These technology has not been displaced for over the last 10 years

Ambiguous allele combinations in PCR-SBT



Estimation of HLA allele

Ambiguous typing combinations

Combination 1 *B*07:21 + B*35:11*

Combination 2 *B*07:18 + B*35:05*

Combination 3 *B*07:09 + B*35:34*

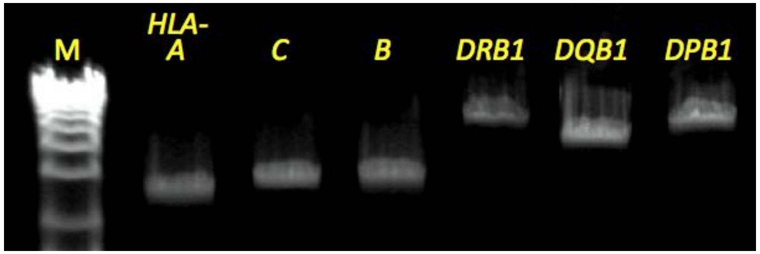
Combination 4 *B*07:24 + B*35:15*

?

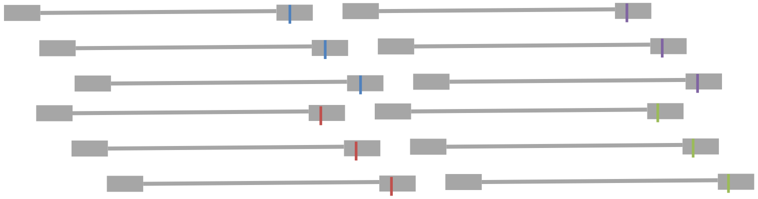
Phase-defined sequencing is very difficult

PCR-based HLA typing

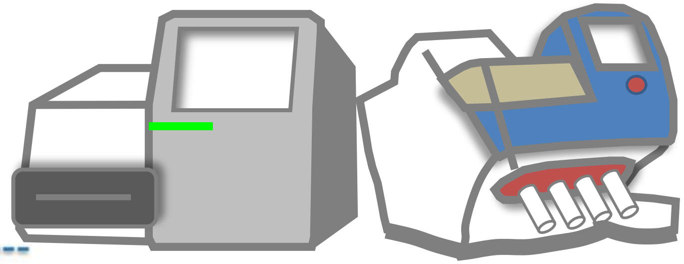
PCR amplicons



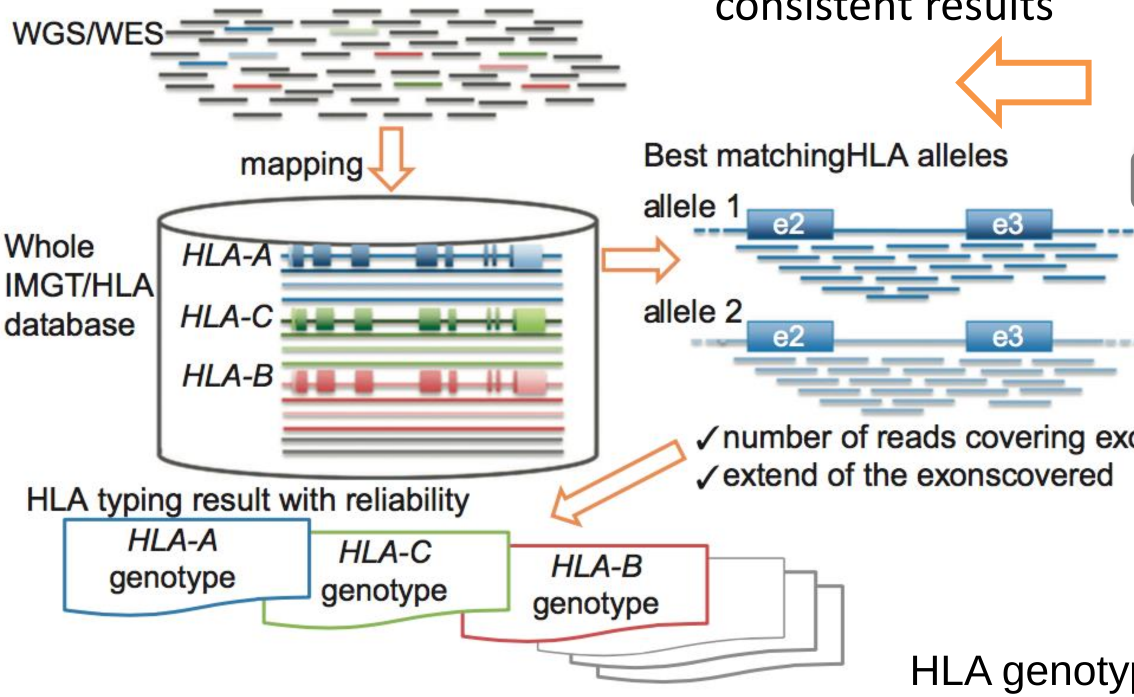
DNA library for NGS

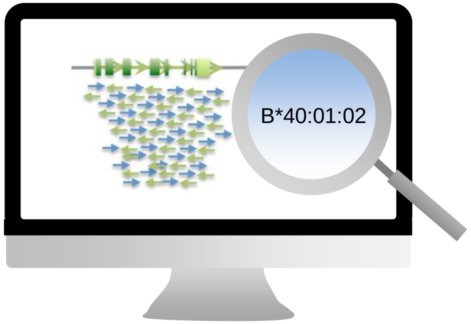


Which NGS platform provides best and consistent results



Sequencing





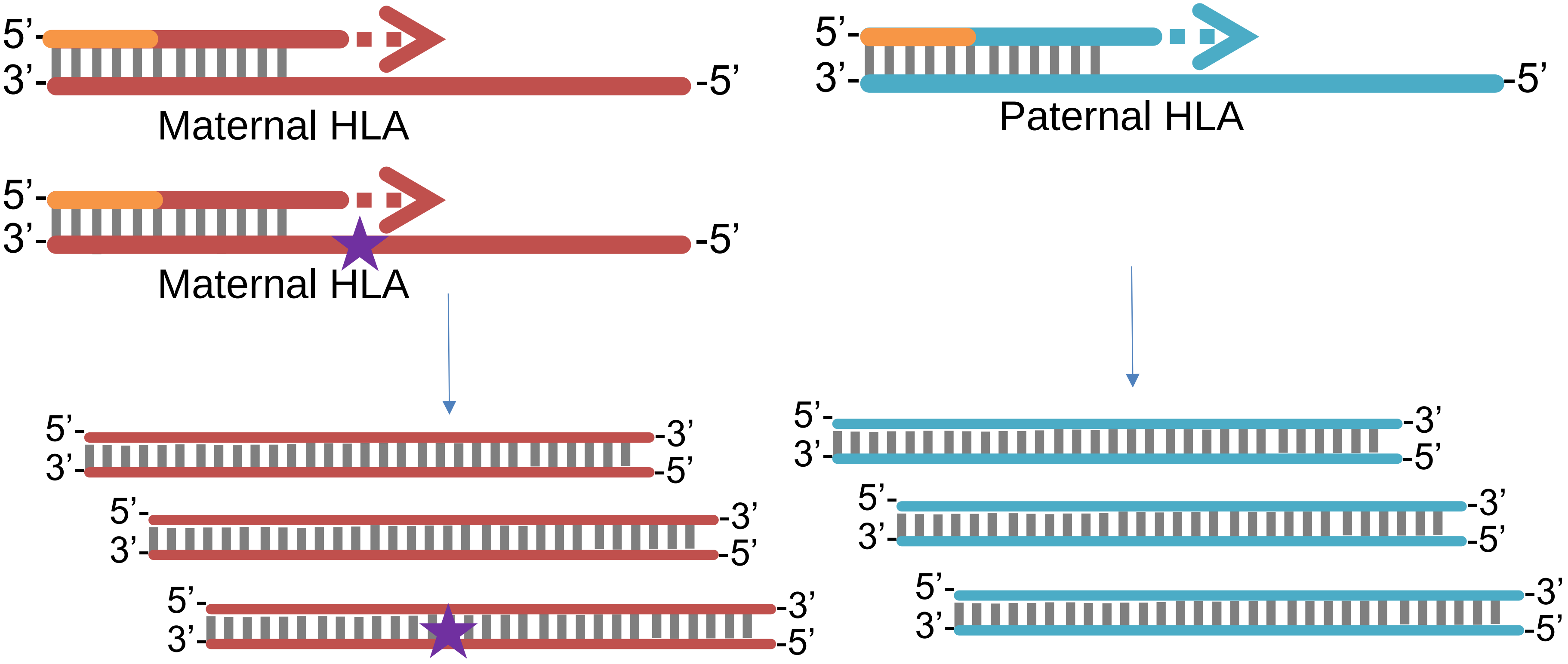
HLA genotype

Hosomichi et al. BMC Genomics 2015

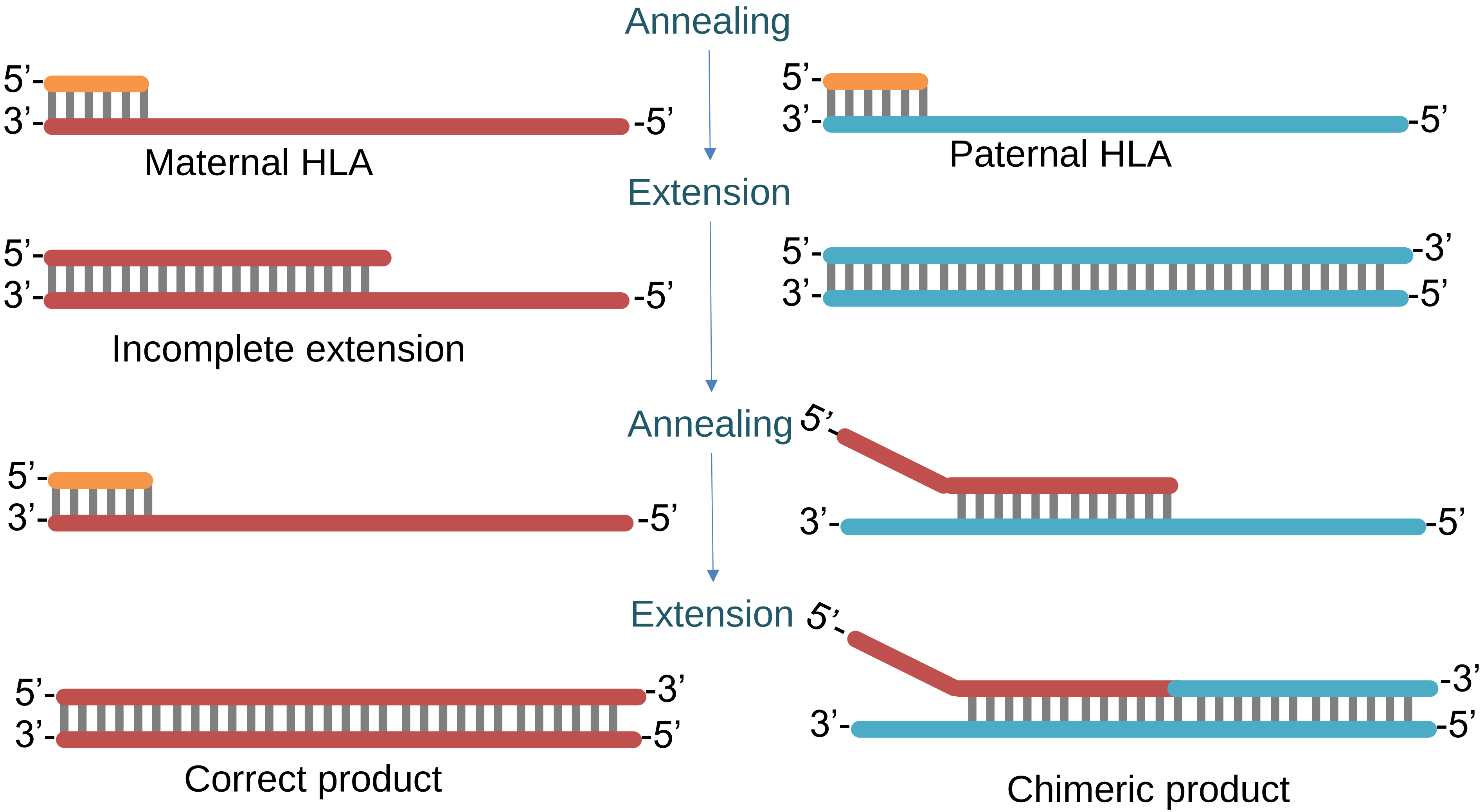
PCR-based HLA typing

Limitations possibly leading to typing errors

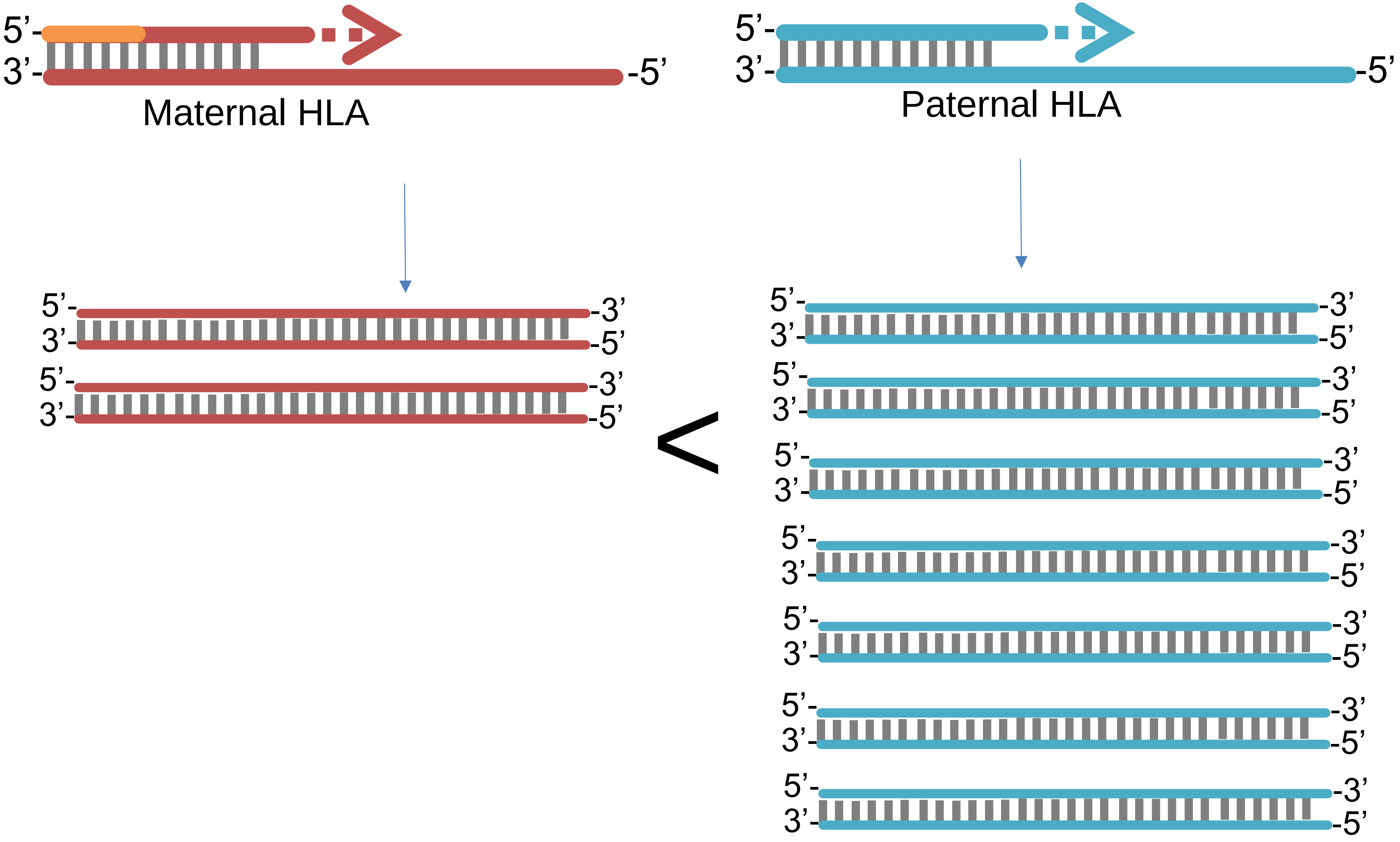
Nucleotide misincorporation
(error rate = < 0.01%)



Chimeric sequences generated by PCR-mediated recombination (chimeric sequence = < 26.4%)

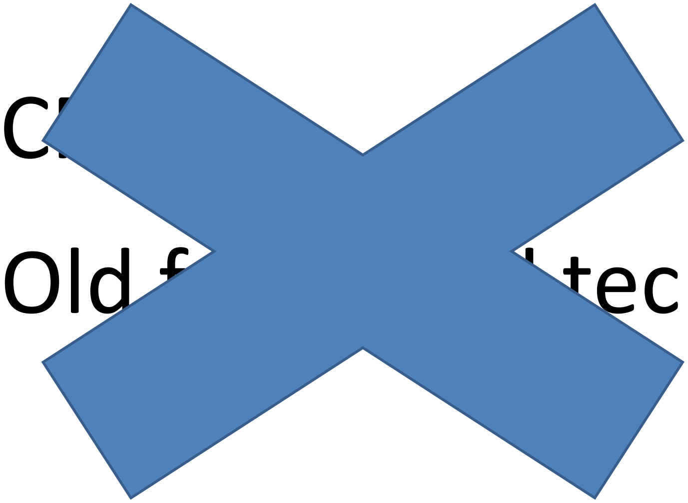


PCR allele dropout or allelic imbalance



PCR

Old fashioned technology



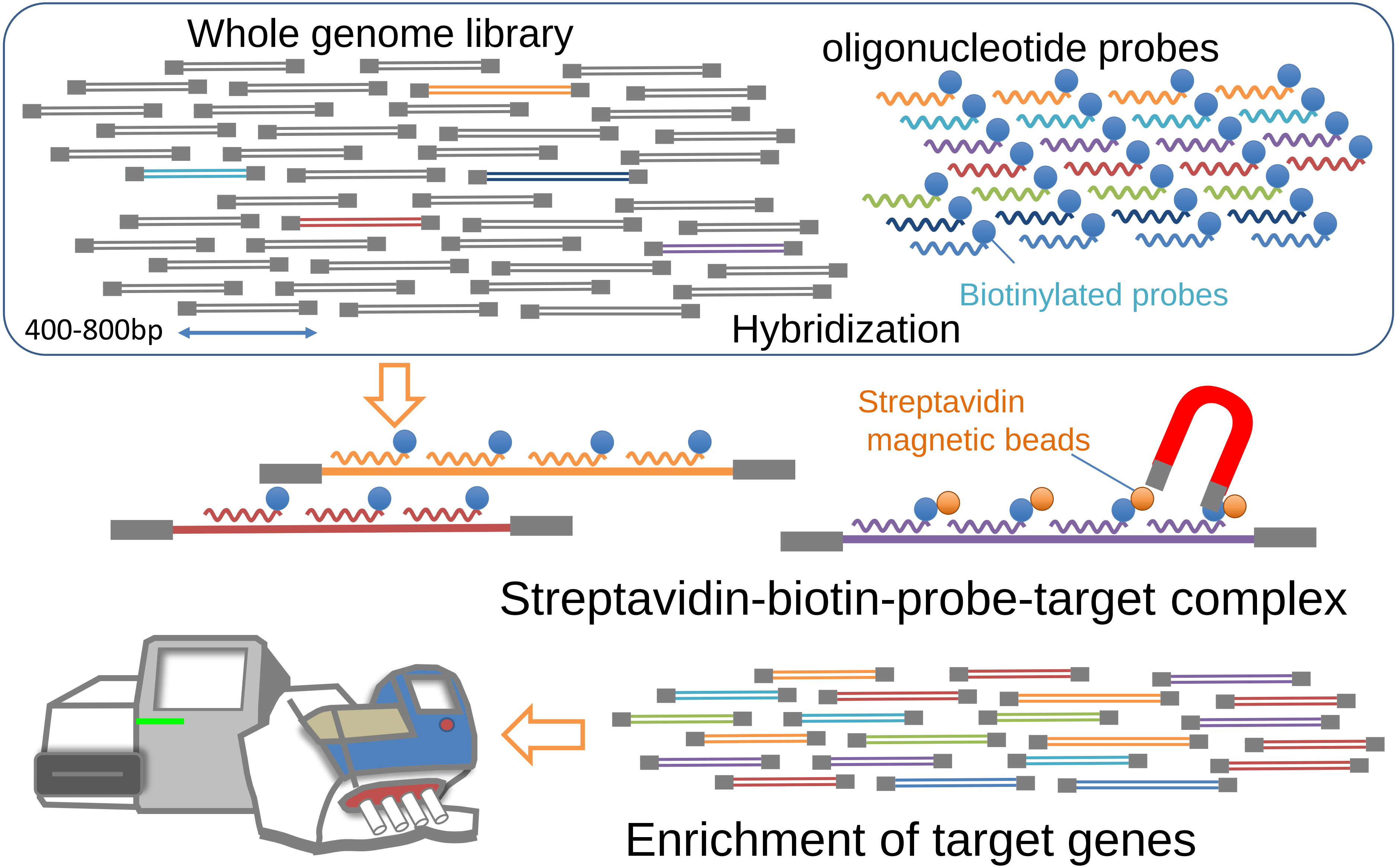
PC

Old f technology

Use a new weapon

Lightsaber

Target capture of HLA gene fragments by hybridization of whole genomic DNA with probes



Whole genome library

oligonucleotide probes

400-800bp

Biotinylated probes

Hybridization

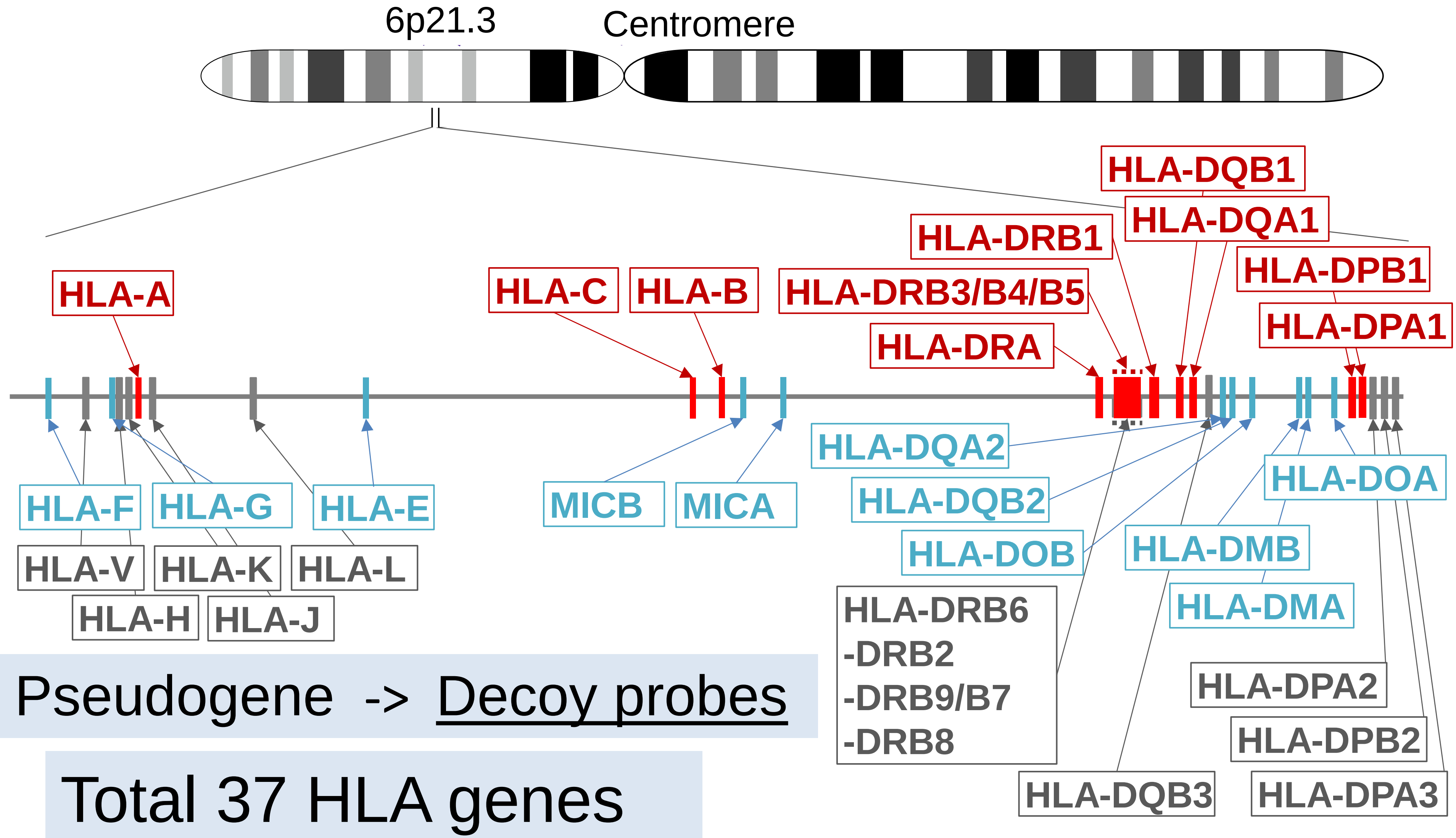
Streptavidin
magnetic beads

Streptavidin-biotin-probe-target complex

Enrichment of target genes

37 HLA genes targeted by capture method

Human chromosome 6

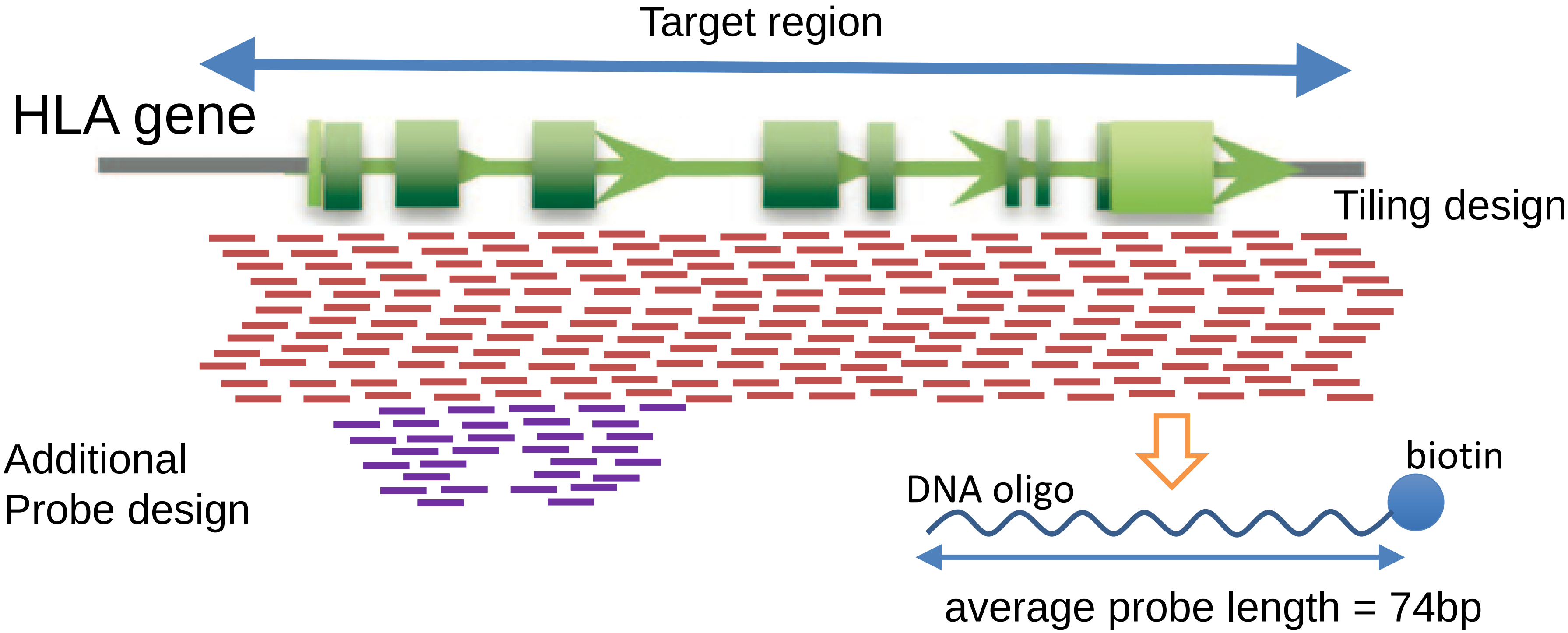


Pseudogene -> Decoy probes

Total 37 HLA genes

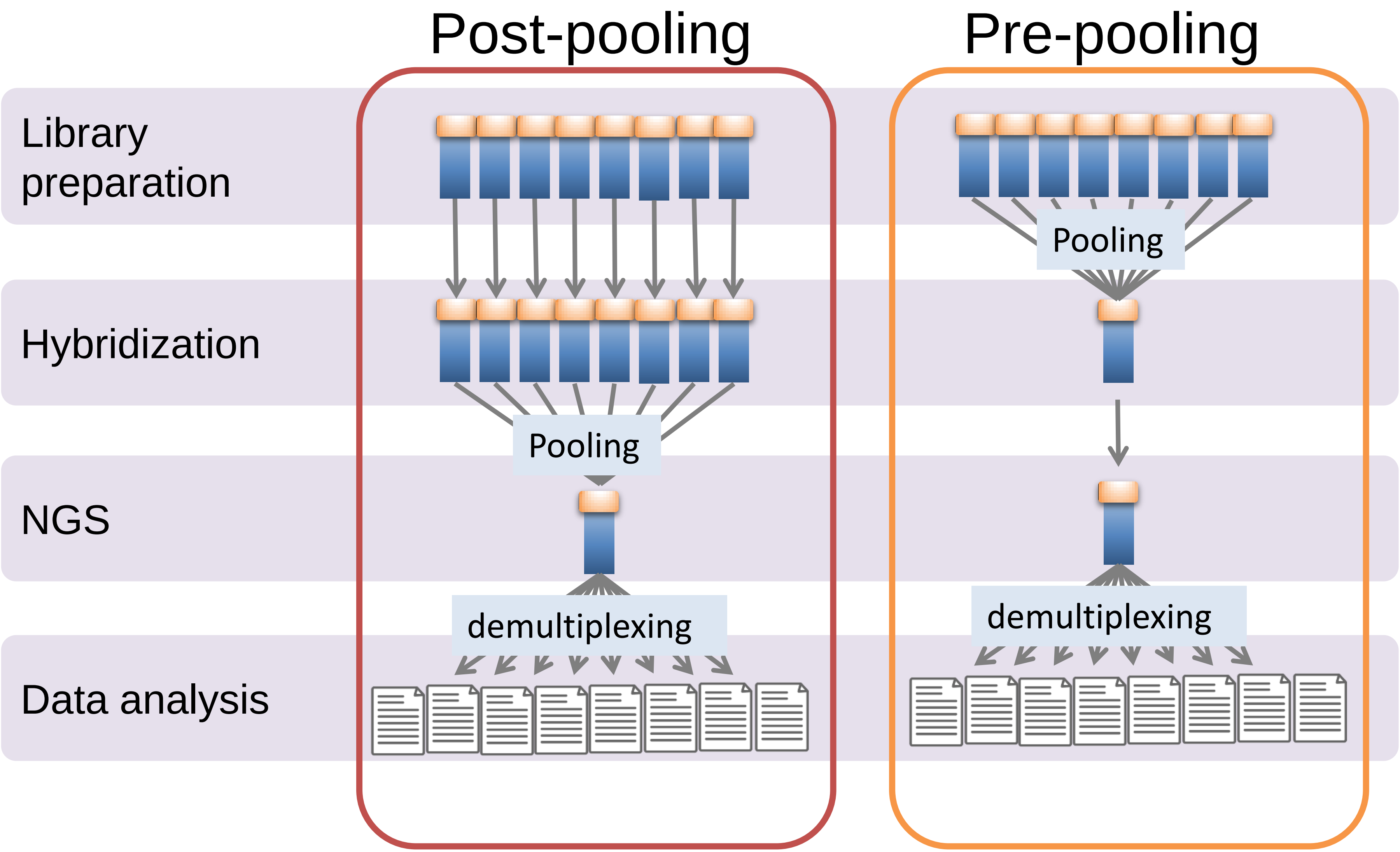
🟥: Classical HLA gene 🟦: Non-classical HLA gene ⬛: HLA pseudogene

Probe design for sequence capture method

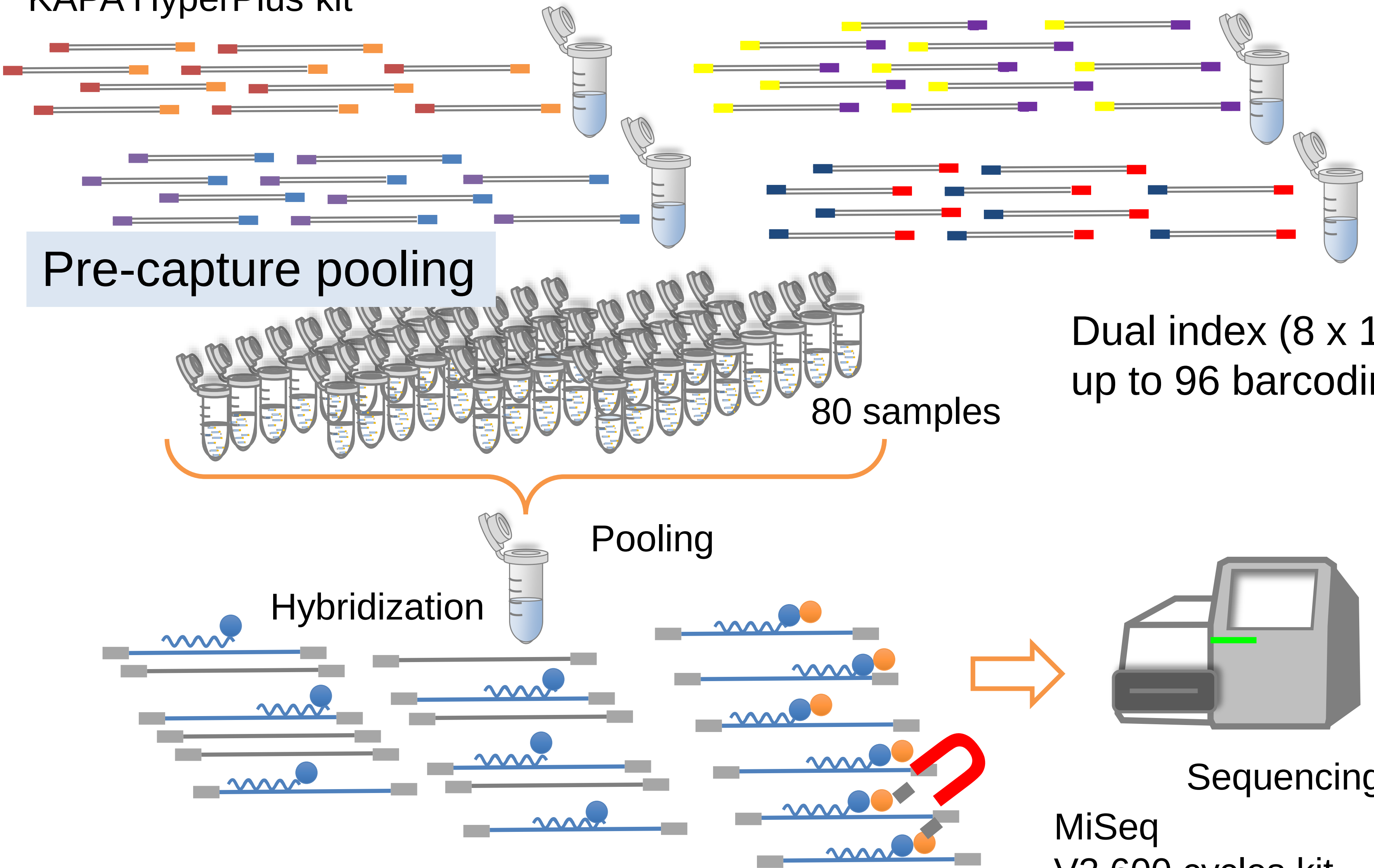


- Entire HLA gene region as target
- Tiling design for high coverage
- Additional design for polymorphic exons

Pre-capture pooling for multiple samples



HLA typing by NGS capture method



KAPA HyperPlus kit

Pre-capture pooling

Dual index (8 x 12)
up to 96 barcoding

80 samples

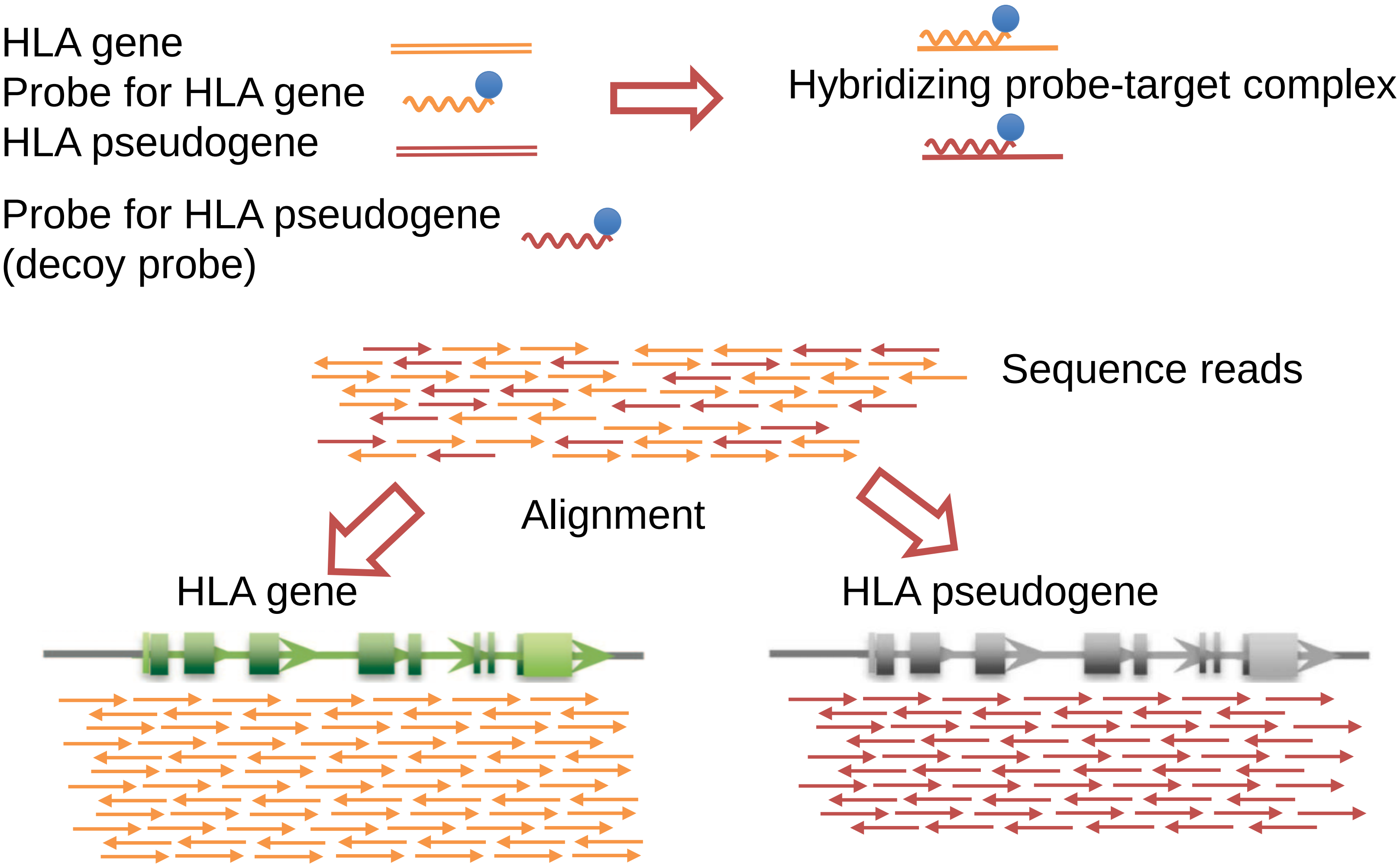
Pooling

Hybridization

Sequencing

MiSeq
V3 600 cycles kit
300bp paired-end reads

Specific and non-specific hybridization of oligonucleotide probes



HLA gene

Probe for HLA gene

HLA pseudogene

Probe for HLA pseudogene (decoy probe)

Hybridizing probe-target complex

Sequence reads

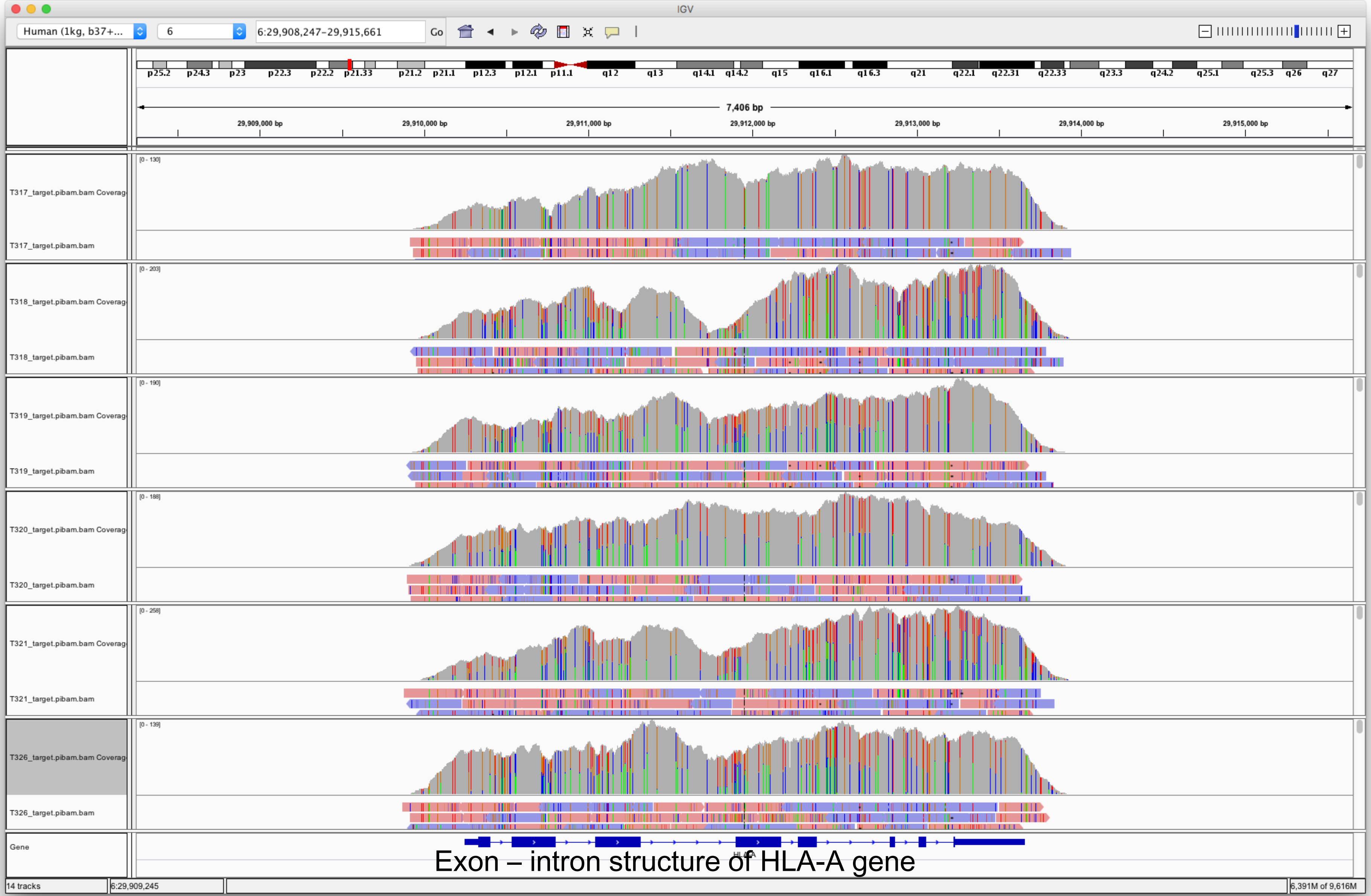
Alignment

HLA gene

HLA pseudogene

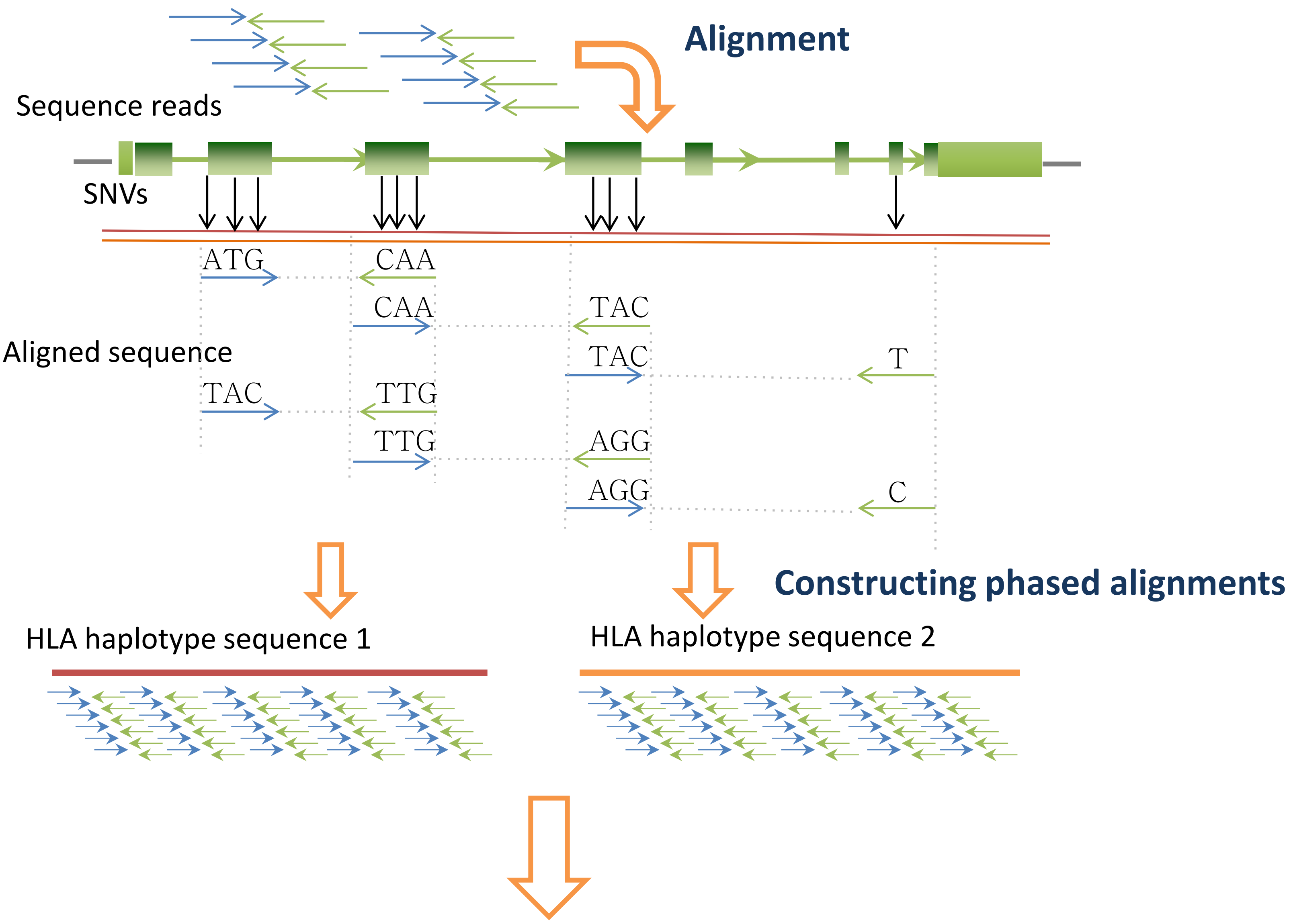
Sequence reads for primary important HLA genes are not affected

Sequence read alignment of HLA-A gene
- IGV Genome viewer image -



Exon – intron structure of HLA-A gene

Alignment to phased two HLA gene sequences



Sequence reads

Alignment

SNVs

Aligned sequence

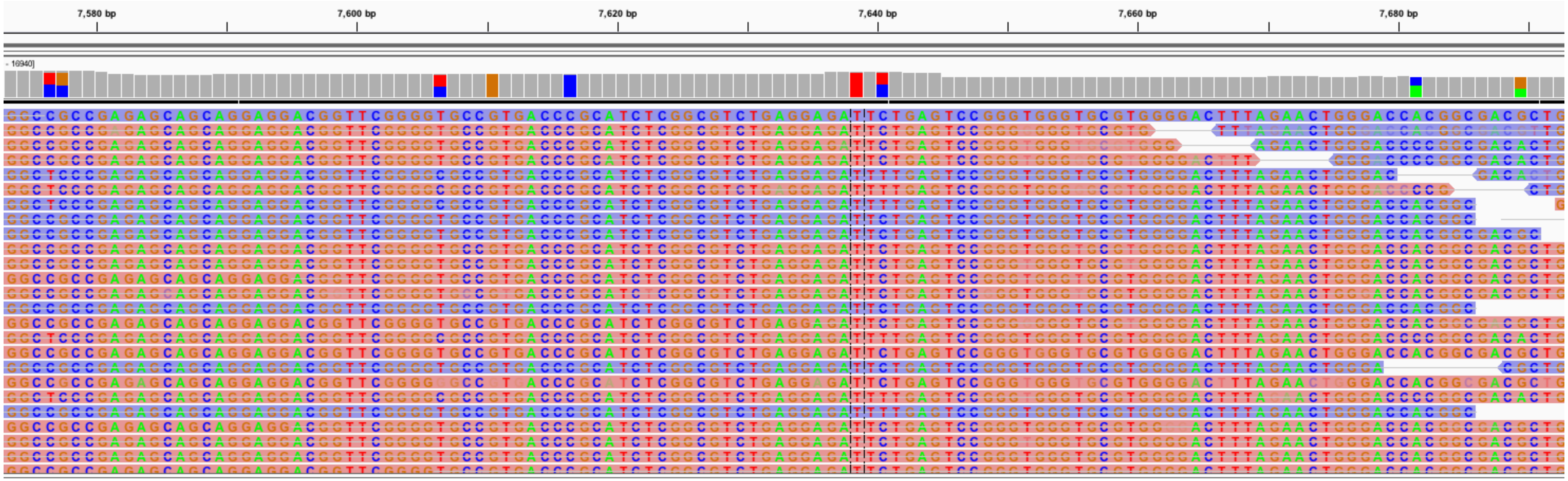
Constructing phased alignments

HLA haplotype sequence 1

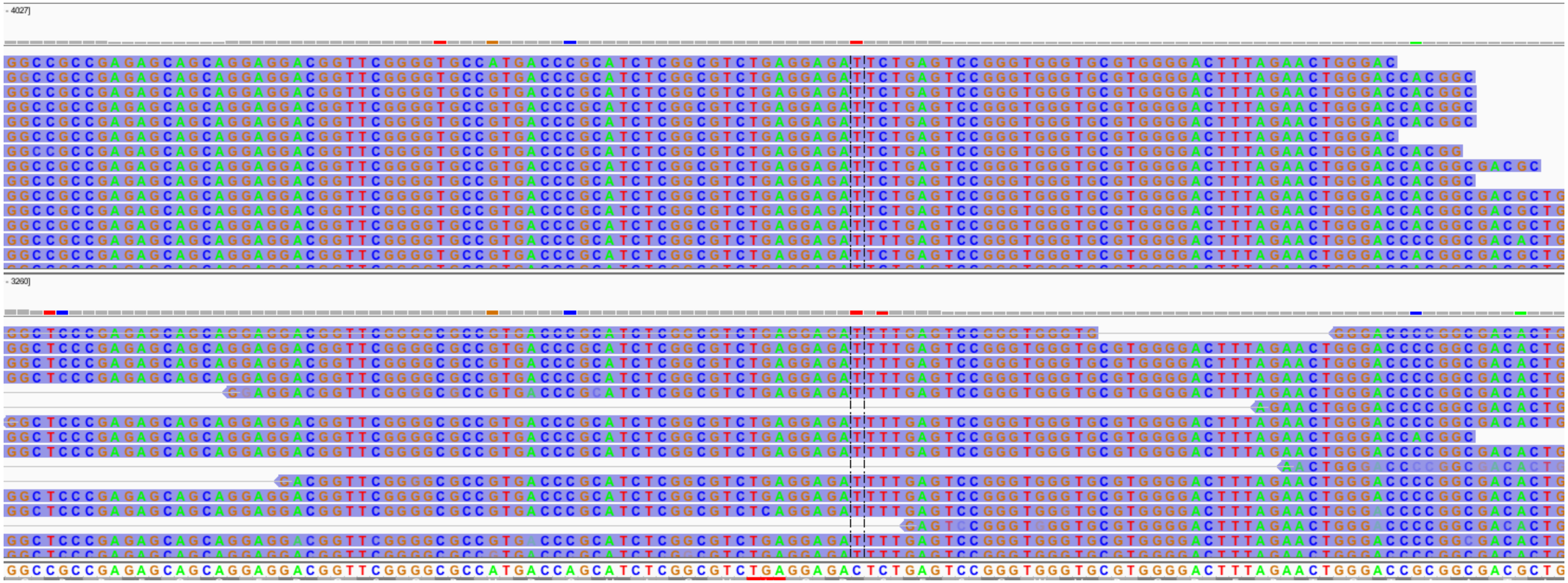
HLA haplotype sequence 2

Database search

Before phasing



After phasing



hap01

hap02

NGS sequencing results

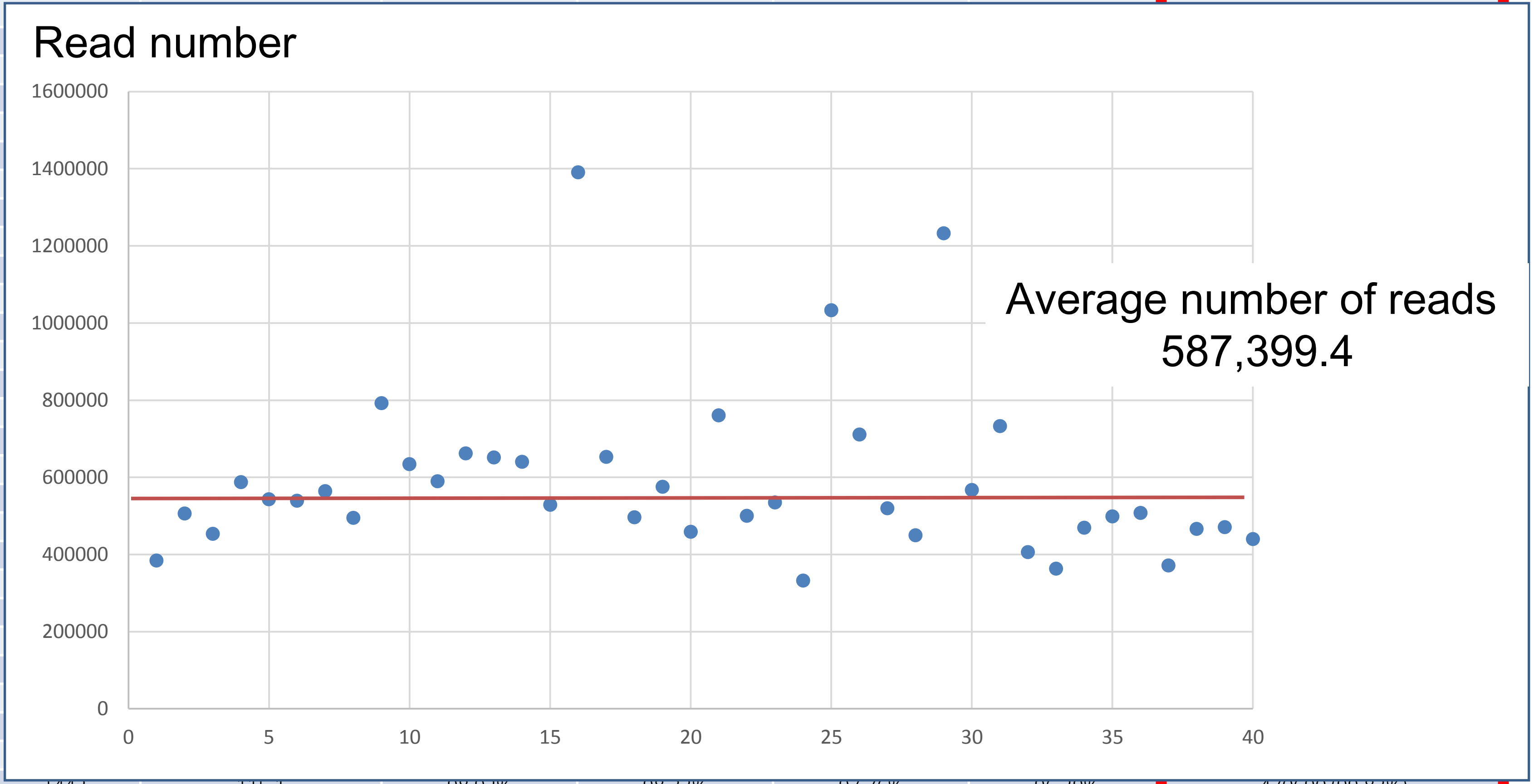
High mapping rate
to human genome

Sample	Average depth	depth >=1	depth >=5	depth >=10	depth >=20	total mapped reads
T317	84.32	100.00%	99.97%	99.84%	99.18%	383480 (99.82%)
T318						505961 (99.80%)
T319						453277 (99.85%)
T320						587357 (99.80%)
T321						542309 (99.83%)
T326						539153 (99.78%)
T328						563587 (99.71%)
T330						494460 (99.87%)
T334						791921 (99.75%)
T342						633337 (99.71%)
T343						589172 (99.69%)
T346	145.36	100.00%	100.00%	99.98%	99.81%	661594 (99.70%)
T349	139.1	97.09%	95.86%	95.00%	94.00%	651119 (99.73%)
T354	141.97	100.00%	99.94%	99.85%	99.28%	639696 (99.77%)
T357	103.27	96.69%	95.11%	94.10%	92.88%	528563 (99.82%)
T359	318.28	99.62%	99.38%	99.21%	98.77%	1390259 (99.71%)
T360	139.18	96.90%	95.75%	95.20%	94.63%	652835 (99.78%)
T369	112.66	99.44%	98.74%	98.16%	96.78%	496244 (99.59%)
T370	117.37	96.89%	95.59%	95.23%	94.41%	575047 (99.77%)
T371	95.02	100.00%	100.00%	99.91%	99.46%	458519 (99.74%)
T372	157.01	99.98%	99.97%	99.95%	99.78%	759796 (99.89%)
T373	113.03	99.59%	98.93%	98.27%	96.82%	499958 (99.78%)
T375	114.62	99.80%	99.60%	99.00%	97.76%	534209 (99.82%)
T378	83.26	97.36%	95.62%	94.80%	93.19%	332040 (99.68%)
T380	235.93	99.98%	99.97%	99.97%	99.94%	1032785 (99.78%)
T394	159.79	99.77%	99.36%	98.82%	98.08%	710761 (99.78%)
T396	118.34	99.31%	98.90%	97.73%	96.44%	519128 (99.81%)
T397	102.18	99.56%	98.90%	98.22%	96.64%	449440 (99.74%)
T398	299.95	100.00%	100.00%	100.00%	99.99%	1232251 (99.73%)
T400	135.95	100.00%	99.96%	99.92%	99.80%	567002 (99.78%)
T417	158.16	99.43%	99.08%	98.64%	97.16%	731950 (99.64%)
T424	108.82	99.84%	99.30%	98.72%	97.32%	405557 (99.48%)
T425	92.93	99.41%	98.80%	97.88%	96.38%	362529 (99.44%)
T426	113.19	100.00%	100.00%	99.99%	99.59%	468668 (99.61%)
T427	124.03	99.99%	99.97%	99.90%	99.45%	498473 (99.67%)
T429	135.66	99.52%	98.96%	98.03%	96.51%	507057 (99.62%)
T433	105.75	98.95%	98.36%	97.65%	96.00%	370756 (99.52%)
T434	123.86	100.00%	99.99%	99.78%	99.28%	465461 (99.59%)
T442	115.1	98.92%	98.33%	97.76%	96.39%	470690 (99.83%)
T451	132.52	99.98%	99.86%	99.53%	98.88%	439573 (99.59%)

NGS sequencing results

Sample	Average depth	depth >=1	depth >=5	depth >=10	depth >=20	total mapped reads
T317	84.32	100.00%	99.97%	99.84%	99.18%	383480 (99.82%)
						505961 (99.80%)
						453277 (99.85%)
						587357 (99.80%)
						542309 (99.83%)
						539153 (99.78%)
						563587 (99.71%)
						494460 (99.87%)
						791921 (99.75%)
T342	154.26	99.04%	98.36%	97.93%	97.12%	633337 (99.71%)
T343	139.3	99.53%	99.06%	98.36%	97.27%	589172 (99.69%)
T442	115.1	98.92%	98.33%	97.76%	96.39%	470690 (99.83%)
T451	132.52	99.98%	99.86%	99.53%	98.88%	439573 (99.59%)

Low variation in the number of reads among DNA samples



Average number of reads 587,399.4

NGS sequencing results

Sample	Average depth	depth >=1	depth >=5	depth >=10	depth >=20	total mapped reads
T317	84.32	100.00%	99.97%	99.84%	99.18%	383480 (99.82%)
T318	103.29	96.80%	94.78%	94.24%	93.15%	505961 (99.80%)
T319	87.05	96.61%	95.34%	94.92%	93.84%	453277 (99.85%)
T320	126.16	99.07%	98.44%	97.94%	96.96%	587357 (99.80%)
T321	107.97	99.43%	98.87%	97.88%	96.18%	542309 (99.83%)
T326	100.58	99.98%	99.97%	99.91%	99.78%	539153 (99.78%)
T328	113.7	100.00%	100.00%	99.97%	99.70%	563587 (99.71%)
T330	102.36	99.98%	99.97%	99.84%	99.48%	494460 (99.87%)
T334	191.2	99.46%	98.94%	98.46%	97.17%	791921 (99.75%)
T342	154.26	99.04%	98.36%	97.93%	97.12%	633337 (99.71%)
T343	139.3	99.53%	99.06%	98.36%	97.27%	589172 (99.69%)
T346	145.36	100.00%	100.00%	99.98%	99.81%	661594 (99.70%)
T349	139.1	97.09%	95.86%	95.00%	94.00%	651119 (99.73%)
T354	141.97	100.00%	99.94%	99.85%	99.28%	639696 (99.77%)
T357	103.27	96.69%	95.11%	94.10%	92.88%	528563 (99.82%)
T359	318.28					1390259 (99.71%)
T360	139.18					652835 (99.78%)
T369	112.66					496244 (99.59%)
T370	117.37					575047 (99.77%)
T371	95.02					458519 (99.74%)
T372	157.01					759796 (99.89%)
T373	113.03					499958 (99.78%)
T375	114.62					534209 (99.82%)
T378	83.26					332040 (99.68%)
T380	235.93					1032785 (99.78%)
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T398	299.95	100.00%	100.00%	100.00%	99.99%	1232251 (99.73%)
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T425	92.93	99.41%	98.80%	97.88%	96.38%	362529 (99.44%)
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T429	135.66	99.52%	98.96%	98.03%	96.51%	507057 (99.62%)
T433	105.75	98.95%	98.36%	97.65%	96.00%	370756 (99.52%)
T434	123.86	100.00%	99.99%	99.78%	99.28%	465461 (99.59%)
T442	115.1	98.92%	98.33%	97.76%	96.39%	470690 (99.83%)
T451	132.52	99.98%	99.86%	99.53%	98.88%	439573 (99.59%)

Average read depths : 133.8

NGS sequencing results

Sample	Average depth	depth >=1	depth >=5	depth >=10	depth >=20	total mapped reads
T317	84.32	100.00%	99.97%	99.84%	99.18%	383480 (99.82%)
T318	103.29	96.80%	94.78%	94.24%	93.15%	505961 (99.80%)
T319	87.05	96.61%	95.34%	94.92%	93.84%	453277 (99.85%)
T320	126.16	99.07%	98.44%	97.94%	96.96%	587357 (99.80%)
T321	107.97	99.43%	98.87%	97.88%	96.18%	542309 (99.83%)
T326	100.58	99.98%	99.97%	99.91%	99.78%	539153 (99.78%)
T328	113.7	100.00%	100.00%	99.97%	99.70%	563587 (99.71%)
T330	102.36	99.98%	99.97%	99.84%	99.48%	494460 (99.87%)
T334	191.2	99.46%	98.94%	98.46%	97.17%	791921 (99.75%)
T342	154.26	99.04%	98.36%	97.93%	97.12%	633337 (99.71%)
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T369	112.66	99.44%	98.74%	98.16%	96.78%	496244 (99.59%)
					94.41%	575047 (99.77%)
					99.46%	458519 (99.74%)
					99.78%	759796 (99.89%)
					96.82%	499958 (99.78%)
					97.76%	534209 (99.82%)
					93.19%	332040 (99.68%)
					99.94%	1032785 (99.78%)
					98.08%	710761 (99.78%)
					96.44%	519128 (99.81%)
T397	102.18	99.56%	98.90%	98.22%	96.64%	449440 (99.74%)
T398	299.95	100.00%	100.00%	100.00%	99.99%	1232251 (99.73%)
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T417	158.16	99.43%	99.08%	98.64%	97.16%	731950 (99.64%)
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T426	113.19	100.00%	100.00%	99.99%	99.59%	468668 (99.61%)
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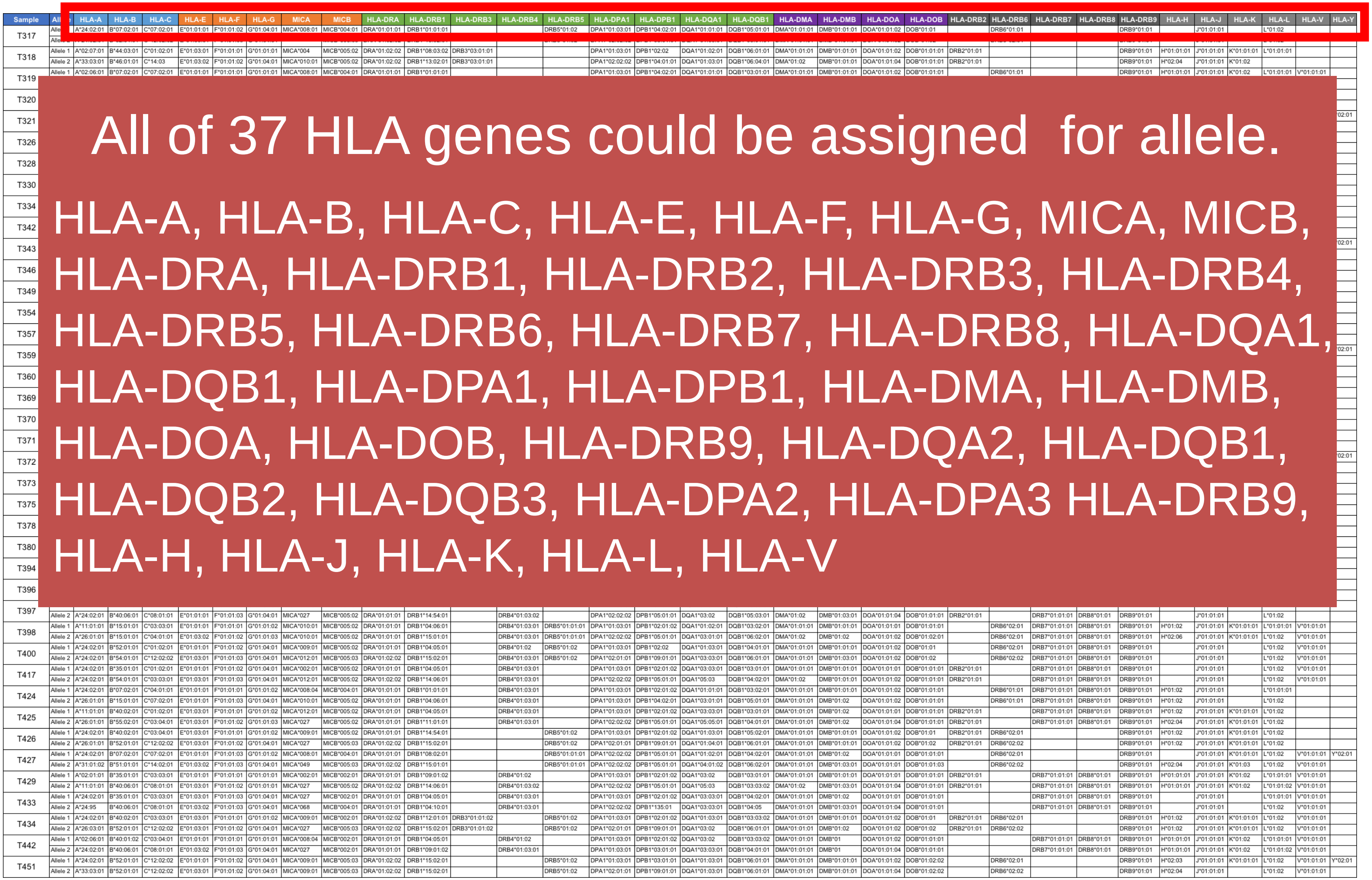
T429	135.66	99.52%	98.96%	98.03%	96.51%	507057 (99.62%)
T433	105.75	98.95%	98.36%	97.65%	96.00%	370756 (99.52%)
T434	123.86	100.00%	99.99%	99.78%	99.28%	465461 (99.59%)
T442	115.1	98.92%	98.33%	97.76%	96.39%	470690 (99.83%)
T451	132.52	99.98%	99.86%	99.53%	98.88%	439573 (99.59%)

More than 97% nucleotide sites have more than x 20 read depths

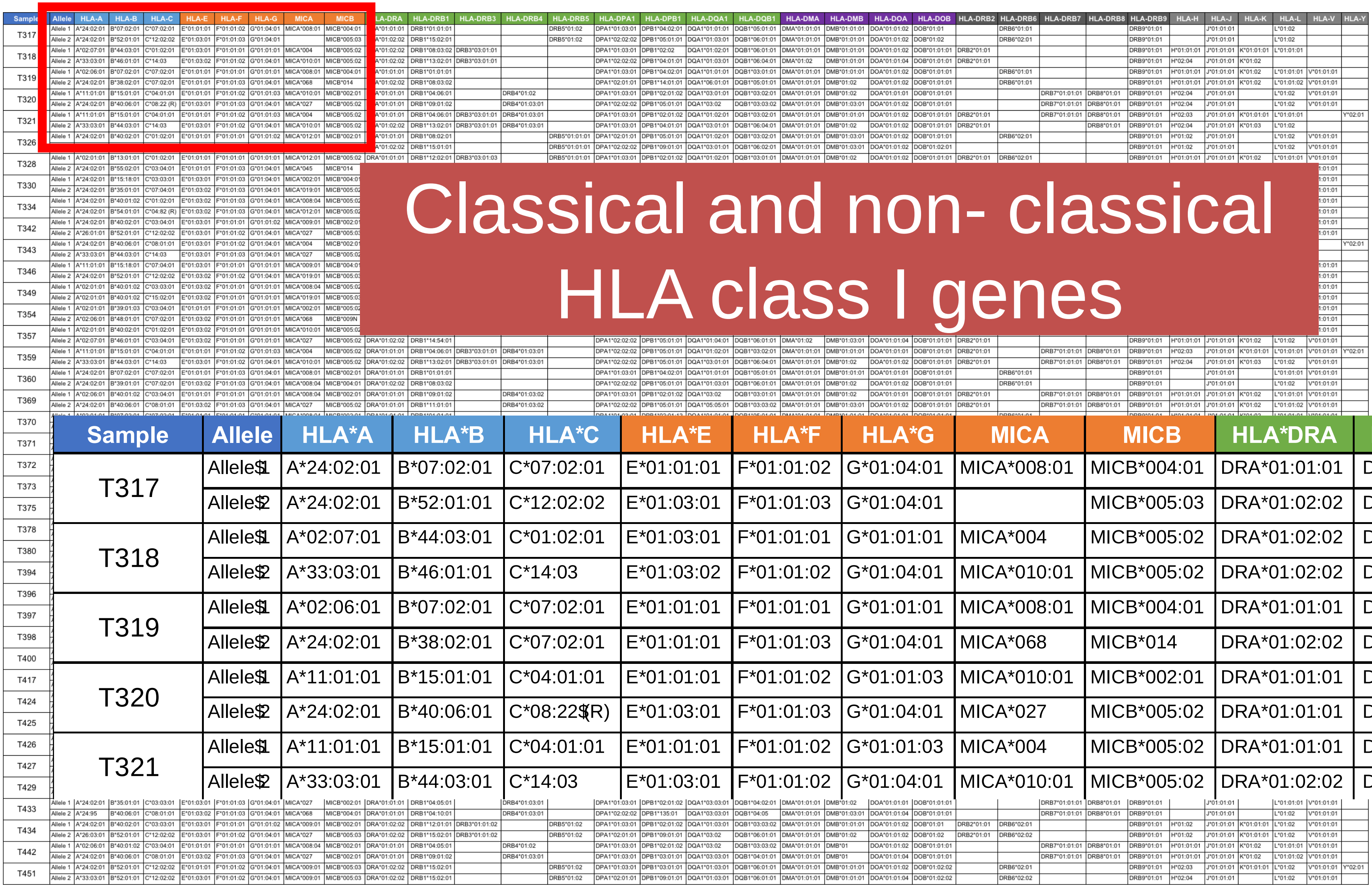
HLA typing results by NGS capture method



All of 37 HLA genes could be assigned for allele.

HLA-A, HLA-B, HLA-C, HLA-E, HLA-F, HLA-G, MICA, MICB, HLA-DRA, HLA-DRB1, HLA-DRB2, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-DRB6, HLA-DRB7, HLA-DRB8, HLA-DQA1, HLA-DQB1, HLA-DPA1, HLA-DPB1, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DOB, HLA-DRB9, HLA-DQA2, HLA-DQB1, HLA-DQB2, HLA-DQB3, HLA-DPA2, HLA-DPA3 HLA-DRB9, HLA-H, HLA-J, HLA-K, HLA-L, HLA-V

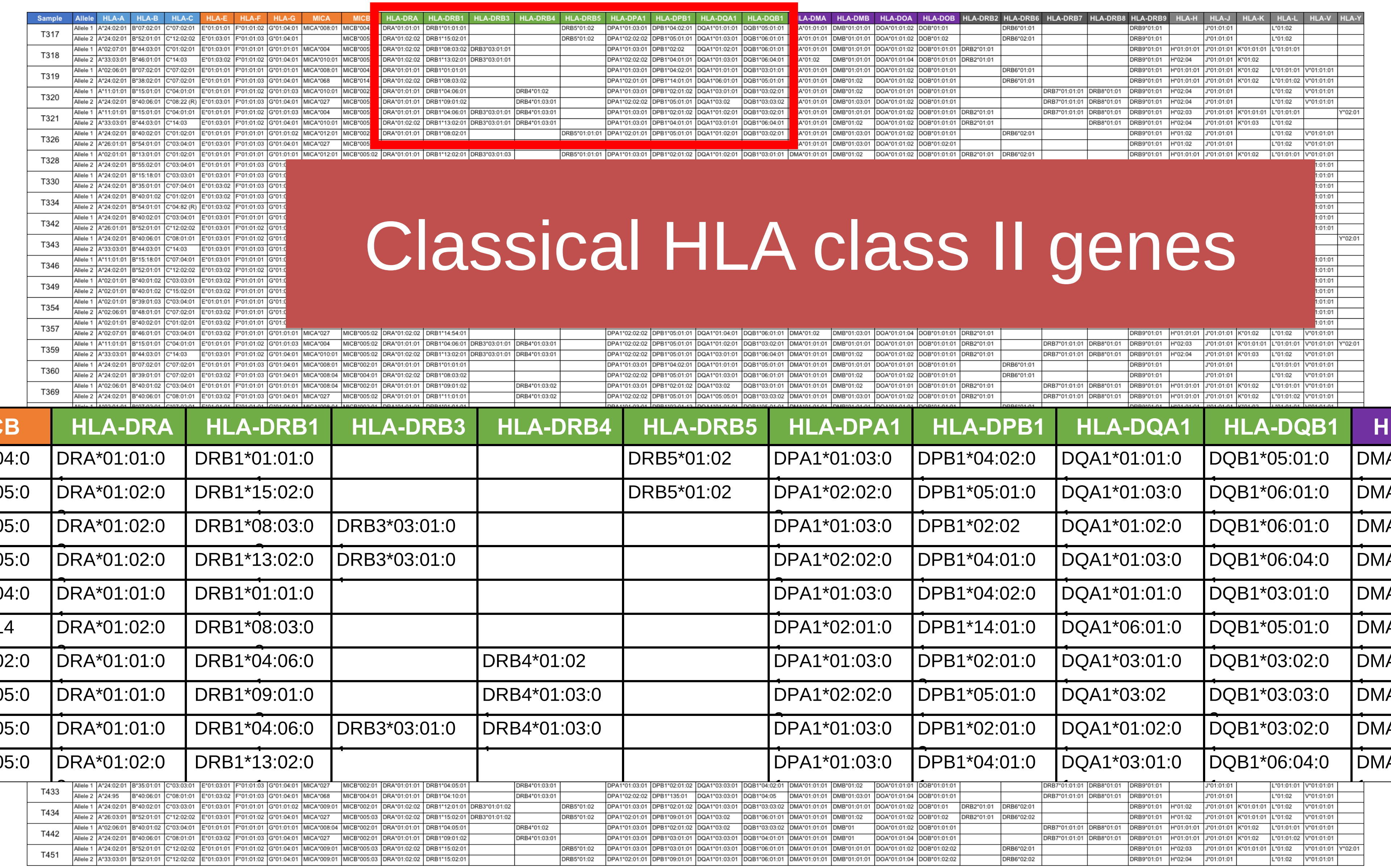
HLA typing results by NGS capture method



Classical and non- classical HLA class I genes

Sample	Allele	HLA*A	HLA*B	HLA*C	HLA*E	HLA*F	HLA*G	MICA	MICB	HLA*DRA	HL
T317	Allele 1	A*24:02:01	B*07:02:01	C*07:02:01	E*01:01:01	F*01:01:02	G*01:04:01	MICA*008:01	MICB*004:01	DRA*01:01:01	DRE
	Allele 2	A*24:02:01	B*52:01:01	C*12:02:02	E*01:03:01	F*01:01:03	G*01:04:01		MICB*005:03	DRA*01:02:02	DRE
T318	Allele 1	A*02:07:01	B*44:03:01	C*01:02:01	E*01:03:01	F*01:01:01	G*01:01:01	MICA*004	MICB*005:02	DRA*01:02:02	DRE
	Allele 2	A*33:03:01	B*46:01:01	C*14:03	E*01:03:02	F*01:01:02	G*01:04:01	MICA*010:01	MICB*005:02	DRA*01:02:02	DRE
T319	Allele 1	A*02:06:01	B*07:02:01	C*07:02:01	E*01:01:01	F*01:01:01	G*01:01:01	MICA*008:01	MICB*004:01	DRA*01:01:01	DRE
	Allele 2	A*24:02:01	B*38:02:01	C*07:02:01	E*01:01:01	F*01:01:03	G*01:04:01	MICA*068	MICB*014	DRA*01:02:02	DRE
T320	Allele 1	A*11:01:01	B*15:01:01	C*04:01:01	E*01:01:01	F*01:01:02	G*01:01:03	MICA*010:01	MICB*002:01	DRA*01:01:01	DRE
	Allele 2	A*24:02:01	B*40:06:01	C*08:22 (R)	E*01:03:01	F*01:01:03	G*01:04:01	MICA*027	MICB*005:02	DRA*01:01:01	DRE
T321	Allele 1	A*11:01:01	B*15:01:01	C*04:01:01	E*01:01:01	F*01:01:02	G*01:01:03	MICA*004	MICB*005:02	DRA*01:01:01	DRE
	Allele 2	A*33:03:01	B*44:03:01	C*14:03	E*01:03:01	F*01:01:02	G*01:04:01	MICA*010:01	MICB*005:02	DRA*01:02:02	DRE

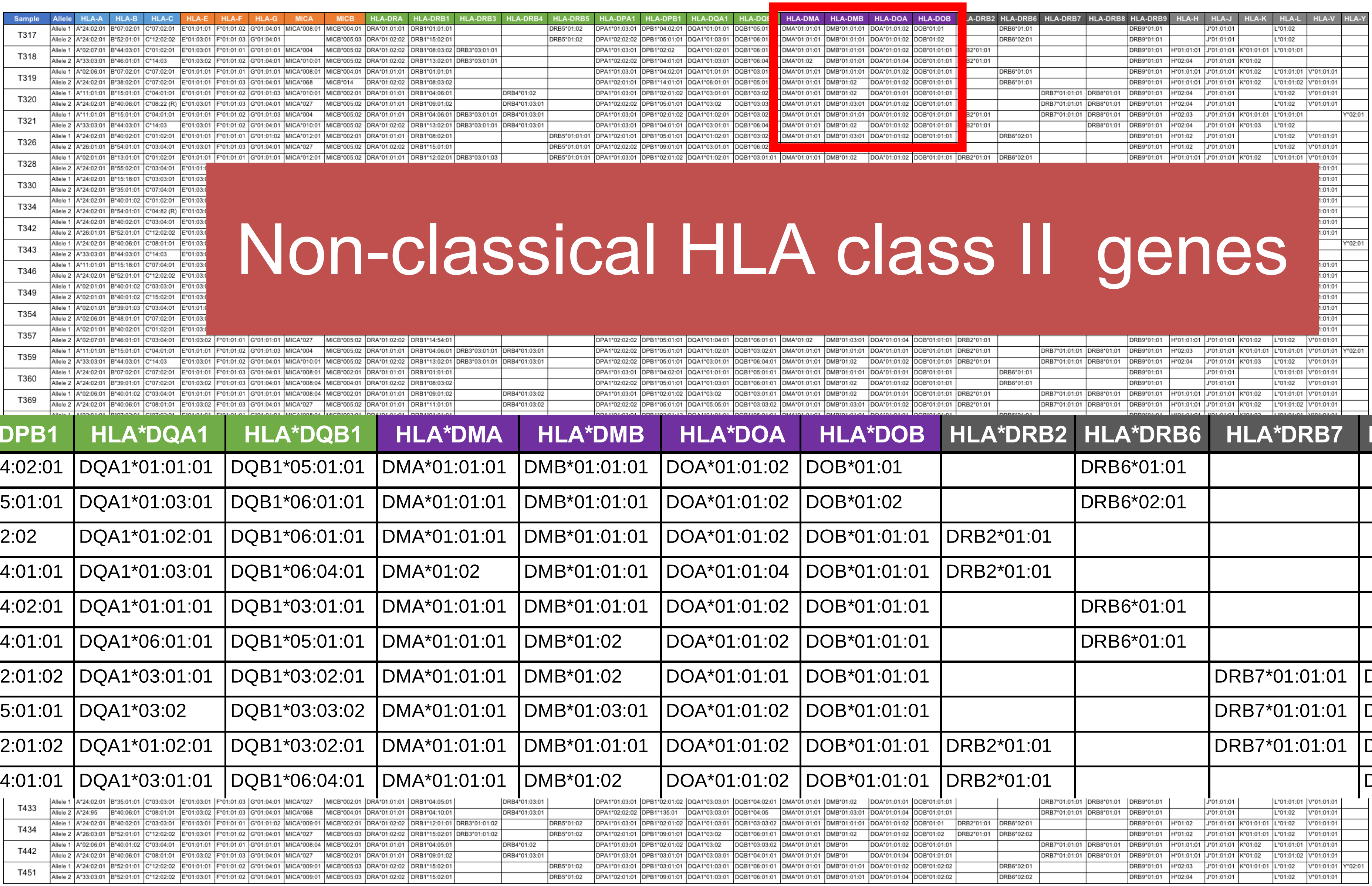
HLA typing results by NGS capture method



Classical HLA class II genes

CB	HLA-DRA	HLA-DRB1	HLA-DRB3	HLA-DRB4	HLA-DRB5	HLA-DPA1	HLA-DPB1	HLA-DQA1	HLA-DQB1	H
04:0	DRA*01:01:0	DRB1*01:01:0			DRB5*01:02	DPA1*01:03:0	DPB1*04:02:0	DQA1*01:01:0	DQB1*05:01:0	DMA
05:0	DRA*01:02:0	DRB1*15:02:0			DRB5*01:02	DPA1*02:02:0	DPB1*05:01:0	DQA1*01:03:0	DQB1*06:01:0	DMA
05:0	DRA*01:02:0	DRB1*08:03:0	DRB3*03:01:0			DPA1*01:03:0	DPB1*02:02	DQA1*01:02:0	DQB1*06:01:0	DMA
05:0	DRA*01:02:0	DRB1*13:02:0	DRB3*03:01:0			DPA1*02:02:0	DPB1*04:01:0	DQA1*01:03:0	DQB1*06:04:0	DMA
04:0	DRA*01:01:0	DRB1*01:01:0				DPA1*01:03:0	DPB1*04:02:0	DQA1*01:01:0	DQB1*03:01:0	DMA
14	DRA*01:02:0	DRB1*08:03:0				DPA1*02:01:0	DPB1*14:01:0	DQA1*06:01:0	DQB1*05:01:0	DMA
02:0	DRA*01:01:0	DRB1*04:06:0		DRB4*01:02		DPA1*01:03:0	DPB1*02:01:0	DQA1*03:01:0	DQB1*03:02:0	DMA
05:0	DRA*01:01:0	DRB1*09:01:0		DRB4*01:03:0		DPA1*02:02:0	DPB1*05:01:0	DQA1*03:02	DQB1*03:03:0	DMA
05:0	DRA*01:01:0	DRB1*04:06:0	DRB3*03:01:0	DRB4*01:03:0		DPA1*01:03:0	DPB1*02:01:0	DQA1*01:02:0	DQB1*03:02:0	DMA
05:0	DRA*01:02:0	DRB1*13:02:0				DPA1*01:03:0	DPB1*04:01:0	DQA1*03:01:0	DQB1*06:04:0	DMA

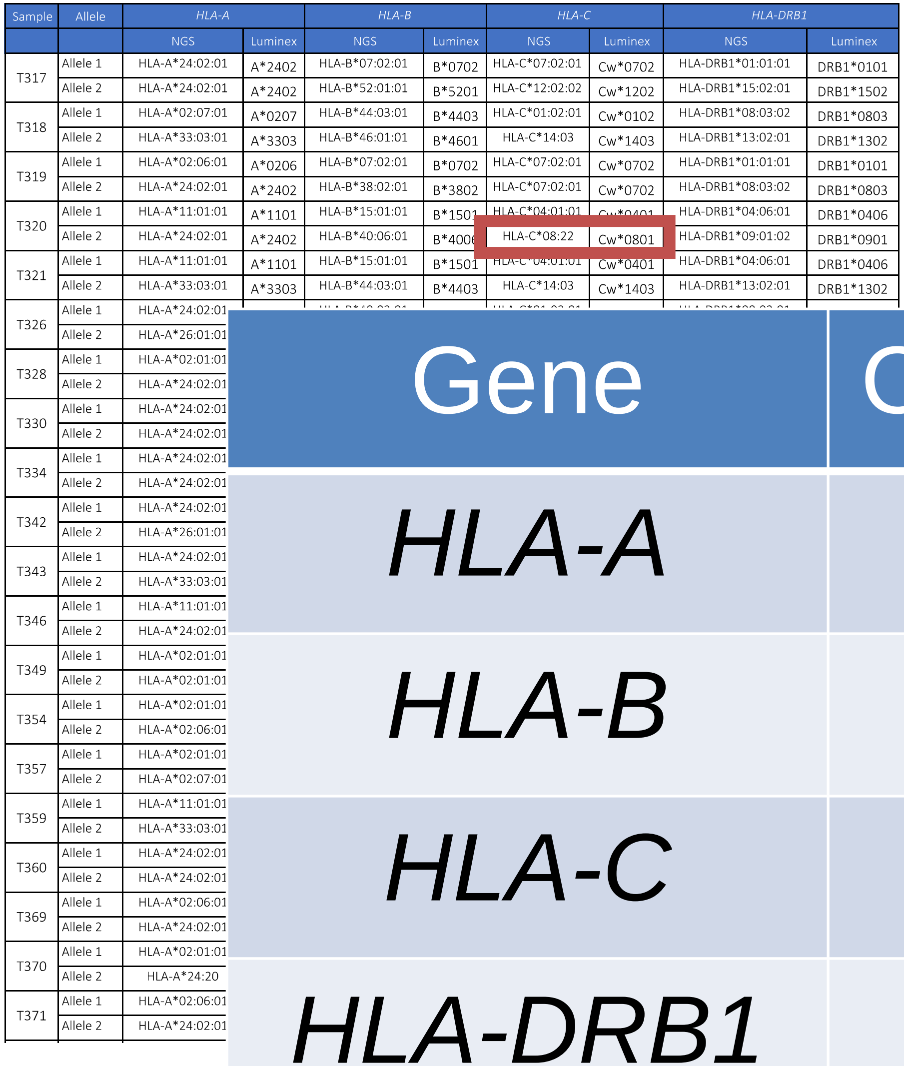
HLA typing results by NGS capture method



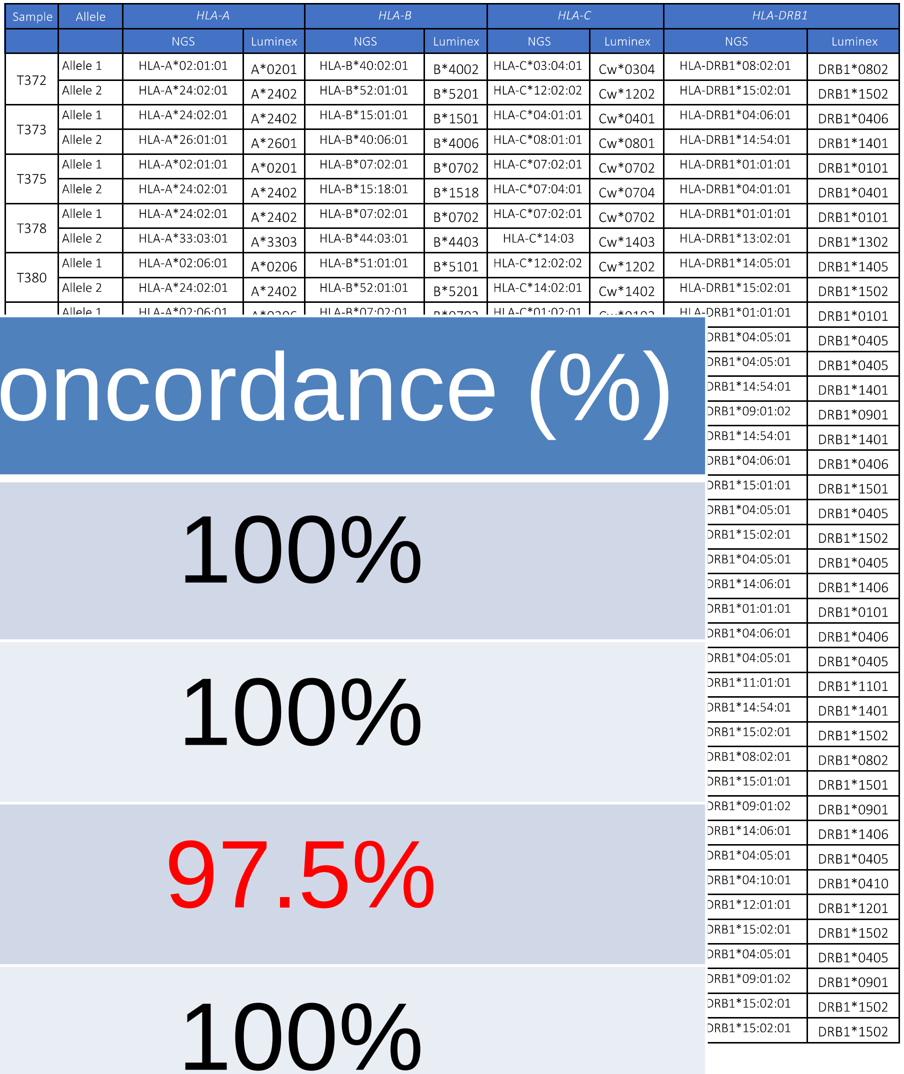
Non-classical HLA class II genes

A*DPB1	HLA*DQA1	HLA*DQB1	HLA*DMA	HLA*DMB	HLA*DOA	HLA*DOB	HLA*DRB2	HLA*DRB6	HLA*DRB7	HL
1*04:02:01	DQA1*01:01:01	DQB1*05:01:01	DMA*01:01:01	DMB*01:01:01	DOA*01:01:02	DOB*01:01		DRB6*01:01		
1*05:01:01	DQA1*01:03:01	DQB1*06:01:01	DMA*01:01:01	DMB*01:01:01	DOA*01:01:02	DOB*01:02		DRB6*02:01		
1*02:02	DQA1*01:02:01	DQB1*06:01:01	DMA*01:01:01	DMB*01:01:01	DOA*01:01:02	DOB*01:01:01	DRB2*01:01			
1*04:01:01	DQA1*01:03:01	DQB1*06:04:01	DMA*01:02	DMB*01:01:01	DOA*01:01:04	DOB*01:01:01	DRB2*01:01			
1*04:02:01	DQA1*01:01:01	DQB1*03:01:01	DMA*01:01:01	DMB*01:01:01	DOA*01:01:02	DOB*01:01:01		DRB6*01:01		
1*14:01:01	DQA1*06:01:01	DQB1*05:01:01	DMA*01:01:01	DMB*01:02	DOA*01:01:02	DOB*01:01:01		DRB6*01:01		
1*02:01:02	DQA1*03:01:01	DQB1*03:02:01	DMA*01:01:01	DMB*01:02	DOA*01:01:01	DOB*01:01:01			DRB7*01:01:01	DR
1*05:01:01	DQA1*03:02	DQB1*03:03:02	DMA*01:01:01	DMB*01:03:01	DOA*01:01:02	DOB*01:01:01			DRB7*01:01:01	DR
1*02:01:02	DQA1*01:02:01	DQB1*03:02:01	DMA*01:01:01	DMB*01:01:01	DOA*01:01:02	DOB*01:01:01	DRB2*01:01		DRB7*01:01:01	DR
1*04:01:01	DQA1*03:01:01	DQB1*06:04:01	DMA*01:01:01	DMB*01:02	DOA*01:01:02	DOB*01:01:01	DRB2*01:01			DR

Concordance between PCR-SSO and NGS



Sample	Allele	*HLA-A*		*HLA-B*		*HLA-C*		*HLA-DRB1*	
		NGS	Luminex	NGS	Luminex	NGS	Luminex	NGS	Luminex
T317	Allele 1	HLA-A*24:02:01	A*2402	HLA-B*07:02:01	B*0702	HLA-C*07:02:01	Cw*0702	HLA-DRB1*01:01:01	DRB1*0101
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*52:01:01	B*5201	HLA-C*12:02:02	Cw*1202	HLA-DRB1*15:02:01	DRB1*1502
T318	Allele 1	HLA-A*02:07:01	A*0207	HLA-B*44:03:01	B*4403	HLA-C*01:02:01	Cw*0102	HLA-DRB1*08:03:02	DRB1*0803
	Allele 2	HLA-A*33:03:01	A*3303	HLA-B*46:01:01	B*4601	HLA-C*14:03	Cw*1403	HLA-DRB1*13:02:01	DRB1*1302
T319	Allele 1	HLA-A*02:06:01	A*0206	HLA-B*07:02:01	B*0702	HLA-C*07:02:01	Cw*0702	HLA-DRB1*01:01:01	DRB1*0101
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*38:02:01	B*3802	HLA-C*07:02:01	Cw*0702	HLA-DRB1*08:03:02	DRB1*0803
T320	Allele 1	HLA-A*11:01:01	A*1101	HLA-B*15:01:01	B*1501	HLA-C*04:01:01	Cw*0401	HLA-DRB1*04:06:01	DRB1*0406
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*40:06:01	B*400	HLA-C*08:22	Cw*0801	HLA-DRB1*09:01:02	DRB1*0901
T321	Allele 1	HLA-A*11:01:01	A*1101	HLA-B*15:01:01	B*1501	HLA-C*04:01:01	Cw*0401	HLA-DRB1*04:06:01	DRB1*0406
	Allele 2	HLA-A*33:03:01	A*3303	HLA-B*44:03:01	B*4403	HLA-C*14:03	Cw*1403	HLA-DRB1*13:02:01	DRB1*1302
T326	Allele 1	HLA-A*24:02:01							
	Allele 2	HLA-A*26:01:01							
T328	Allele 1	HLA-A*02:01:01							
	Allele 2	HLA-A*24:02:01							
T330	Allele 1	HLA-A*24:02:01							
	Allele 2	HLA-A*24:02:01							
T334	Allele 1	HLA-A*24:02:01							
	Allele 2	HLA-A*24:02:01							
T342	Allele 1	HLA-A*24:02:01							
	Allele 2	HLA-A*26:01:01							
T343	Allele 1	HLA-A*24:02:01							
	Allele 2	HLA-A*33:03:01							
T346	Allele 1	HLA-A*11:01:01							
	Allele 2	HLA-A*24:02:01							
T349	Allele 1	HLA-A*02:01:01							
	Allele 2	HLA-A*02:01:01							
T354	Allele 1	HLA-A*02:01:01							
	Allele 2	HLA-A*02:06:01							
T357	Allele 1	HLA-A*02:01:01							
	Allele 2	HLA-A*02:07:01							
T359	Allele 1	HLA-A*11:01:01							
	Allele 2	HLA-A*33:03:01							
T360	Allele 1	HLA-A*24:02:01							
	Allele 2	HLA-A*24:02:01							
T369	Allele 1	HLA-A*02:06:01							
	Allele 2	HLA-A*24:02:01							
T370	Allele 1	HLA-A*02:01:01							
	Allele 2	HLA-A*24:20							
T371	Allele 1	HLA-A*02:06:01							
	Allele 2	HLA-A*24:02:01							



Sample	Allele	*HLA-A*		*HLA-B*		*HLA-C*		*HLA-DRB1*	
		NGS	Luminex	NGS	Luminex	NGS	Luminex	NGS	Luminex
T372	Allele 1	HLA-A*02:01:01	A*0201	HLA-B*40:02:01	B*4002	HLA-C*03:04:01	Cw*0304	HLA-DRB1*08:02:01	DRB1*0802
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*52:01:01	B*5201	HLA-C*12:02:02	Cw*1202	HLA-DRB1*15:02:01	DRB1*1502
T373	Allele 1	HLA-A*24:02:01	A*2402	HLA-B*15:01:01	B*1501	HLA-C*04:01:01	Cw*0401	HLA-DRB1*04:06:01	DRB1*0406
	Allele 2	HLA-A*26:01:01	A*2601	HLA-B*40:06:01	B*4006	HLA-C*08:01:01	Cw*0801	HLA-DRB1*14:54:01	DRB1*1401
T375	Allele 1	HLA-A*02:01:01	A*0201	HLA-B*07:02:01	B*0702	HLA-C*07:02:01	Cw*0702	HLA-DRB1*01:01:01	DRB1*0101
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*15:18:01	B*1518	HLA-C*07:04:01	Cw*0704	HLA-DRB1*04:01:01	DRB1*0401
T378	Allele 1	HLA-A*24:02:01	A*2402	HLA-B*07:02:01	B*0702	HLA-C*07:02:01	Cw*0702	HLA-DRB1*01:01:01	DRB1*0101
	Allele 2	HLA-A*33:03:01	A*3303	HLA-B*44:03:01	B*4403	HLA-C*14:03	Cw*1403	HLA-DRB1*13:02:01	DRB1*1302
T380	Allele 1	HLA-A*02:06:01	A*0206	HLA-B*51:01:01	B*5101	HLA-C*12:02:02	Cw*1202	HLA-DRB1*14:05:01	DRB1*1405
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*52:01:01	B*5201	HLA-C*14:02:01	Cw*1402	HLA-DRB1*15:02:01	DRB1*1502
	Allele 1	HLA-A*02:06:01		HLA-B*07:02:01		HLA-C*01:02:01		HLA-DRB1*01:01:01	DRB1*0101
								DRB1*04:05:01	DRB1*0405
								DRB1*04:05:01	DRB1*0405
								DRB1*14:54:01	DRB1*1401
								DRB1*09:01:02	DRB1*0901
								DRB1*14:54:01	DRB1*1401
								DRB1*04:06:01	DRB1*0406
								DRB1*15:01:01	DRB1*1501
								DRB1*04:05:01	DRB1*0405
								DRB1*15:02:01	DRB1*1502
								DRB1*04:05:01	DRB1*0405
								DRB1*14:06:01	DRB1*1406
								DRB1*01:01:01	DRB1*0101
								DRB1*04:06:01	DRB1*0406
								DRB1*04:05:01	DRB1*0405
								DRB1*11:01:01	DRB1*1101
								DRB1*14:54:01	DRB1*1401
								DRB1*15:02:01	DRB1*1502
								DRB1*08:02:01	DRB1*0802
								DRB1*15:01:01	DRB1*1501
								DRB1*09:01:02	DRB1*0901
								DRB1*14:06:01	DRB1*1406
								DRB1*04:05:01	DRB1*0405
								DRB1*04:10:01	DRB1*0410
								DRB1*12:01:01	DRB1*1201
								DRB1*15:02:01	DRB1*1502
								DRB1*04:05:01	DRB1*0405
								DRB1*09:01:02	DRB1*0901
								DRB1*15:02:01	DRB1*1502
								DRB1*15:02:01	DRB1*1502

Gene	Concordance (%)
HLA-A	100%
HLA-B	100%
HLA-C	97.5%
HLA-DRB1	100%

Discrepancy of alleles defined between NGS capture and Luminex methods

Sample	Allele	*HLA-A*		*HLA-B*		*HLA-C*		*HLA-DRB1*	
		NGS	Luminex	NGS	Luminex	NGS	Luminex	NGS	Luminex
T320	Allele 1	HLA-A*11:01:01	A*1101	HLA-B*15:01:01	B*1501	HLA-C*04:01:01	Cw*0401	HLA-DRB1*04:06:01	DRB1*0406
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*40:06:01	B*4006	HLA-C*08:22	Cw*0801	HLA-DRB1*09:01:02	DRB1*0901

HLA-C*08:01:01 ? (Luminex)
or
HLA-C*08:22 ? (NGS-capture)

Sample	Allele	*HLA-A*		*HLA-B*		*HLA-C*		*HLA-DRB1*	
		NGS	Luminex	NGS	Luminex	NGS	Luminex	NGS	Luminex
T334	Allele 1	HLA-A*24:02:01	A*2402	HLA-B*40:01:02	B*4001	HLA-C*01:02:01	Cw*0102	HLA-DRB1*04:05:01	DRB1*0405
	Allele 2	HLA-A*24:02:01	A*2402	HLA-B*54:01:01	B*5401	HLA-C*04:82	Cw*0401	HLA-DRB1*14:06:01	DRB1*1406

HLA -C*04:01 ? (Luminex)
or
HLA-C*04:82 ? (NGS-capture)

Nucleotide sequences of HLA-C:08:01 and -C*08:22

```
                             -20                  -15                  -10                   -5                      1
C*08:01:01   ATG CGG GTC ATG GCG CCC CGA  ACC CTC ATC CTG CTG CTC TCG  GGA  GCC  CTG GCC CTG ACC GAG ACC TGG GCC  T|GC
C*08:22      ATG CGG GTC ATG GCG CCC CGA  ACC CTC ATC CTG CTG CTC TCG  GGA  GCC  CTG GCC CTG ACC GAG ACC TGG GCC  T|GC

                              5                   10                   15                    20                     25
C*08:01:01   TCC CAC TCC ATG AGG TAT TTC  TAC ACC GCC GTG TCC CGG CCC  GGC  CGC  GGA GAG CCC CGC TTC ATC GCA GTG  GGC
C*08:22      TCC CAC TCC ATG AGG TAT TTC  TAC ACC GCC GTG TCC CGG CCC  GGC  CGC  GGA GAG CCC CGC TTC ATC GCA GTG  GGC

                             30                   35                   40                    45                     50
C*08:01:01   TAC GTG GAC GAC ACG CAG TTC  GTG CAG TTC GAC AGC GAC GCC  GCG  AGT  CCA AGA GGG GAG CCG CGG GCG CCG  TGG
C*08:22      TAC GTG GAC GAC ACG CAG TTC  GTG CAG TTC GAC AGC GAC GCC  GCG  AGT  CCA AGA GGG GAG CCG CGG GCG CCG  TGG
```

1 SNV in exon 6

```
                       320
C*08:01:01   GGG  AGC  TGC  TCT  CAG
C*08:22      GGG  AGC  TAC  TCT  CAG
```

```
                             255                  260                  265                   270                    275
C*08:01:01   GGA GAA GAG CAG AGA TAC ACG  TGC CAT GTG CAG CAC GAG GGG  CTG  CCA  GAG CCC CTC ACC CTG AGA TGG G|GG  CCA
C*08:22      GGA GAA GAG CAG AGA TAC ACG  TGC CAT GTG CAG CAC GAG GGG  CTG  CCA  GAG CCC CTC ACC CTG AGA TGG G|GG  CCA

                             280                  285                  290                   295                    300
C*08:01:01   TCT TCC CAG CCC ACC ATC CCC  ATC GTG GGC ATC GTT GCT GGC  CTG  GCT  GTC CTG GCT GTC CTA GCT GTC CTA  GGA
C*08:22      TCT TCC CAG CCC ACC ATC CCC  ATC GTG GGC ATC GTT GCT GGC  CTG  GCT  GTC CTG GCT GTC CTA GCT GTC CTA  GGA

                             305                  310                  315                                          325
C*08:01:01   GCT GTG ATG GCT GTT GTG ATG  TGT AGG AGG AAG AGC TCA G|GT  GGA  AAA  GGA GGG AG  TGC TCT CAG GCT GCG  T|CC
C*08:22      GCT GTG ATG GCT GTT GTG ATG  TGT AGG AGG AAG AGC TCA G|GT  GGA  AAA  GGA GGG AG  TAC TCT CAG GCT GCG  T|CC

                             330                  335                  340
C*08:01:01   AGC AAC AGT GCC CAG GGC TCT  GAT GAG TCT CTC ATC GCT TGT  AAA  G|CC  TGA
C*08:22      AGC AAC AGT GCC CAG GGC TCT  GAT GAG TCT CTC ATC GCT TGT  AAA  G|CC  TGA
```

Nucleotide sequences of *HLA-C*04:01* and *-C*04:82*

```
                             -20                                  -15                                  -10                                  -5                           1
C*04:01:01:01  ATG CGG GTC ATG GCG CCC CGA  ACC CTC ATC CTG CTG CTC TCG  GGA  GCC  CTG GCC CTG ACC GAG ACC TGG GCC  G|GC
C*04:82        ATG CGG GTC ATG GCG CCC CGA  ACC CTC ATC CTG CTG CTC TCG  GGA  GCC  CTG GCC CTG ACC GAG ACC TGG GCC  G|GC

                              5                                   10                                   15                                   20                           25
C*04:01:01:01  TCC CAC TCC ATG AGG TAT TTC  TCC ACA TCC GTG TCC TGG CCC  GGC  CGC  GGG GAG CCC CGC TTC ATC GCA GTG  GGC
C*04:82        TCC CAC TCC ATG AGG TAT TTC  TCC ACA TCC GTG TCC TGG CCC  GGC  CGC  GGG GAG CCC CGC TTC ATC GCA GTG  GGC

                             30                                   35                                   40                                   45                           50
C*04:01:01:01  TAC GTG GAC GAC ACG CAG TTC  GTG CGG TTC GAC AGC GAC GCC  GCG  AGT  CCA AGA GGG GAG CCG CGG GAG CCG  TGG
C*04:82        TAC GTG GAC GAC ACG CAG TTC  GTG CGG TTC GAC AGC GAC GCC  GCG  AGT  CCA AGA GGG GAG CCG CGG GAG CCG  TGG
```

9 bp insertion in exon 5

```
                  300
C*04:01:01:01  GTC  ...  ...  ...  CTA
C*04:82        GTC  CTA  GCT  GTC  CTA
```

```
                            255                                  260                                  265                                  270                           275
C*04:01:01:01  GGA GAA GAG CAG AGA TAC ACG  TGC CAT GTT CAG CAC GAG GGG  CTG  CCG  GAG CCC CTC ACC CTG AGA TGG  A|AG CCG
C*04:82        GGA GAA GAG CAG AGA TAC ACG  TGC CAT GTT CAG CAC GAG GGG  CTG  CCG  GAG CCC CTC ACC CTG AGA TGG  A|AG CCG

                            280                                  285                                  290                                  295
C*04:01:01:01  TCT TCC CAG CCC ACC ATC CCC  ATC GTG GGC ATC GTT GCT GGC  CTG  GCT  GTC CTG GCT GTC CTA GCT GTC  ...  ...  ...  TA
C*04:82        TCT TCC CAG CCC ACC ATC CCC  ATC GTG GGC ATC GTT GCT GGC  CTG  GCT  GTC CTG GCT GTC CTA GCT GTC  CTA  GCT  GTC  TA

                            305                                  310                                  315                                  320                           325
C*04:01:01:01  GGA GCT ATG GTG GCT GTT GTG  ATG TGT AGG AGG AAG AGC TCA  G|GT GGA  AAA GGA GGG AGC TGC TCT CAG GCT  GCG
C*04:82        GGA GCT ATG GTG GCT GTT GTG  ATG TGT AGG AGG AAG AGC TCA  G|GT GGA  AAA GGA GGG AGC TGC TCT CAG GCT  GCG

                            330                                  335                                  340
C*04:01:01:01  T|CC AGC AAC AGT GCC CAG GGC  TCT GAT GAG TCT CTC ATC GCT  TGT  AAA  G|CC TGA
C*04:82        T|CC AGC AAC AGT GCC CAG GGC  TCT GAT GAG TCT CTC ATC GCT  TGT  AAA  G|CC TGA
```

Pharmacogenomics of HLA loci

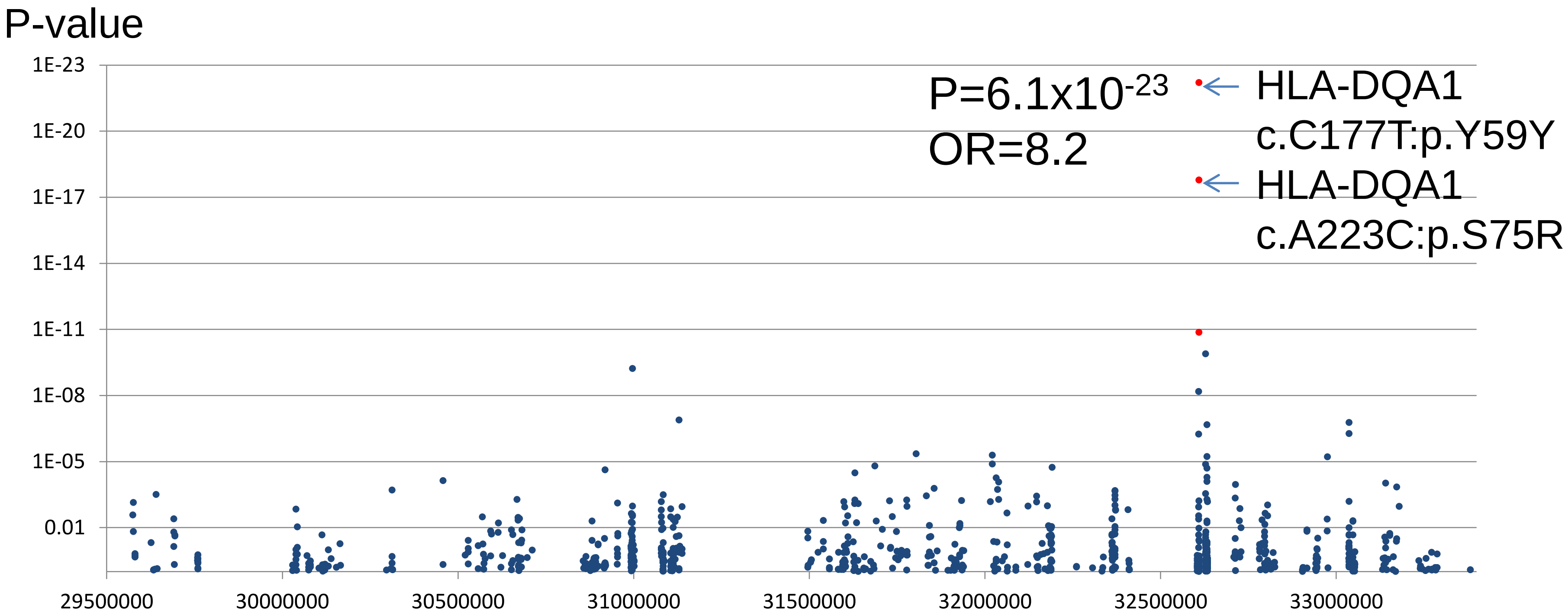
Methimazol (anti-thyroid drug) induced agranulocytosis

40 patients with agranulocytosis
after administration of antithyroid drug

Case-control study with HLA alleles

Dr.Uchino (Noguchi Hospital)

Regional plots of association results in the entire HLA region

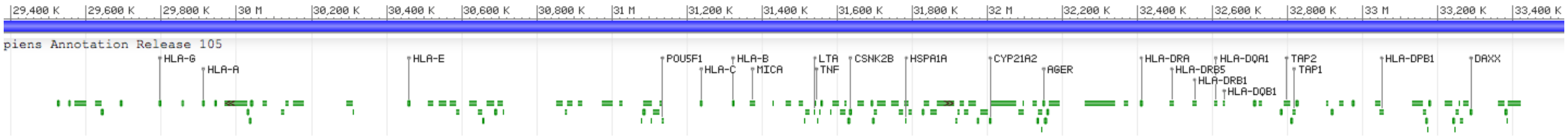


$P=6.1\text{x}10^{-23}$

OR=8.2

← HLA-DQA1 c.C177T:p.Y59Y

← HLA-DQA1 c.A223C:p.S75R



Conclusion

Completed sequencing of HLA genes with large scale, accurate, and cost effective manner.

PCR-SSO (Luminex)

HLA: 200 US$ for one locus
1200 US$ for 6 loci

60 US$/ sample for all loci

If you do pursue a career in a science, technology, engineering or math-related field, the Force will be with us! Remember, the Death Star's power to destroy a planet, or even a whole star system, is insignificant next to the power of the Force.

This Isn't the Petition Response You're Looking For
By Paul Shawcross

Awake your force!

May all the force be with you

Thanks!!