IUIS 2025 VIENNA

19th International Congress of Immunology

August 17–22, 2025 | Vienna Austria

Study of the expressed repertoires of the adaptive immune responses: example of mouse T cell receptors

Myriam Croze

https://www.imgt.org

Immunological Genome Project

Open Source immgenT

IMGT® (International ImmunoGenetics information system) provides databases and tools based on the IMGT-ONTOLOGY for in-depth exploration of the adaptive immune response.

Axis I

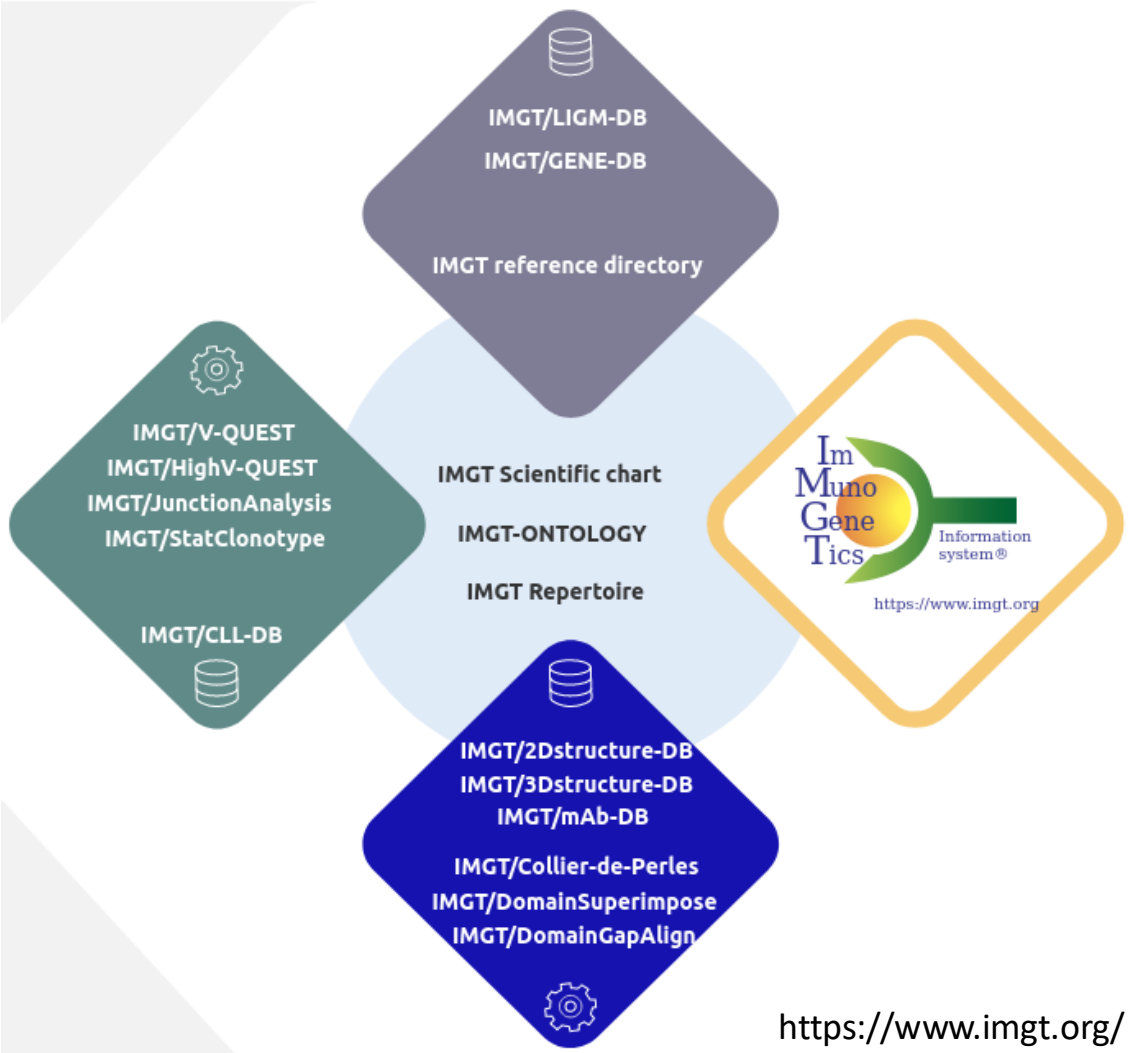
Understanding the adaptive immune response by deciphering the immunoglobulins (IG) and T cell receptor (TR) genes on the genomic loci of jawed vertebrates.

Axis II

Analysis and exploration of the expressed IG and TR repertoires based on comparison with IMGT reference directories in normal and pathological situations.

Axis III

2D and 3D structure databases and tools for analysis of the adaptive immune proteins and engineered antibodies and TR.



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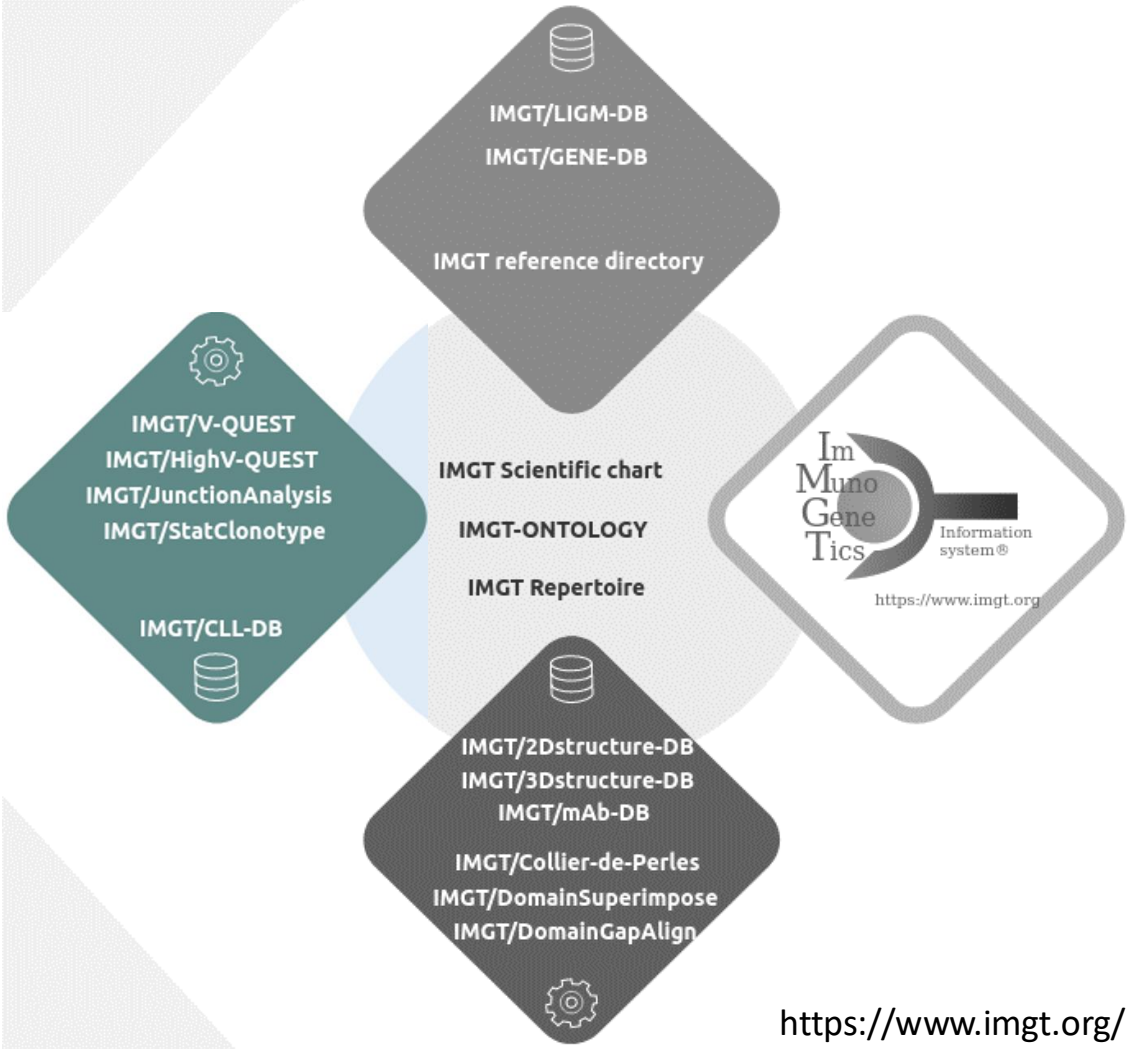


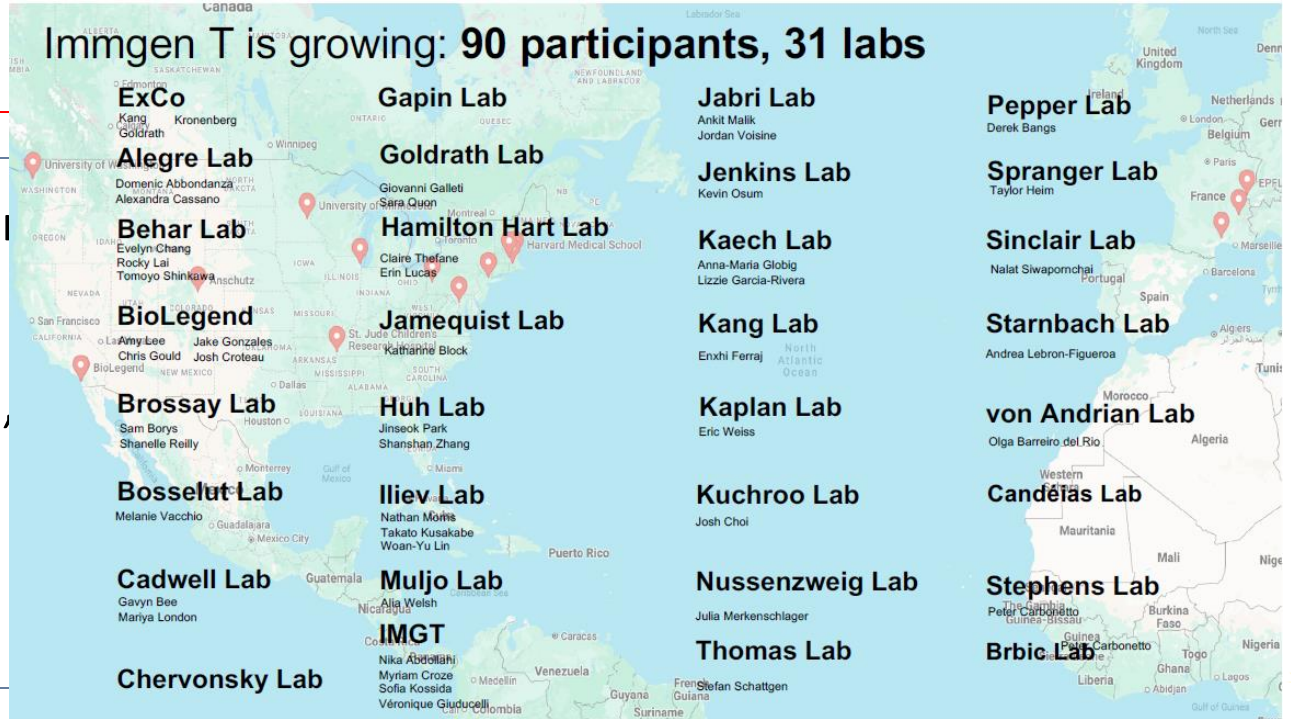
https://www.imgt.org/

➢ Collaboration between **IMGT®** and **immgenT project** to study the expressed T cell receptor (TR) repertoires of the adaptive immune response in mouse

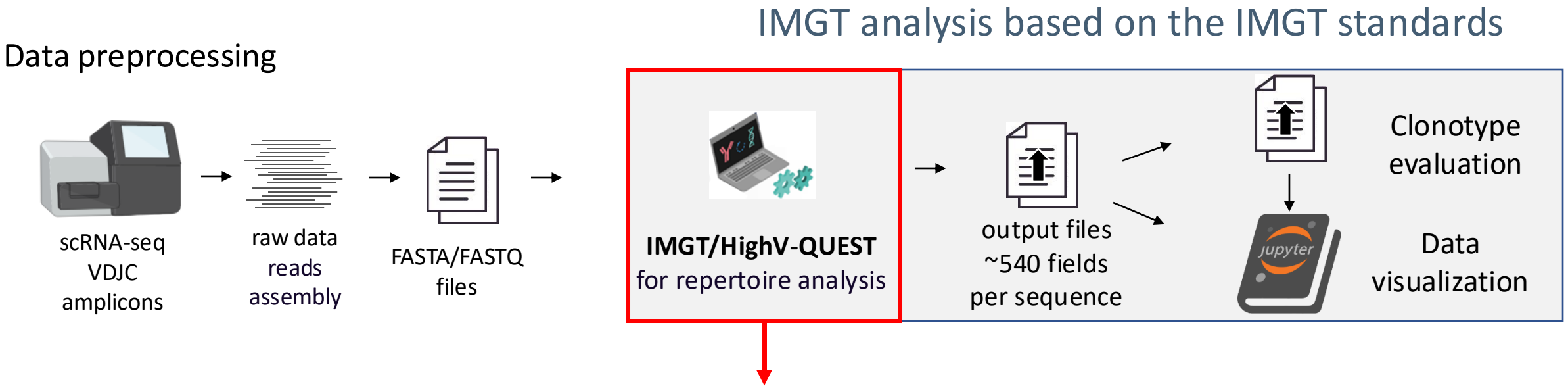
- Principal investigator of the project: **Pr. Christophe Benoist** from Harvard Medical School (HMS)
- Collaboration with **Dr. Liang Yang** from HMS, and **Dr. Serge Candéias** from the CEA.
- The project includes 90 participants from 31 labs

- Single cells RNAseq data from mouse (C57BL/6J strai

  conditions:
  - Different tissues
  - Different infections (virus, bacteria,
  - Different ages
  - Cancer
  - ….



- Fasta files for each chain are analysed with IMGT/HighV-QUEST to get the 11 output files.
- Analyses and visualization of the data



Giudicelli, V., Brochet, X., Lefranc, M.-P. Cold Spring Harb Protoc. 2011 Jun 1;2011(6). pii: pdb.prot5633. doi: 10.1101/pdb.prot5633.

Identifies the germline V, D and J genes and alleles

1. Alignment for V-GENE and allele identification

Closest V-REGIONs (evaluated from the V-REGION first nucleotide to the 2nd-CYS codon)

		Score	Identity
L06615	Homsap IGHV3-30*04 F	1260	93.06% (268/288 nt)
KC713945	Homsap IGHV3-30-3*03 F	1260	93.06% (268/288 nt)
M83134	Homsap IGHV3-30*01 F	1251	92.71% (267/288 nt)
M77300	Homsap IGHV3-30*09 F	1251	92.71% (267/288 nt)
M77324	Homsap IGHV3-30*14 F	1251	92.71% (267/288 nt)

Alignment with FR-IMGT and CDR-IMGT delimitations

```
                                <---------------------------------- FR1-IMGT ---------------
AB012909                        gaggtgcagctgttggagtctgggggga...ggcgtggtccagcctgggaggtccctgaga
L06615 Homsap IGHV3-30*04 F     c-----------g--------------...------------------------------
KC713945 Homsap IGHV3-30-3*03 F c-----------g--------------...------------------------------
M83134 Homsap IGHV3-30*01 F     c-----------g--------------...------------------------------
M77300 Homsap IGHV3-30*09 F     c-----------g--------------...------------------------------
M77324 Homsap IGHV3-30*14 F     c-----------g--------------...------------------------------
```

Analyses of the V-(D)-J junction (IMGT/JunctionAnalysis)

Analysis of the JUNCTION

D-REGION is in reading frame 1

Click on mutated (underlined) nucleotide to see the original one:

Input	V name	3'V-REGION	N1	D-REGION	N2	5'J-REGION	J name	D name	Vmut	Dmut	Jmut	Ngc	JUNCTION decryption
AB012909	Homsap IGHV3-30*04 F	tgtgcgag...	g	......acagctttctta.	acgc	....ctatgacttctgg	Homsap IGHJ4*02 F	Homsap IGHD5-18*01 F	0	3	2	4/5	(8)-3{1}-6(13)-1{4}-4(13)

Translation of the JUNCTION

Click on mutated (underlined) amino acid to see the original one:

	104	105	106	107	108	109	110	113	114	115	116	117	118	Frame	CDR3-IMGT length	Molecular mass	pI	PhysicoChemical Descriptor
	C	A	R	T	A	F	F	N	A	Y	D	F	W					
AB012909	tgt	gcg	agg	aca	gct	ttc	ttt	aac	gcc	tat	gac	ttc	tgg	+	11	1,611.8	6.15	CARTAFFNAYDFW

Be aware that some allele reference sequences may be incomplete or from cDNAs. In those cases, IMGT/JunctionAnalysis uses automatically the allele *01 for the analysis of the JUNCTION.

Description of mutations

9. V-REGION mutation and AA change table

FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT
c1>g, Q1>E (+ + -) g13>t, V5>L (+ - +) g70>a, A24>I (+ - +) c71>t, A24>I (+ - +)	g112>c, A38>P (- - -)	c118>a, H40>T (+ - -) a119>c, H40>T (+ - -) g163>a, V55>S (- - -) t164>g, V55>S (- - -)	t177>c, D59 a190>t, N64>Y (- - -)	c198>t, Y66 t199>a, Y67>K (- - -) c201>g, Y67>K (- - -) c203>t, A68>V (+ - +) g211>a, V71>M (+ - -) t226>c, F76>L (+ - -) c265>t, L89 c268>g, Q90>E (+ + -) g284>c, R95>T (- - -)	a318>g, R106 g319>a a320>c

Full annotation of the V-DOMAIN

13. Annotation by IMGT/Automat

```
Label                   Location/Qualifiers
V-D-J-REGION            1..355
                        /CDR_length="[8.8.11]"
                        /FR_length="[25.17.38.11]"
                        /nucleotide sequence
                        gaggtgcagctgttggagtctgggggaggcgtggtccagcctgggaggtccctgagactc
                        tcctgtatagcctctggattcaccttcagtagctatcctatgacctgggtccgccaggct
                        ccaggcaaggggctggagtgggtggcaagtatatcatatgacggaagttataaatataag
                        gtagactccatgaagggccgactcaccatctccagagacaattccaagaacacgctgtat
                        ttggaaatgaacagcctgacagctgaggacacggctgtgtattactgtgcgaggacagct
                        ttctttaacgcctatgacttctggggccagggaaccctggtcaccgtctcctcag
                        /translation
                        EVQLLESGGGVVQPGRSLRLSCIASGFTFSSYPMTWVRQAPGKGLEWVASISYDGSYKYK
                        VDSMKGRLTISRDNSKNTLYLEMNSLTAEDTAVYYCARTAFFNAYDFWGQGTLVTVSS
V-REGION                1..293
                        /allele="Homsap IGHV3-30*04 F or Homsap IGHV3-30-3*03 F"
                        /gene="Homsap IGHV3-30 or Homsap IGHV3-30-3"
                        /nucleotide sequence
                        gaggtgcagctgttggagtctgggggaggcgtggtccagcctgggaggtccctgagactc
                        tcctgtatagcctctggattcaccttcagtagctatcctatgacctgggtccgccaggct
```

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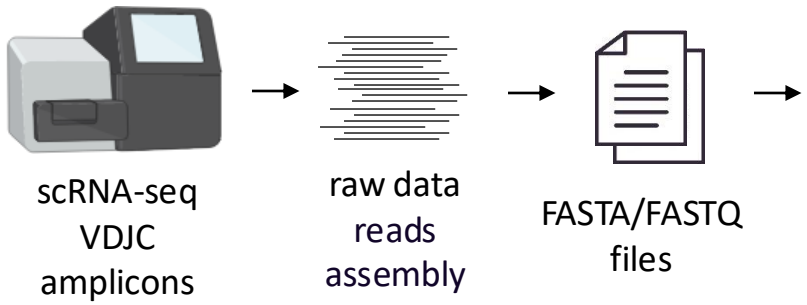
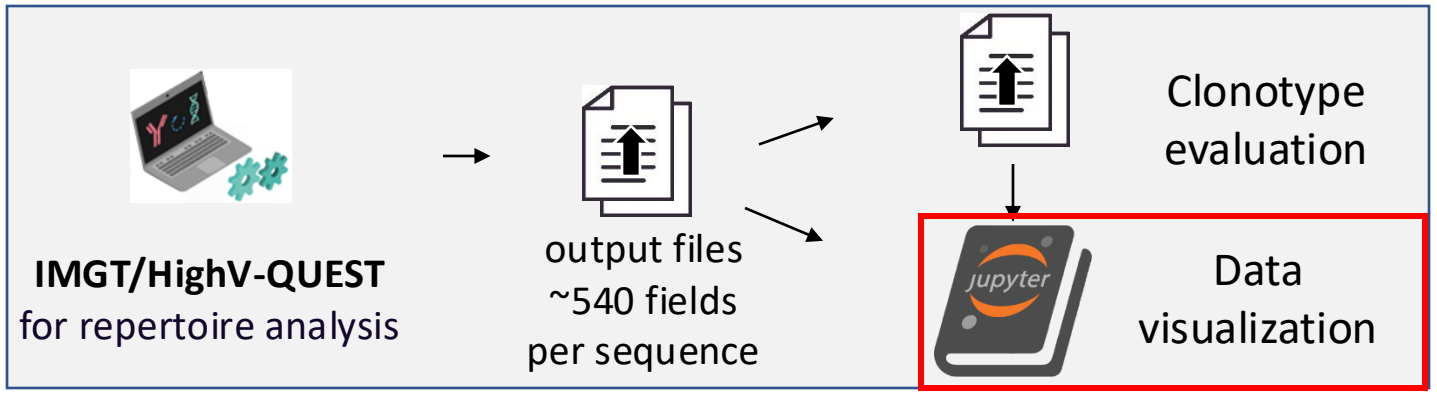
Data preprocessing



IMGT analysis based on the IMGT standards



1. V and J genes abundance:

TRA V gene and allele composition in thymus

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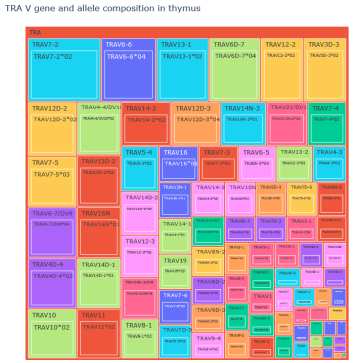
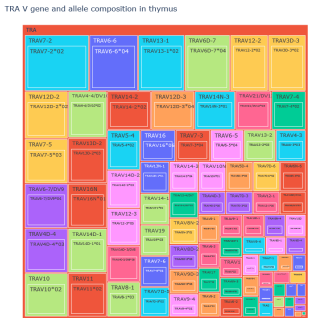


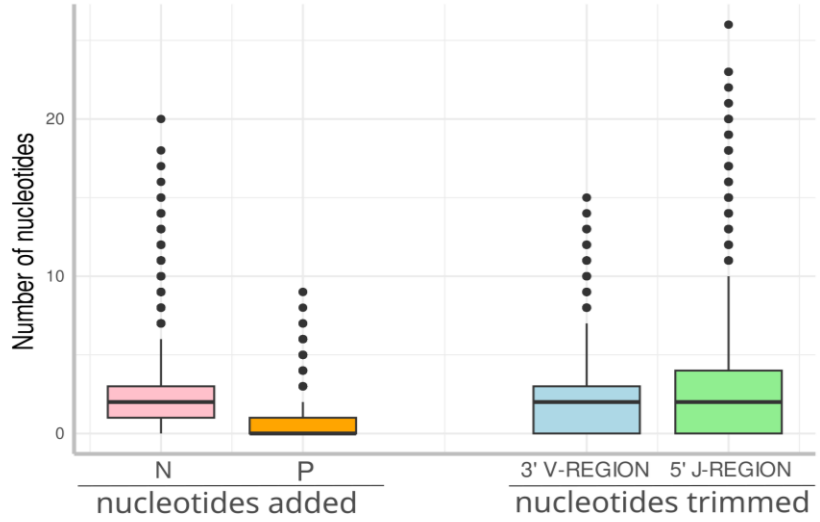
2. Preference for V-J genes pairing in chain rearrangement

1. V and J genes abundance:



2. Preference for V-J genes pairing in chain rearrangement

3. Nucleotide trimmed, N-diversity and Palindrome:



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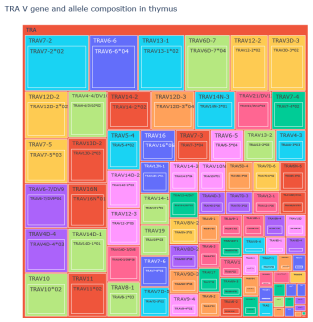

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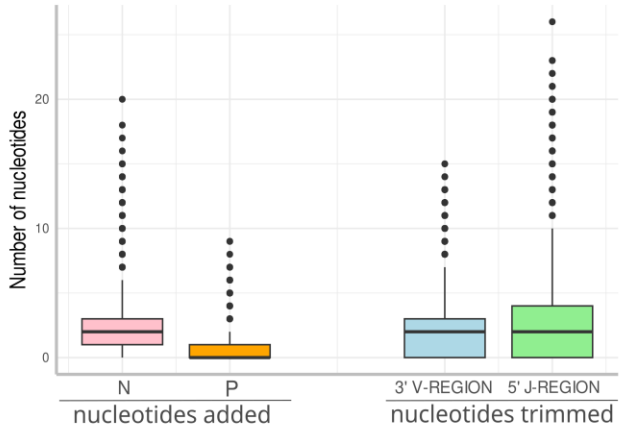
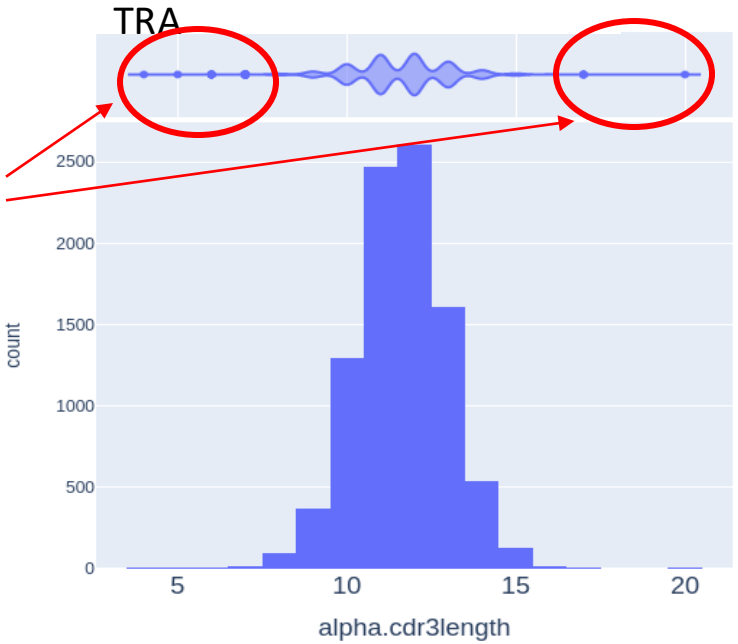


4. CDR3-IMGT length distribution

- Outliers with short (< 7 AA) or long (>16 AA) CDR3
- Identification of unusual rearrangements



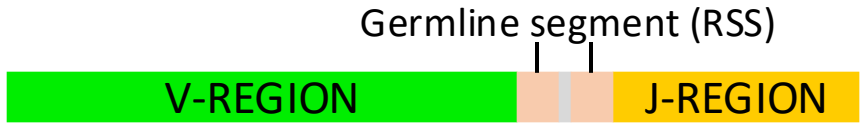
➢ Identification of unusual rearrangements

TRDD in TRA

TRDD with TRDJ1 in TRA

TRBD1 + TRBD2 in TRB

Germline segments (RSS) in TRA and TRB



Two V-REGION in TRA and TRB

Two J-REGION in TRA and TRB

Capture of unrelated germline sequence in TRA and TRB

➢ Conclusion

-> Collaboration IMGT and ImmgenT project: analysis of expressed TR repertoires in mouse with IMGT/HighV-QUEST tool and visualisation of data:

- Identification of V, D and J genes and alleles
- V-(D)-J junction analysis: nucleotide trimmed, N-diversity, palindrome and CDR3 length
- Unusual rearrangements identified: two J or V genes, germline segments, TRDD gene in alpha, etc

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IGH

Thank you for your attention

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Dr. Véronique Giudicelli

Dr. Nika Abdollahi

Université Montpellier

cnrs

Immunological Genome Project

Open Source immgenT

https://www.immgen.org/ImmGenT/

Pr. Christophe Benoist

Dr. David Zemmour

Dr. Liang Yang

Dr. Serge Candéias

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Conflict of interest disclosure

☑ I have no potential conflict of interest to report

❑ I have the following potential conflict(s) of interest to report:

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supported by ÖGAI
Austrian Society for Allergology and Immunology

Local Congress Organizers:

Rudolf Valenta (Congress President)

Wilfried Ellmeier, Barbara Bohle

Medical University of Vienna, Austria

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