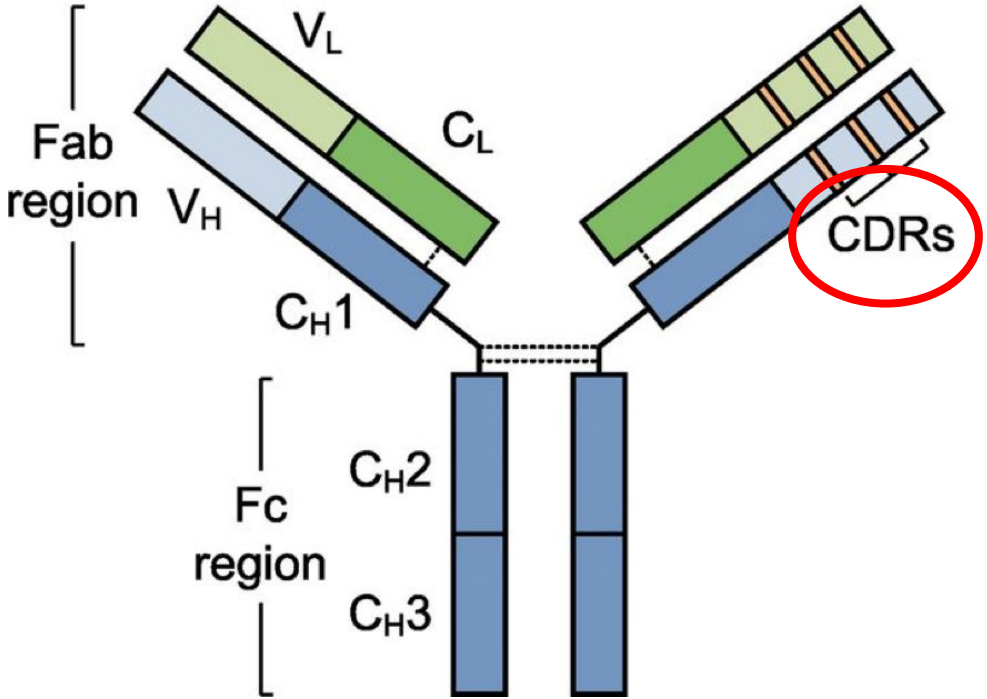
Analysis of VH replacement and gene conversion-like events in the joint diversity of IgH

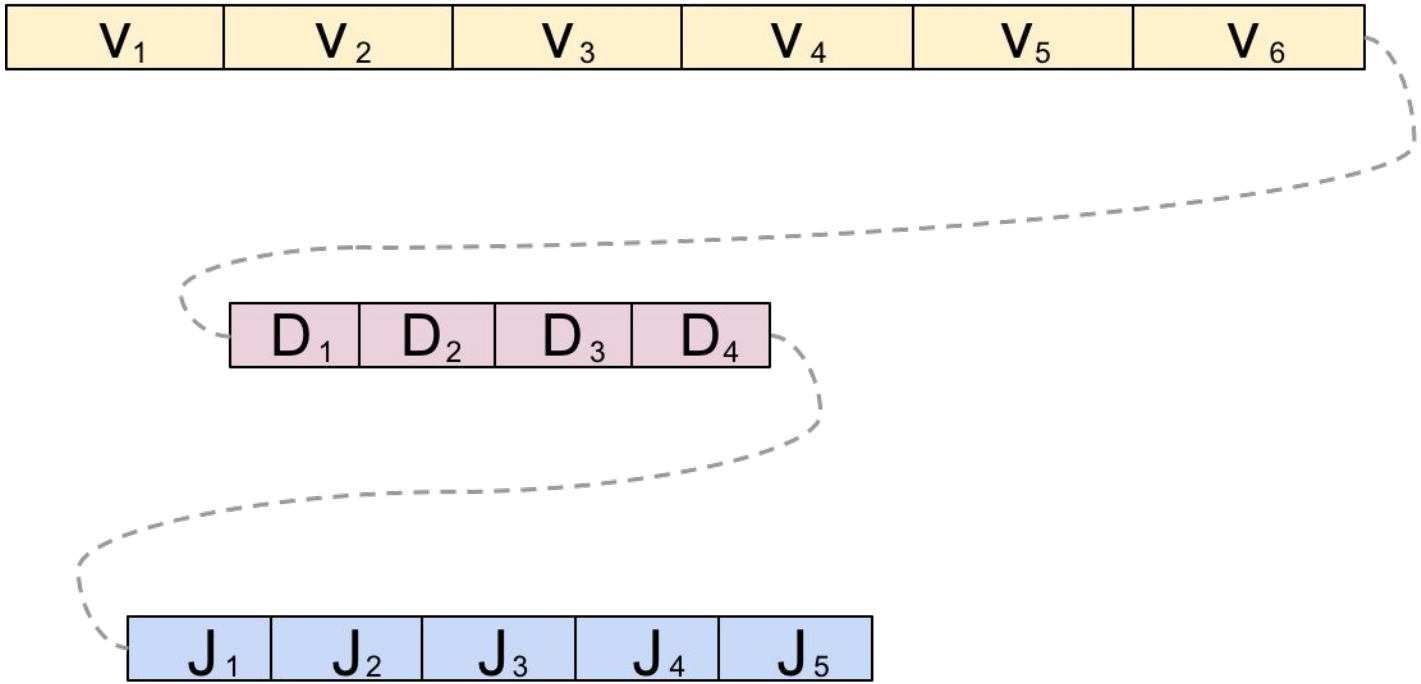
Anastasiya Vinogradova
Adel Gazizova

Oksana Ayzsilnieks, Andrey Slabodkin,
Maria Chernigovskaya

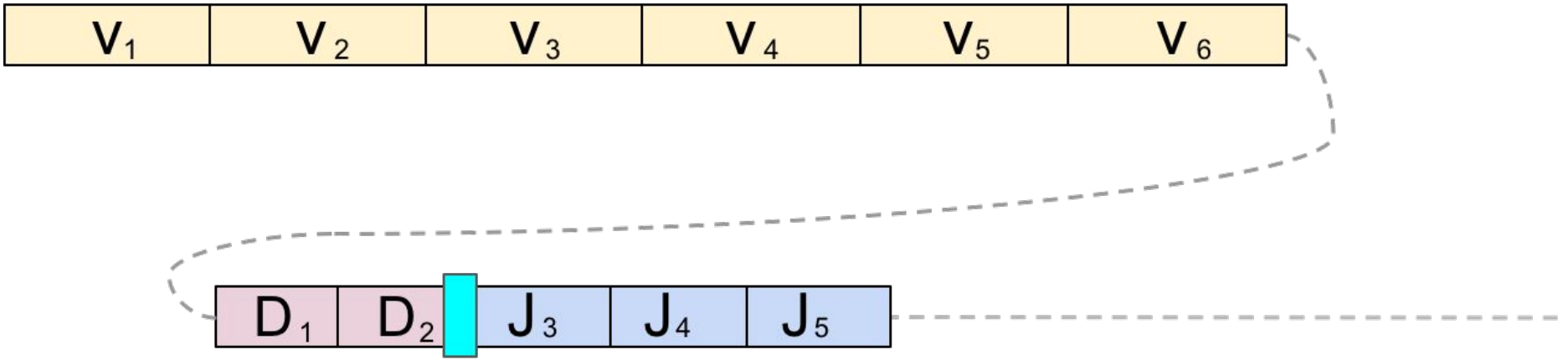
Antibodies structure



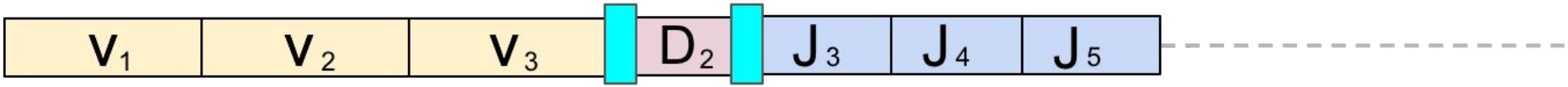
VDJ recombination



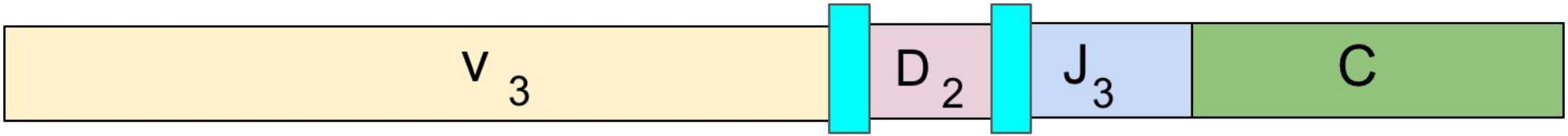
VDJ recombination



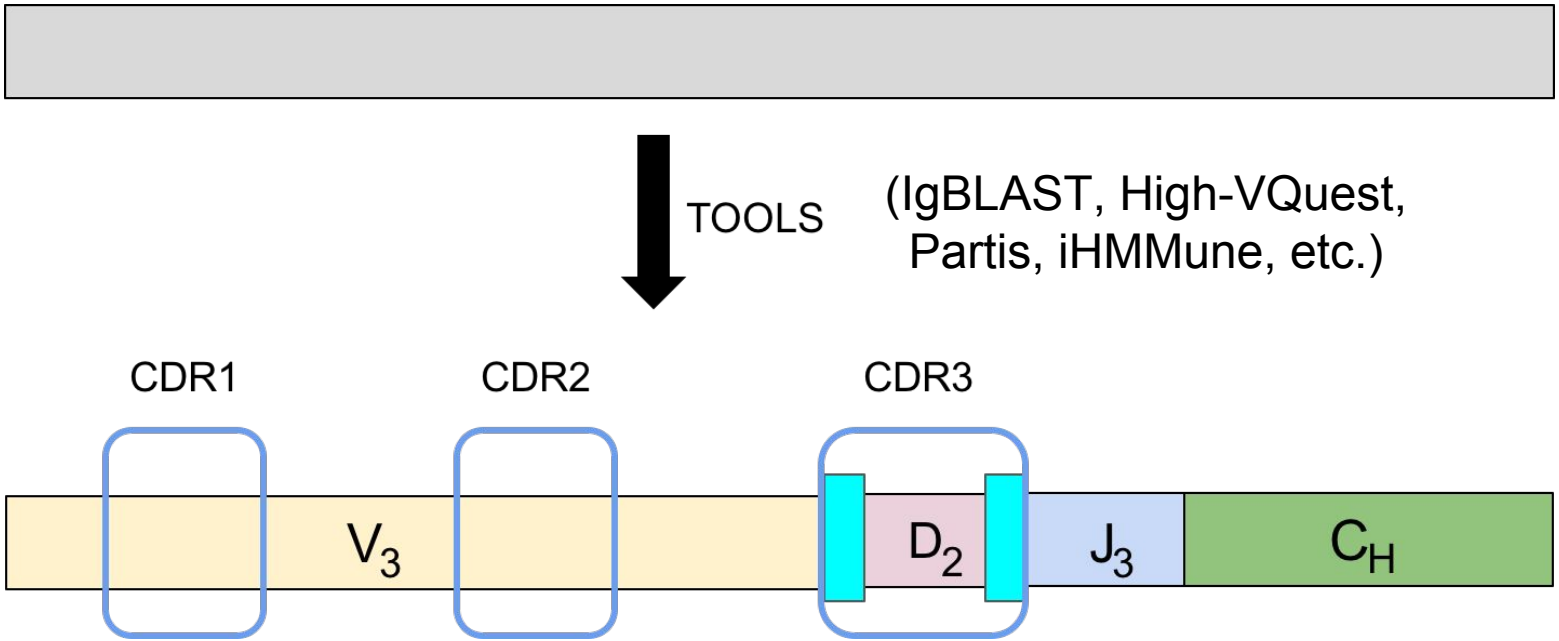
VDJ recombination



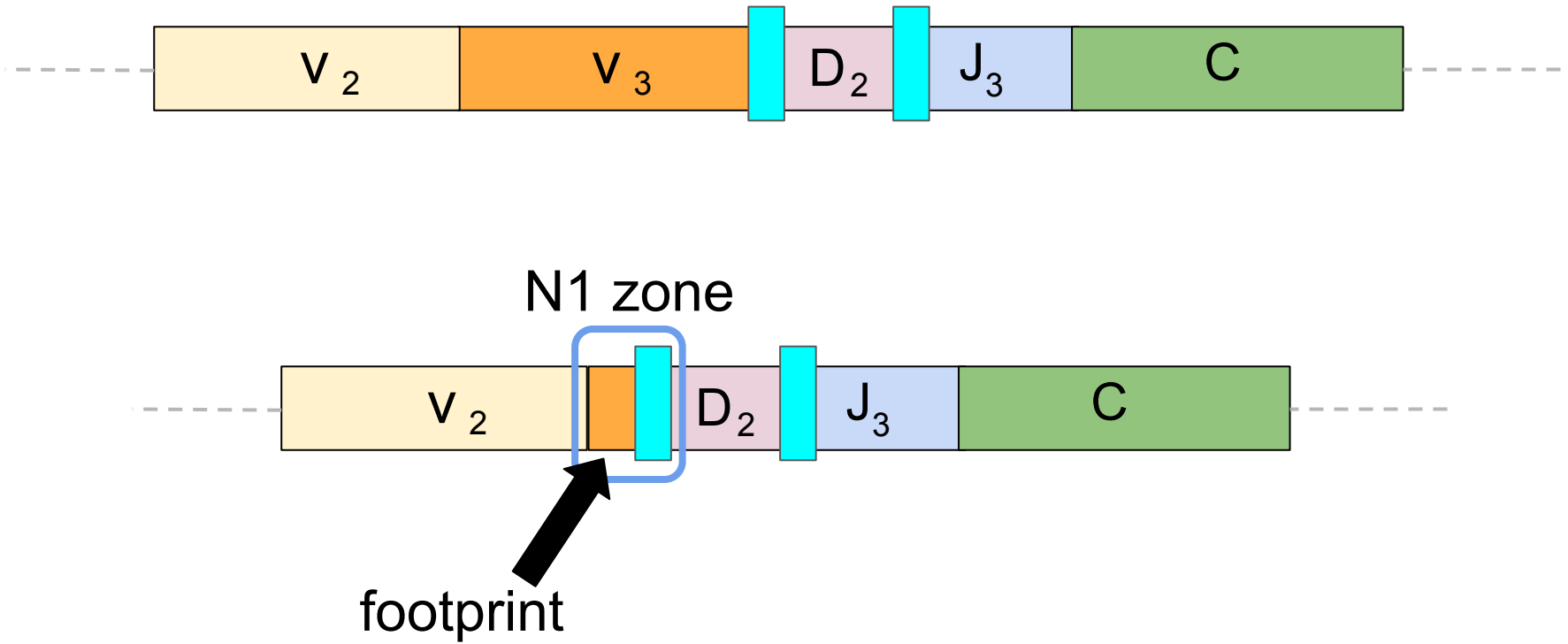
VDJ recombination



Annotation


TOOLS
(IgBLAST, High-VQuest,
Partis, iHMMune, etc.)
CDR1
CDR2
CDR3
V3
D2
J3
CH

VH replacement

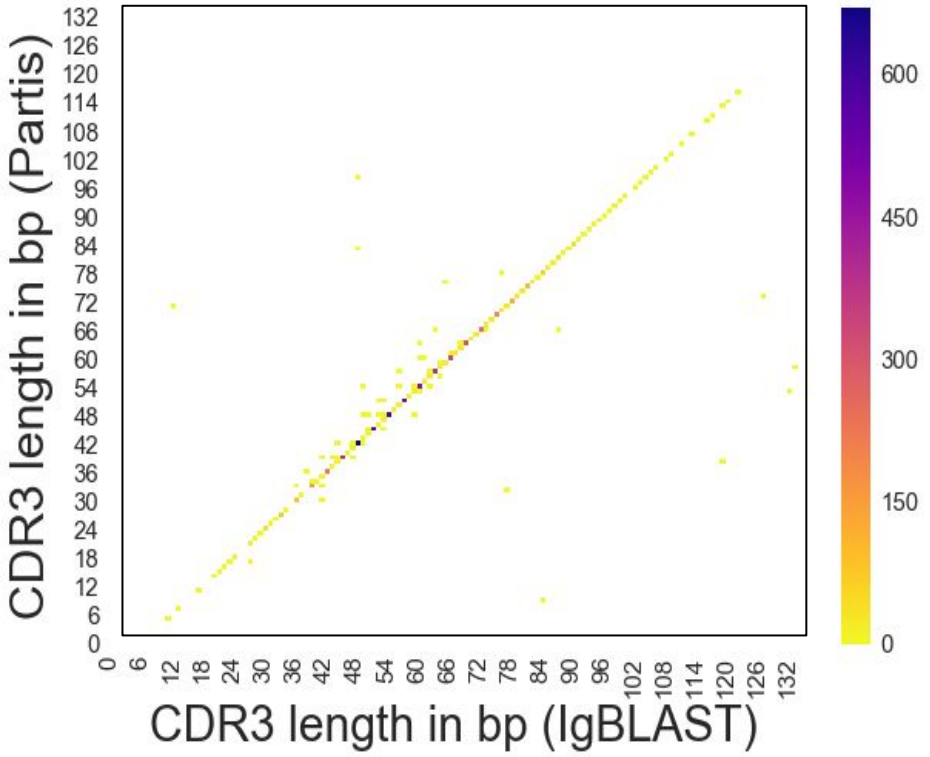


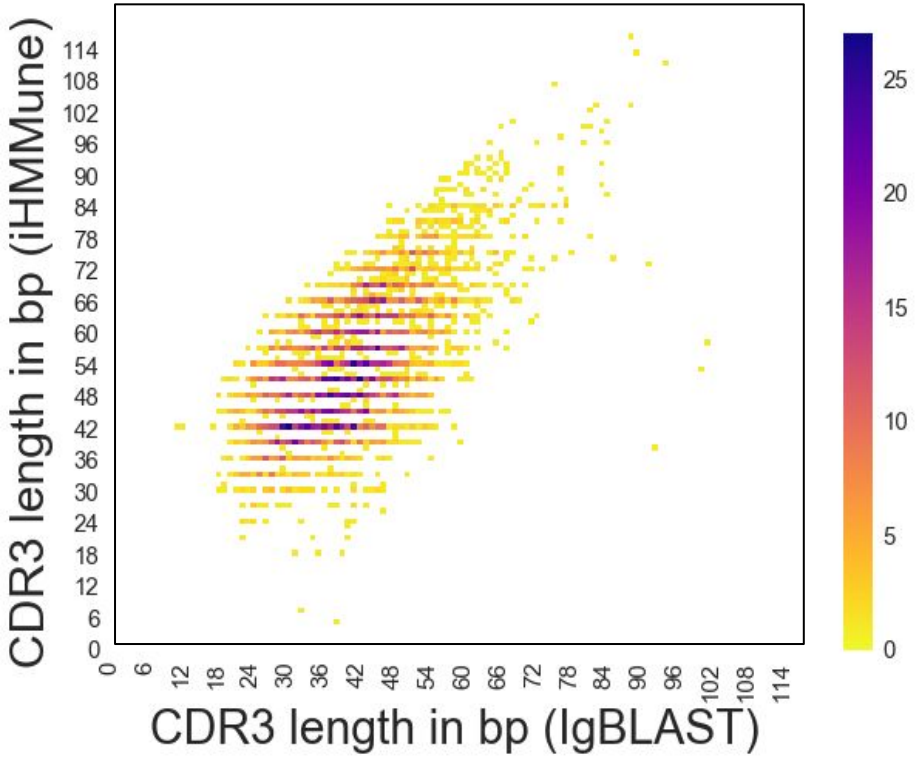
Goals of the project

1. Identify VH replacement (VHR) in sequences
2. Associate found VHRs to phenotypes
3. Detect phenotype groups that significantly differ from each other

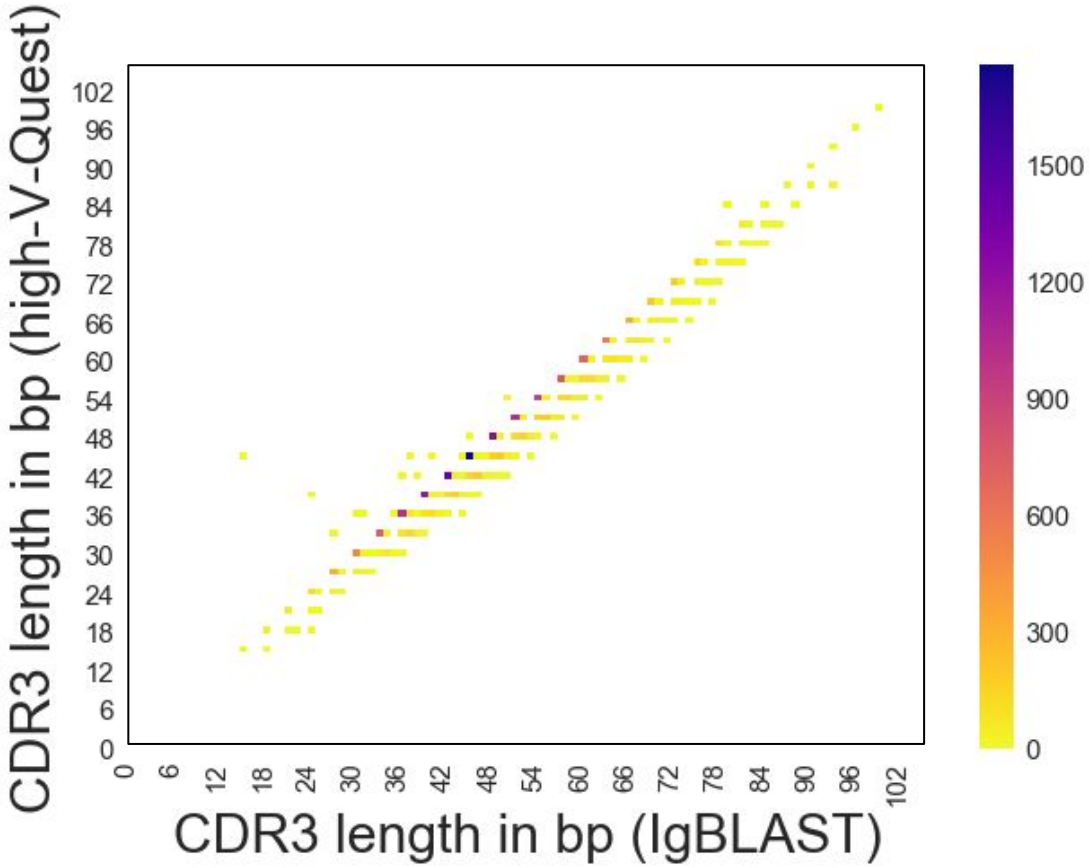
Results

CDR3 length: Partis, iHMMune vs IgBLAST



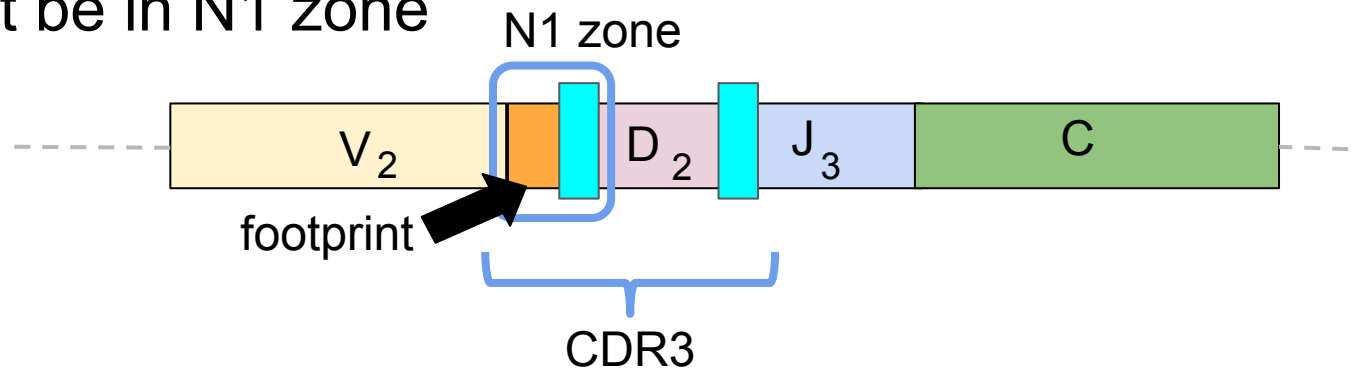


CDR3 length: High-VQuest vs IgBLAST

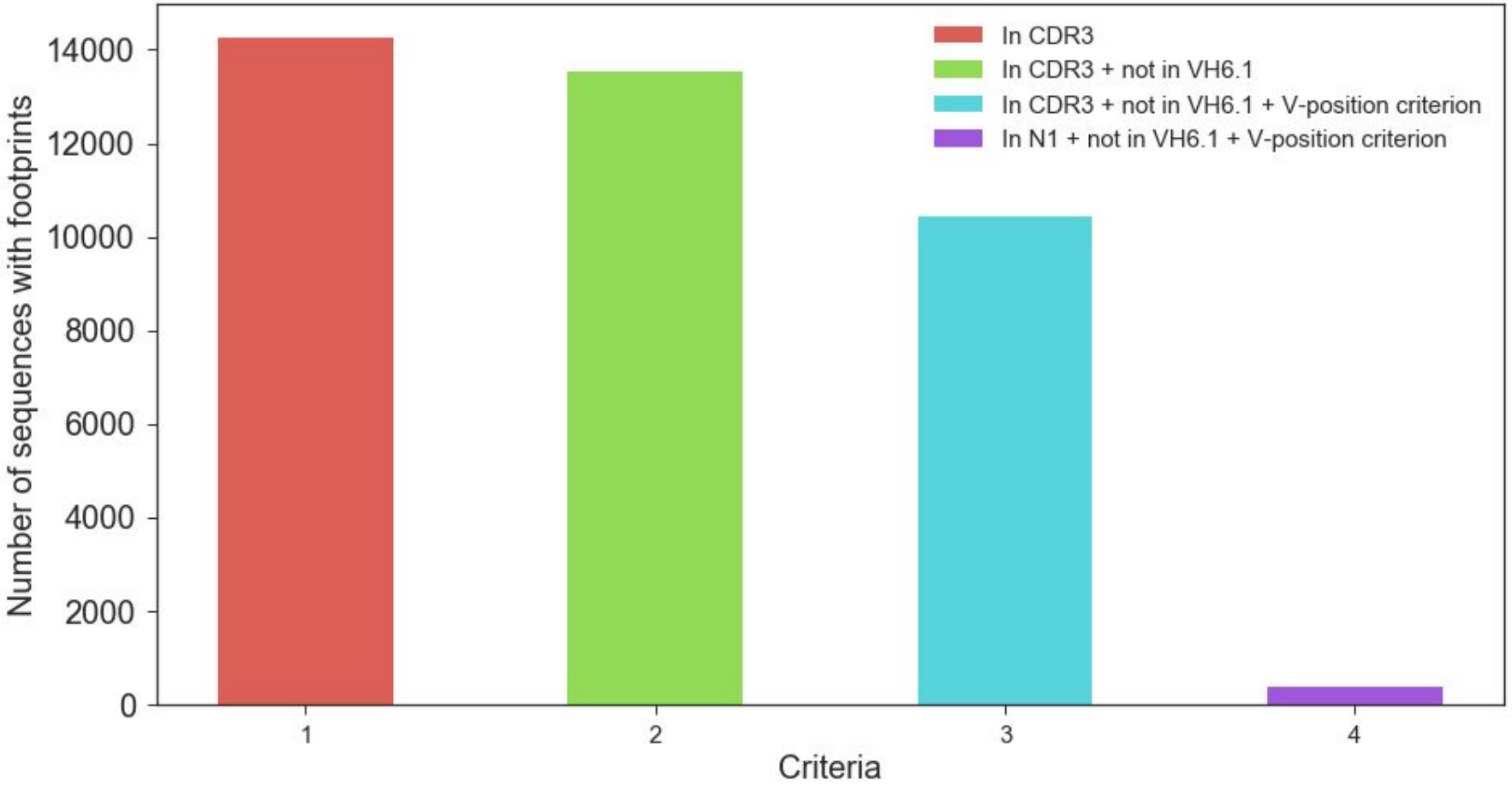


Footprints criteria

1. Footprint must be in CDR3
2. Footprints can’t be in VH6.1 gene
3. Footprint V gene must be located before sequence V gene in the locus
4. Footprint must be in N1 zone



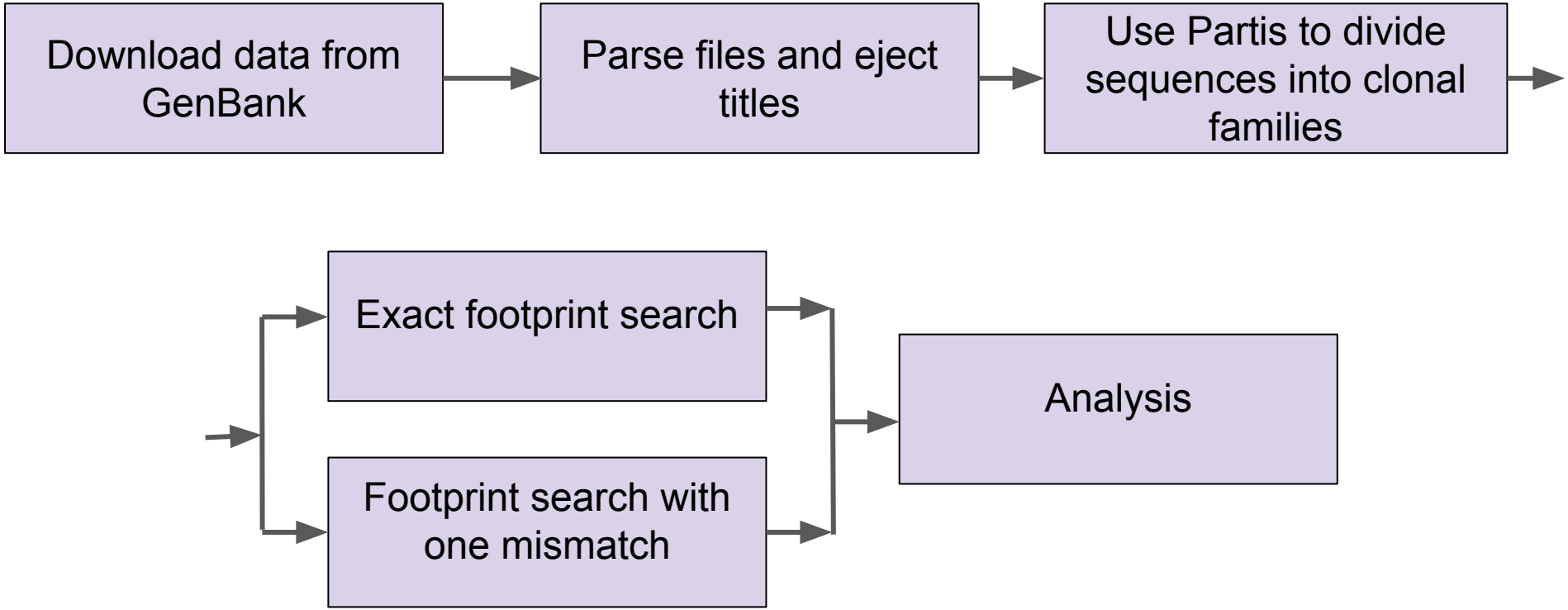
Footprints criteria



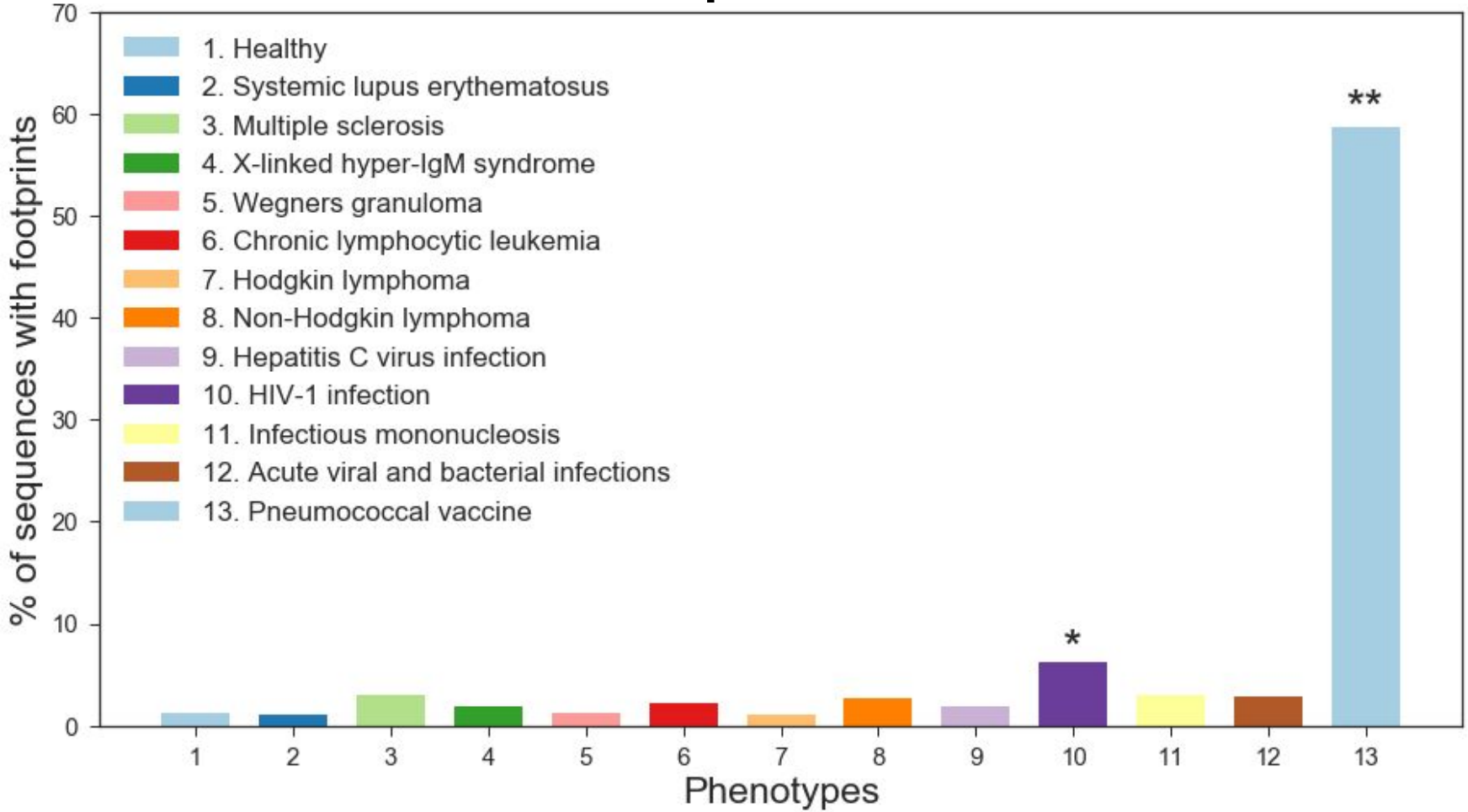
Phenotypes

- Healthy people
- People with:
  - autoimmune diseases
  - lymphomas
  - leukemia
  - chronic infections
  - acute infections

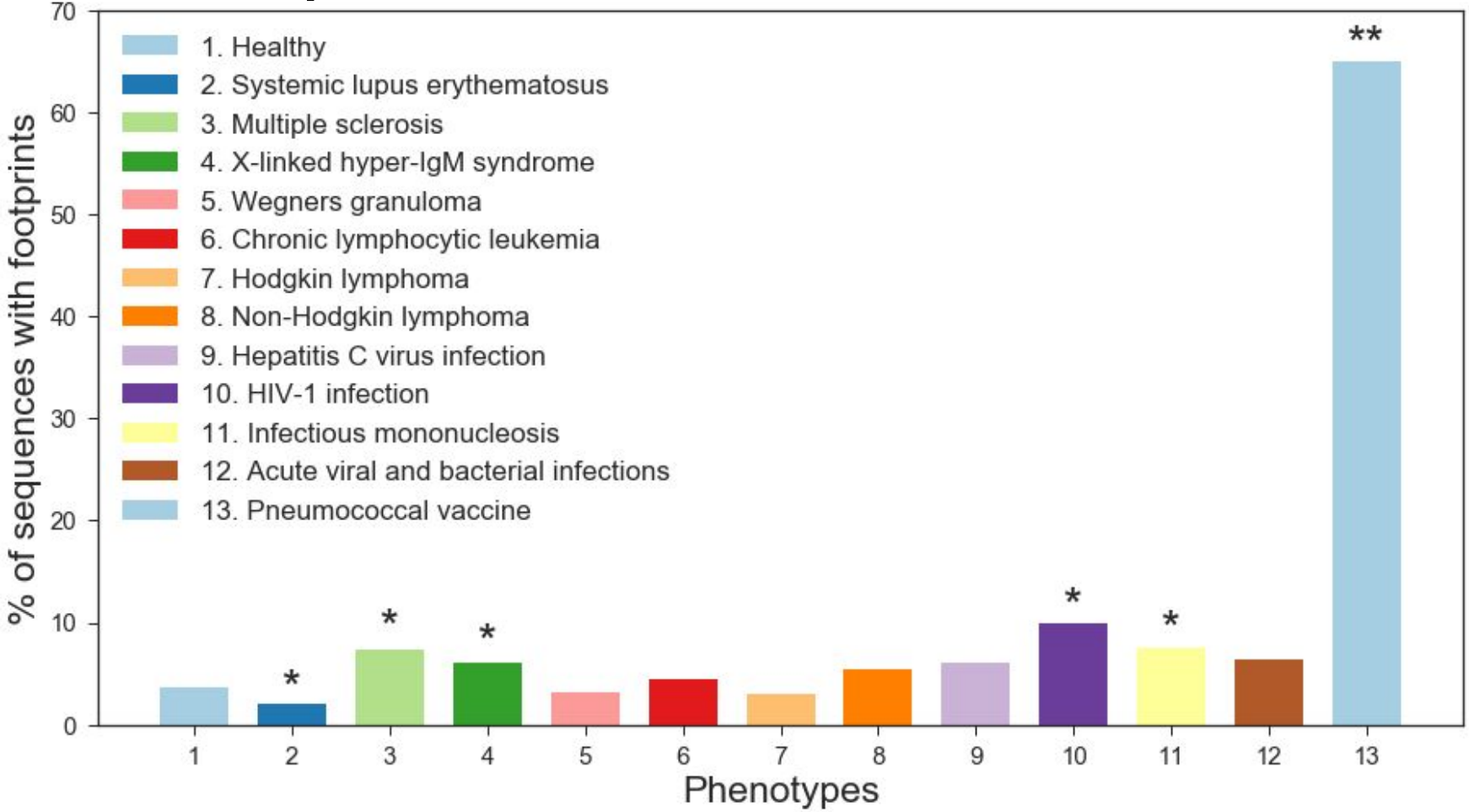
Pipeline for phenotypes detection



Exact footprint search



Footprint search with 1 mismatch

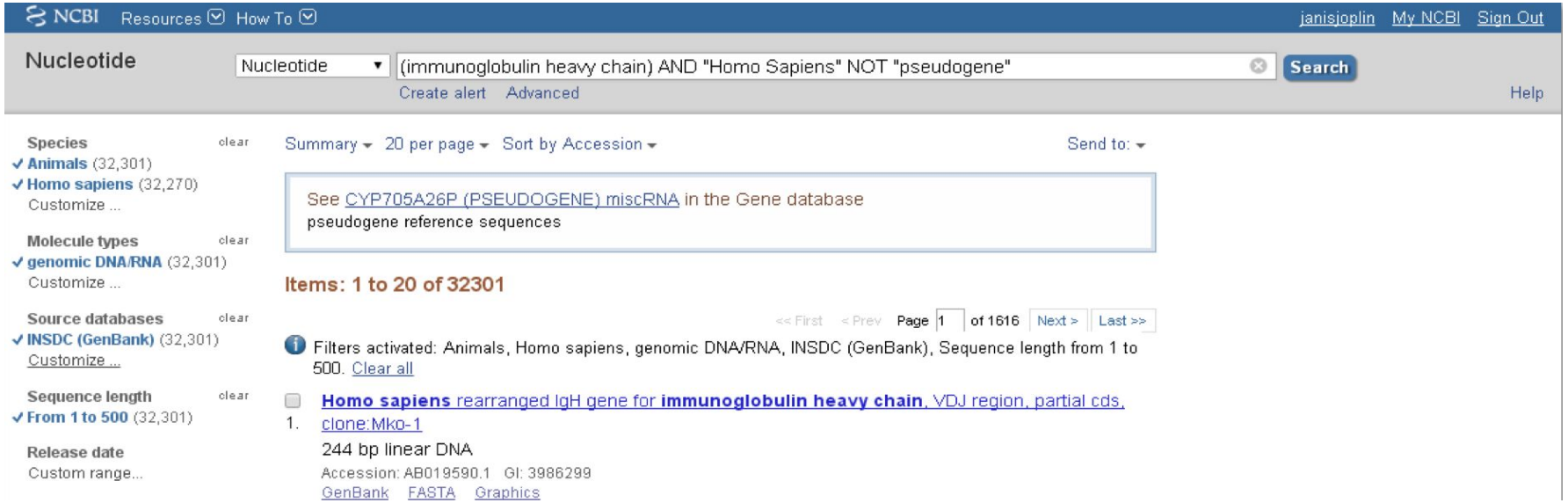


Results

1. We compared IGH annotation tools based on alignment and HMM
2. We created pipeline that searches footprints in IGH sequences
3. We analysed human IGH sequences with different phenotypes

Thank you for your attention!

Used dataset

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1|A model for the development of human IgD-only B cells: Genotypic analyses suggest their generation in superantigen driven immune responses.txt
2|Altered V(D)J recombination underlies the skewed immunoglobulin repertoires in normal and malignant B-cell precursors from fetal origin.txt
3|Amino acid sequence based PCR primers for amplification of rearranged human heavy and light chain immunoglobulin variable region genes.txt
4|Analysis of immunoglobulin VH genes suggests marginal zone B-cell lymhomas recognize similar antigens.txt
5|Analysis of rearranged immunoglobulin heavy chain variable region genes obtained from a bone marrow transplant (BMT) recipient.txt
6|Analysis of somatic hypermutation in X-linked hyper-IgM syndrome shows specific deficiencies in mutational targeting.txt
7|Analysis of the heavy chain repertoire of human peripheral B cells using single-cell polymerase chain reaction.txt
8|Analysis of the human VH gene repertoire. Differential effects of selection and somatic hypermutation on human peripheral CD5(+)!IgM+ and CD5(-)!IgM+ B cells.txt
9|Analysis of the immunoglobulin repertoire expressed by human fetal IgM- and IgM+ B cells reveals the impact of specific selection mechanism.txt
10|Analysis of VH genes rearranged in single B cells contained in dermal infiltrates of patients with Mycosis fungoides.txt
11|Antibodies against homoserine lactones.txt
12|Antibodies to acetylcholine receptor in parous women with myasthenia: evidence for immunization by fetal antigen.txt
13|Antibody repertoire analysis utilizing HIV-virus like particles identify novel quaternary epitopes on HIV-1 trimeric envelope.txt
14|Antigen selected B lymphocytes in Wegener's granuloma.txt
15|Autoantigen induced clonal expansion in immortalized B cells from the peripheral blood of multiple sclerosis patients.txt
16|B-cell clonalities in HCV infection.txt
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- Healthy people: N = 2742
- Systemic lupus erythematosus: N = 1257
- Multiple sclerosis: N = 202
- X-linked hyper-IgM syndrome: N = 994
- Wegners granuloma: N = 160
- Chronic lymphocytic leukemia: N = 741
- Hodgkin lymphoma: N = 98
- Non-Hodgkin lymphomas: N = 328
- Hepatitis C: N = 317
- HIV-1: N = 80
- Infectious mononucleosis: N = 130
- Acute viral and bacterial infections: N = 249
- Pneumococcal vaccine: N = 97

HMM