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

[Diagram of antibody structure with labeled regions: Fab region, V_L, C_L, V_H, C_H1, C_H2, C_H3, Fc region, CDRs]
VDJ recombination

\[ V_1 \quad V_2 \quad V_3 \quad V_4 \quad V_5 \quad V_6 \]

\[ D_1 \quad D_2 \quad D_3 \quad D_4 \]

\[ J_1 \quad J_2 \quad J_3 \quad J_4 \quad J_5 \]
VDJ recombination
VDJ recombination
VDJ recombination
Annotation

(tools) (IgBLAST, High-VQuest, Partis, iHMMune, etc.)

CDR1  CDR2  CDR3

V₃  D₂  J₃  C_H
VH replacement

N1 zone

footprint
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

Diagram:

- CDR3
- N1 zone
- Footprint
- V2, D2, J3, C
Footprints criteria

![Footprints criteria graph](image-url)
Phenotypes

- Healthy people
- People with:
  - autoimmune diseases
  - lymphomas
  - leukemia
  - chronic infections
  - acute infections
Pipeline for phenotypes detection

Download data from GenBank → Parse files and eject titles → Use Partis to divide sequences into clonal families

Exact footprint search → Footprint search with one mismatch → Analysis
Footprint search with 1 mismatch

- Healthy
- Systemic lupus erythematosus
- Multiple sclerosis
- X-linked hyper-IgM syndrome
- Wegners granuloma
- Chronic lymphocytic leukemia
- Hodgkin lymphoma
- Non-Hodgkin lymphoma
- Hepatitis C virus infection
- HIV-1 infection
- Infectious mononucleosis
- Acute viral and bacterial infections
- Pneumococcal vaccine

% of sequences with footprints

Phenotypes
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!
1. A model for the development of human IgD-only B cells: Genotypic analyses suggest their generation in superantigen driven immune responses.
2. Altered V(D)J recombination underlies the skewed immunoglobulin repertoires in normal and malignant B-cell precursors from fetal origin.
3. Amino acid sequence based PCR primers for amplification of rearranged human heavy and light chain immunoglobulin variable region genes.
4. Analysis of immunoglobulin VH genes suggests marginal zone B-cell lymphomas recognize similar antigens.
5. Analysis of rearranged immunoglobulin heavy chain variable region genes obtained from a bone marrow transplant (BMT) recipient.
6. Analysis of somatic hypermutation in X-linked hyper-IgM syndrome shows specific deficiencies in mutational targeting.
7. Analysis of the heavy chain repertoire of human peripheral B cells using single-cell polymerase chain reaction.
9. Analysis of the immunoglobulin repertoire expressed by human fetal IgM- and IgM+ B cells reveals the impact of specific selection mechanism.
10. Analysis of VH genes rearranged in single B cells contained in dermal infiltrates of patients with Mycosis fungoides.
11. Antibodies against homoserine lactones.
12. Antibodies to acetylcholine receptor in paroxysmal women with myasthenia: evidence for immunization by fetal antigen.
14. Antigen selected B lymphocytes in Wegener's granuloma.
15. Antigen induced clonal expansion in immortalized B cells from the peripheral blood of multiple sclerosis patients.
16. B-cell clonalities in HCV infection.
Healthy people: N = 2742
Systemic lupus erythematosus: N = 1257
Multiple sclerosis: N = 202
X-linked hyper-IgM syndrome: N = 994
Wegner's 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