Vidjil, une plateforme web pour l’étude de populations lymphocytaires par NGS

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Bonsai bioinformatics
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GBMHM/Inca

June 23, 2017
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Conflicts of interest

MS: Novartis funded his living expenses for a 2-day workshop in Dieppe, France
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1. Monitor the immune response (vaccine, immunotherapy)

2. Identify markers for leukemia stratification and follow-up
The Adaptive Immune System

- Lymphocyte B
- Lymphocyte T
- Anticorps (Ig)
- Antigène
- Cellule présentatrice d'antigène
- Fragment d'antigène
- Récepteur des cellules T (TR)
TCR and Antibody Specificity – V(D)J Recombination
TCR and Antibody Specificity – V(D)J Recombination

AGG TCA ATAC GAT GACT GGG GTC
AG CTC ATAC GTC AGG GAG

V: 50 to 200  D: 5 to 30  J: 20 to 60
Sequence: 100 to 350
V(D)J recombinations are responsible for receptor diversity.
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Diversity region
Immune Repertoire Sequencing (RepSeq)
Strategies – Sequencing millions of V(D)J recombinations from T-cells or B-cells

DNA
RNA

a) CDR3 specific primer

b) Consensus PCR primers

c) Capture probe

d) RNA-Seq

Quantitative PCR

HTS
Rep-Seq
Immune Repertoire Sequencing (RepSeq)

Identification of all VDJ recombinations
Immune Repertoire Sequencing (RepSeq)
Identification of all VDJ recombinations

V2 J6

V3 J5

V3 J5

V3 J5

V3 J5

V3 J5

V1 J4

V1 J3

V1 J5
Immune Repertoire Sequencing (RepSeq)
Identification of all VDJ recombinations

20%  50%  30%
Childhood leukemias
Concentration du lymphocyte cancèreux

Pourcentage

Concentration du lymphocyte cancèreux

Jours

Pourcentage

Jours
Concentration du lymphocyte cancéreux

Pourcentage

Jours

Concentration du lymphocyte cancéreux

Pourcentage

Jours

Concentration du lymphocyte cancéreux

Pourcentage

Jours

Concentration du lymphocyte cancéreux

Pourcentage

Jours

Concentration du lymphocyte cancéreux

Pourcentage

Jours

Concentration du lymphocyte cancéreux

Pourcentage

Jours

Concentration du lymphocyte cancéreux

Pourcentage

Jours
A strong collaboration with Lille hospital since 2011

N. Grardel
N. Duployez
A. Caillault
M. Figeac
S. Sebda
C. Preudhomme
Vidjil Platform

High-throughput Repertoire Sequencing (RepSeq) analysis

Web Application

Algorithm

Client

Patient database

Server

C++

Javascript, d3.js

Python, web2py, AJAX

- all the Vidjil components are open-source (GPL v3)
- code on http://www.vidjil.org/ and on GitHub
- continuous integration, > 2,000 unit and functional tests

Duez et al., PLOS One, 2016
<table>
<thead>
<tr>
<th>merge</th>
<th>align</th>
<th>to IMGT/V-QUEST</th>
<th>to IgBlast</th>
<th>to Blast</th>
<th>4 clones, 738 494 reads (90.53%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRGV3 1/11/2 J1</td>
<td>49.30%</td>
<td>★</td>
<td>i GCCACCTGGGACAGCTCCC-TT-GTTC-ATTATAAGAAACTCTTTGGCAGTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRGV3 4/1/2 J1</td>
<td>41.23%</td>
<td>★</td>
<td>i GCCACCTGGG---A---T---G---T---ATTATAAGAAACTCTTTGGCAGTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRGV3 3/16/3 J1</td>
<td>0.0021%</td>
<td>★</td>
<td>i GCCG--CTGGAGACCCAAATGTTGACGGGTTATAAGAAACTCTTTGGCAGTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRGV3 5/4/2 J1</td>
<td>+</td>
<td>★</td>
<td>i GCCACCTGGG---GC---CA---AT---T---A---TA---AGAAACTCTTTGGCAGTG</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Web application: traceability– Reports for medical records
Patient database and server

Autonomous RepSeq analysis pipeline in a clinical/research lab
Patient database and server

Autonomous RepSeq analysis pipeline in a clinical/research lab

Upload

L1413893.fastq
Patient database and server

Autonomous RepSeq analysis pipeline in a clinical/research lab

Upload

Process

upload list
L1413893.fastq

last processing | status
2015-02-09 | RUNNING
Patient database and server

Autonomous RepSeq analysis pipeline in a clinical/research lab

Upload

Process

Analyze

upload list

L1413893.fastq

last processing  status
2015-02-09  RUNNING

see the result: multi
Web Application, October 2014 to June 2017

Public test server app.vidjil.org, >100 users, including 30 regular users

10,000 samples
Web Application, October 2014 to June 2017
Public test server app.vidjil.org, >100 users, including 30 regular users

1,000
ALL/CLL patients at diagnosis in 5 labs
Web Application, October 2014 to June 2017

Public test server app.vidjil.org, >100 users, including **30 regular users**
Web Application, October 2014 to June 2017
Public test server app.vidji1.org, >100 users, including 30 regular users
Lille, 2015: routine diagnosis of patients with ALL
5 tubes, mainly BIOMED-2 primers

January-March
34 patients
3 patients with Sanger failure
comparison with IMGT and igBlast

January-December
120 patients

Y. Ferret, A. Caillault et al., British J. of Haematology, 2016
Analyze your immune repertoire data with Vidjil

Interactively process all lymphocyte receptors

Ready-to-use platform to handle HTS/RepSeq data
Analyze your immune repertoire data with **Vidjil**

**Interactively process all lymphocyte receptors**

Ready-to-use platform to handle HTS/RepSeq data

**Open-source software**

Feel free to use: app.vidjil.org
Feel free to contribute: git.vidjil.org
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**New academic and industrial collaborations**
ALL/CLL diagnosis and follow-up, other pathologies
Immunological studies, immune monitoring