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To cite this version:
Méline Wery, Emmanuelle Becker, Franck Auge, Charles Bettembourg, Olivier Dameron, et al.. Identification of causal signature using omics data integration and network reasoning-based analysis. JOBIM 2019 - Journées Ouvertes Biologie, Informatique et Mathématiques, Jul 2019, Nantes, France. pp.1. hal-02193860

HAL Id: hal-02193860
https://inria.hal.science/hal-02193860
Submitted on 24 Jul 2019

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Identification of causal signature using omics data integration and network reasoning-based analysis

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Introduction

Identifying a pathological signature for a complex disease remains a challenge.

The actual definition of a signature in the context of a disease is:

- a set of features able to separate two populations
- based on statistical test

Features can be further used as candidate therapeutic targets.

Objective: Pathological signature based on individual features

⇒ Individualize the identification of signature based on patient specific information (Polymorphism + Gene expression)
⇒ Integrate multi-omics data with prior knowledge on interaction network

Method

Part 1: Discretization of omics data

Genotyping

<table>
<thead>
<tr>
<th>Gene</th>
<th>SNP with HIGH impact</th>
<th>Yes</th>
<th>No</th>
<th>Undefined value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQTL</td>
<td>Filter and discretization over gene expression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Value in {1; -1}</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Part 2: One-by-one patient approach

One biological network
KRF¹ (Pathway Commons)

Mapping the Genotyping data for each patient

Dynamic of the system?
Regulatory dependancies?
Need to clamp other variables (= MIS²) in order to explain the phenotype based on the genotype?

Gene expression

Analysis of each gene expression

Interval of expression for each gene in control population

Value in: \{-1, 0, 1\}

Stable state of the system
Gene Expression
Phenotype

Part 3: Identifying Minimal Intervention Set (MIS)

Conclusion & Perspectives

Diagnosis signature from literature is insufficient for complex disease
Identify a signature by taking into account the dependencies of regulation

Causal signature ⇒ Minimal set of MIS between patients
⇒ New stratification of patients
⇒ Enrich signature with clinical criteria
⇒ Propose candidate therapeutic targets

References

3 Videla, S. et al. (2017). Bioinformatics