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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**.

## Limits of current approaches

1. Limited to one omic layer
2. Require a clear stratification of population
3. Identified features = mix causes, consequences and noise
4. Limited to the most striking effects ⇒ regulation ?

**Objective :** Pathological signature based on individual features

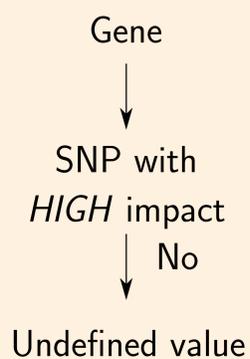
⇒ **Individualize** the identification of signature based on patient specific information (Polymorphism + Gene expression)

⇒ **Integrate multi-omics data with prior knowledge on interaction network**

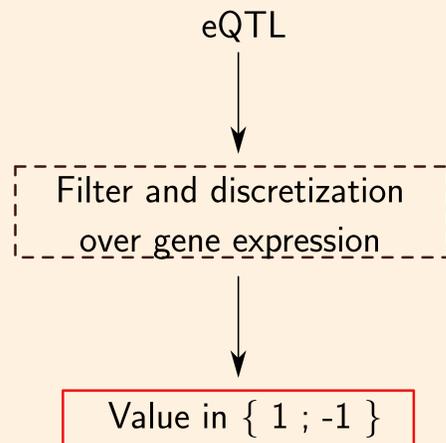
## Method

### Part 1 : Discretization of omics data

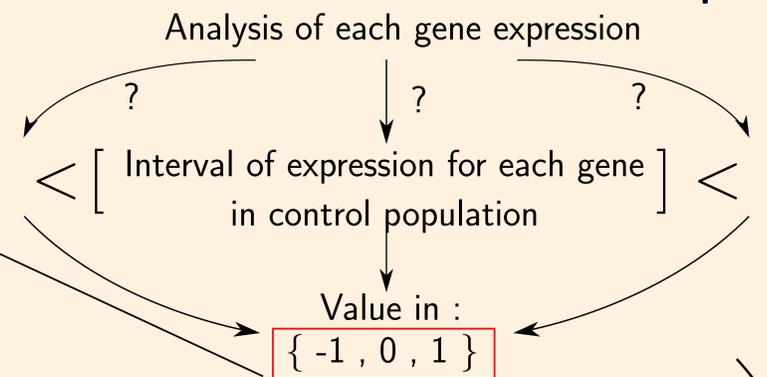
#### Genotyping



#### By patient



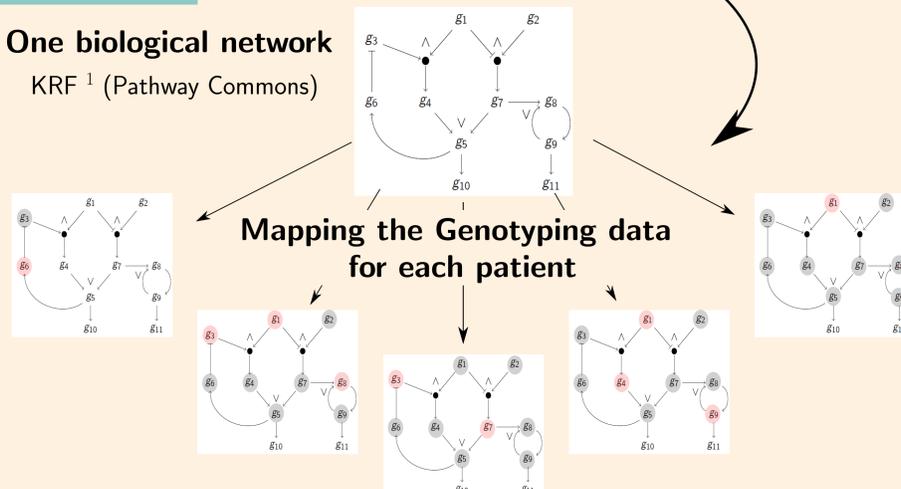
#### Gene expression



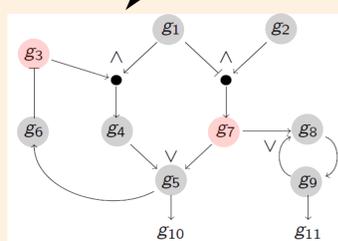
### Part 2 : One-by-one patient approach

#### One biological network

KRF<sup>1</sup> (Pathway Commons)



### Part 3 : Identifying Minimal Intervention Set (MIS)



Dynamic of the system ?  
Regulatory dependencies ?

Need to clamp other variables (= MIS<sup>2</sup>)  
in order to  
explain the phenotype based on the genotype ?  
Caspo<sup>3</sup>

Stable state of the system

=  
Gene Expression  
=  
Phenotype

<sup>1</sup> Blavy, P. et al (2014) BMC Systems Biology

<sup>2</sup> Samaga, R. et al (2010) Journal of Computational Biology

<sup>3</sup> Videla, S. et al.. (2017). Bioinformatics

## 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