

Building handprints of complex diseases – severe asthma as a proof of concept



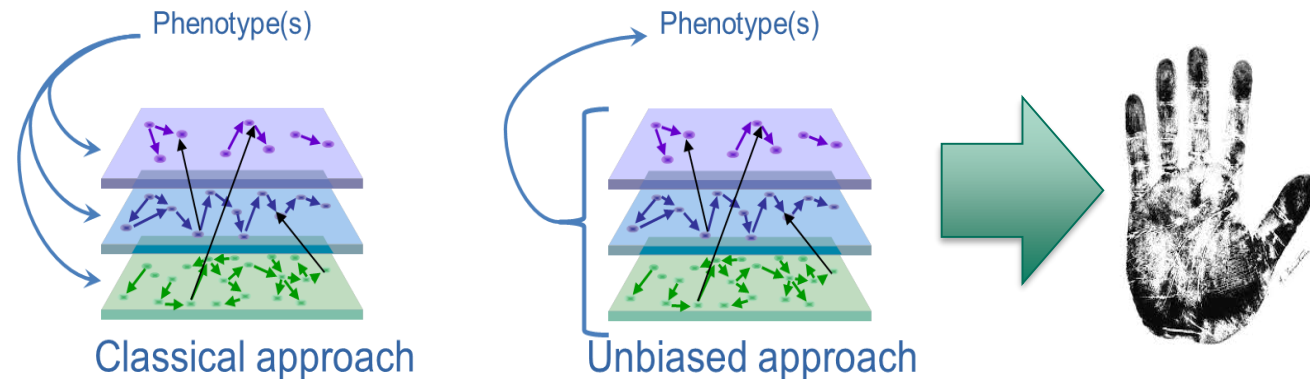
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Rationale

U-BIOPRED hypothesis

Revisiting disease stratification using molecular information

Integrating omics data using an innovative systems biology methodology



Methods

Framework developed during U-BIOPRED and eTRIKS projects

Data hosted in tranSMART

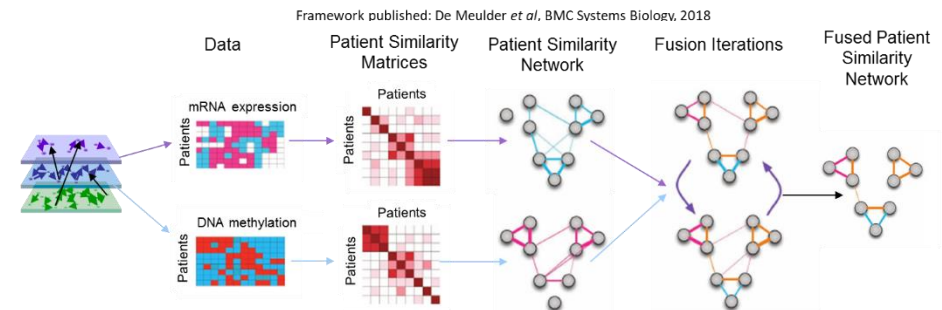
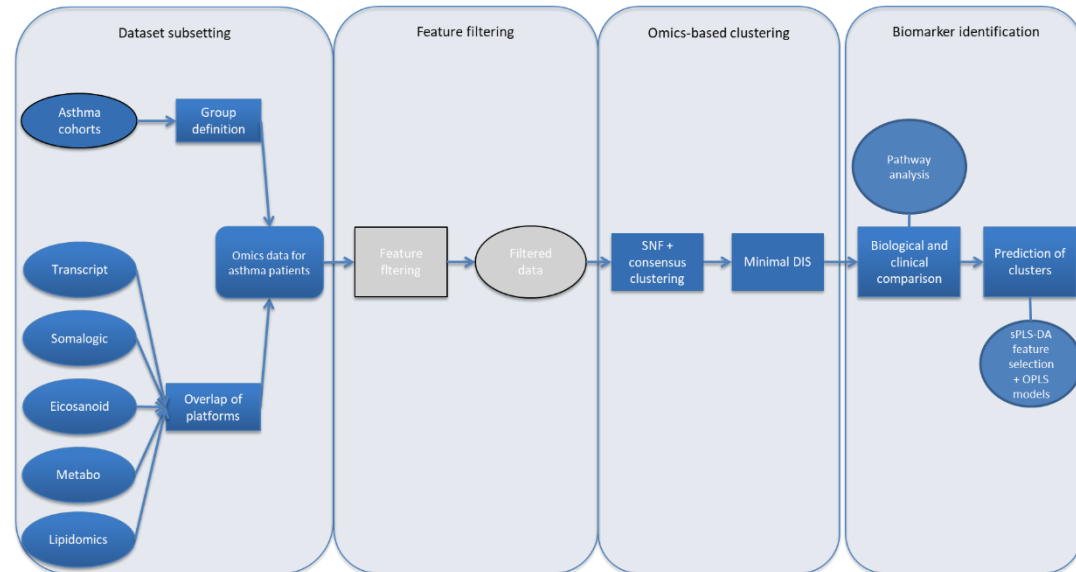
Data fusion: SNF (Wang *et al*, Nature methods, 2011)

Clustering: Consensus clustering with spectral clustering (Wilkerson *et al*, Bioinformatics, 2010)

Deviation from ideal stability (Lefaudeux *et al*, JACI, 2016)

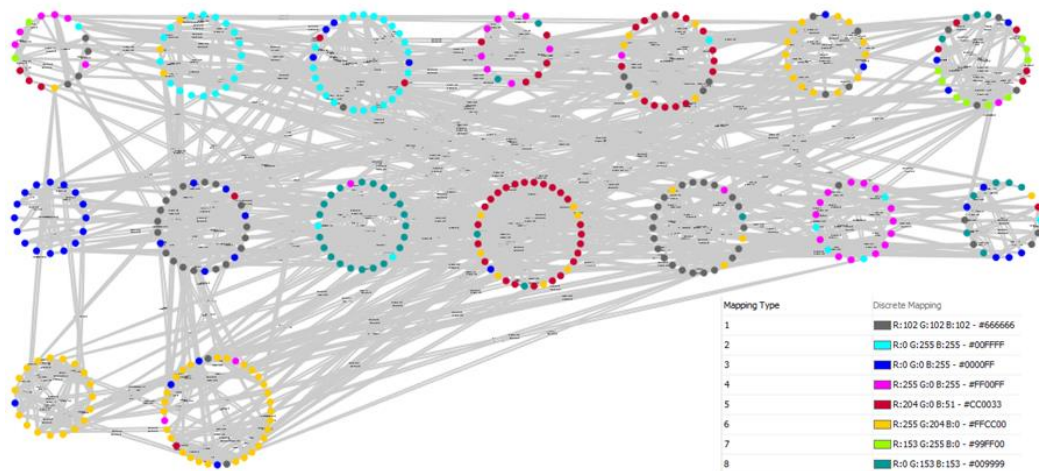
Pathway analysis: g:Profiler (Reimand *et al*, NAR 2016)

Prediction: mixOmics DIABLO (Singh *et al*, 2016)



Similarity network fusion for aggregating data types on a genomic scale, B. Wang *et al*, Nature Methods 11, 333–337 (2014), doi:10.1038/nmeth.2810

Clusters



Cluster	Clinical	Biological
2	Low FEV1 and FVC, high macrophages, high ICS and low OCS	Type-1 interferon signaling, cytokine signaling in immune system
3	Female, high FVC, low neutrophils, no OCS	Histone demethylation, dioxygenase activity
5	Younger, early onset, high macrophages, high medication	Interleukin 3, 5 and GM-CSF signaling, platelet activation, response to oxygen compounds
6	Older, high BMI, high OCS	Influenza infection, Selenocysteine synthesis, regulation of macrophages

Predictive modelling

Prediction based on clinical variables alone is not conclusive

Prediction based on omics variables:

- Selecting necessary and sufficient predictors of groups
- Across several omis platforms
- Exploring the correlations between features

Example for cluster 2

