



HAL
open science

Identification of Driver Nodes in Genetic Networks Regulating Macrophage Activation

Giulia Bassignana, Jennifer Fransson, Olivier Colliot, Violetta Zujovic,
Fabrizio de Vico Fallani

► **To cite this version:**

Giulia Bassignana, Jennifer Fransson, Olivier Colliot, Violetta Zujovic, Fabrizio de Vico Fallani. Identification of Driver Nodes in Genetic Networks Regulating Macrophage Activation. Conference on Complex Systems - CSS, Sep 2018, Thessaloniki, Greece. hal-01967797

HAL Id: hal-01967797

<https://hal.science/hal-01967797>

Submitted on 1 Jan 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Identification of Driver Nodes in Genetic Networks Regulating Macrophage Activation

G. Bassignana^{1,2}, J. Fransson¹, O. Colliot^{1,2}, V. Zujovic¹, F. De Vico Fallani^{1,2}. (1) Sorbonne Univ, UPMC Univ Paris 06, Inserm U-1127, CNRS UMR-7225, Institut du Cerveau et de la Moelle Epinière, 47 Boulevard de l'Hôpital, 75013 Paris, France, giulia.bassignana@gmail.com. (2) Inria Paris, Aramis project-team, 2 Rue Simone IFF, 75012 Paris, France.

Macrophage cells play an important role in the Multiple Sclerosis disease. They are known to participate both to the degenerative process, myelin destruction, and to the regenerative one, coordinating remyelination. The correct genetic activation of macrophage phenotypes permits a correct remyelinating response [1], thus the possibility to steer it towards a healthy state while acting on a limited number of genes (drivers) would be greatly advantageous.

We modeled macrophage activation as a network (Figure 1.a), where nodes correspond to genes involved in phosphorylation and directed links corresponded to significant activations as retrieved from the STRING Database [2]. We adopted the structural controllability framework [3], mapping the Kalman controllability criterion into the maximum cardinality matching on a graph, to identify the driver nodes. Because different configuration of driver nodes are in general possible, we repeated the analysis $R=60000$ times and shuffled the order of the nodes in the adjacency matrix in order to explore different configurations. We defined the node *driverness* as the frequency of times a nodes is selected as driver over R iterations.

Our work is a preliminary step towards the identification of the genes influencing the inflammatory process of macrophages, a crucial mechanism in multiple sclerosis' disease.

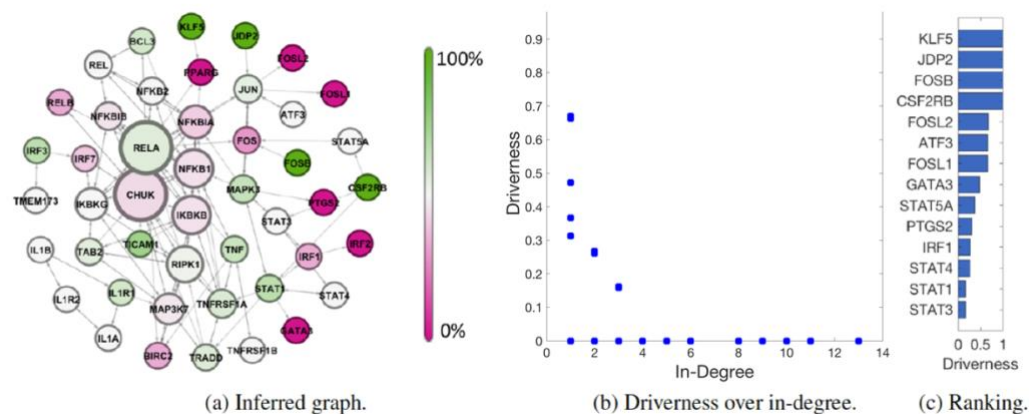


Figure 1: (a) Inferred network of genes involved in phosphorylation, 46 nodes and 168 directed edges. Size of the nodes corresponds to their degree, color to percentage of outgoing links. (b) Driverness of the nodes over their in-degree. (c) Genes ranked by driverness.

References

- [1] V.E. Miron et al., *Nature Neuroscience*, 16 (2013) 1211-1218.
- [2] D. Szklarczyk et al., *Nucleic Acids Res.*, 45 (2017) D362-D368.
- [3] Y.Y. Liu, J.J. Slotine, A.L. Barabasi, *Nature*, 473 (2011) 167-173.