Identification of Driver Nodes in Genetic Networks Regulating Macrophage Activation

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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 an 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.

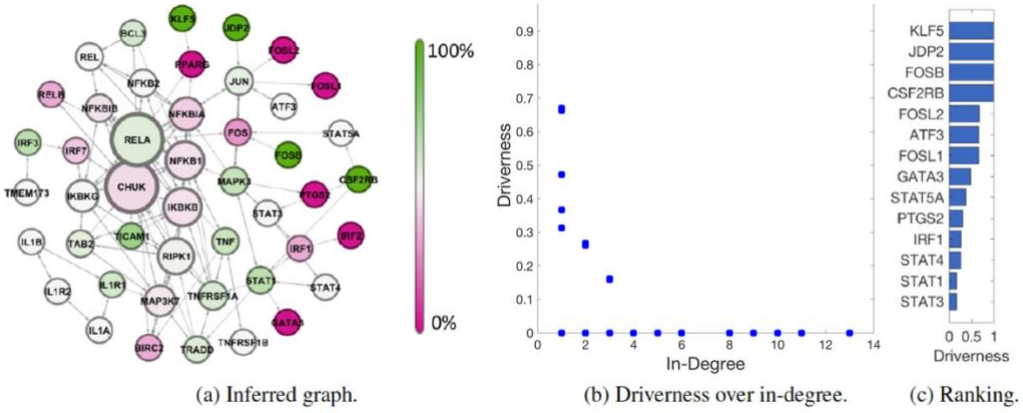

Figure 1: (a) Inferred network of genes involved in phosphorylation, 46 nodes and 168 directed edges. Size of the nodes corresponds to their degree, color to percentage of outgoing links. (b) Driverness of the nodes over their in-degree. (c) Genes ranked by driverness.

References

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[3] Y.Y. Liu, J.J. Slotine, A.L. Barabsi, *Nature*, 473 (2011) 167-173.