

### CT 2.1.3

## Viral Networks, connecting virus-human interaction networks to population disease patterns

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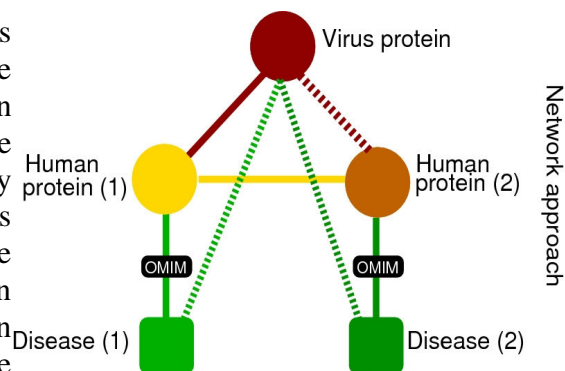
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### Introduction

To discover the underlying principles that translate genomic information to observed phenotypes (e.g., diseases) the study of global properties of cellular networks is essential. Any perturbation to the network, originated by a virus or drug, impacts not just the locally targeted subnetwork but spreads through out the network. This global cascading damage spreading in cellular networks is largely not understood. We have developed a method that provides a new approach to study virus-human interactions and its correlations with diseases. Our method is not specific to the virus reported here, and it involves the utilization of protein-protein interaction data obtained from various experimental methods with gene-disease correlations and patient medical history data.

We have applied the method described in this paper to the Epstein-Barr virus (EBV) for which the virus-host interactome has been experimentally measured (Ref. 1). The first step in our method is to combine the EBV-human protein-protein interactome with the gene-disease map provided by the Online Mendelian Inheritance in Man database (OMIM) (Ref. 2). This integration provides a full map of potential links from virus proteins to diseases, which we name the EBV diseasome network.

As shown in Fig.1, the human proteins which are first or second degree interactors of virus proteins in the human interactome are used to construct the diseasome map. An experimentally measured interaction between a virus protein and a human protein can be associated with a disease if the human protein is associated with that disease in the OMIM database. These diseases are “first-degree” diseases potentially caused



by the virus. Secondary protein

interactions, the proteins that the human protein interacts with, are also included in this construction, since these neighboring proteins can also be significantly affected by the virus. Hence the diseases associated with these neighboring proteins can also be correlated with the virus as “second-degree” diseases.

### Results

An interesting observation the developed EBV diseasome network provides is that the diseases highly associated with EBV in the medical literature do appear in this

network, and they are either first or second degree diseases. Merging all the diseases associated with EBV from two websites (wikipedia.org and emedicine.com) we obtained a comprehensive EBV-associated disease list. Of these 21 diseases listed in Table I, 15 of them appear in the EBV network. When we remove all the pathways that do not belong to diseases that are related to EBV in literature, we end up with a connected dense network. This resulting topology is quite interesting and unexpected. In contrary, a randomly chosen non-literature based disease set yields a disconnected sparse network.

In order to quantify the disease-disease correlations, we also investigated patient medical history data in connection to EBV disease. We find that an interesting modularity appears on the diseaseome among the diseases that appear more often than expected by chance in EBV carrying patients. This result and the fact that EBV diseaseome includes the diseases that appear to be correlated with EBV in literature reveal that cellular network analysis provides useful and unexplored insights into human diseases.

### **Acknowledgement**

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### **References**

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