Network Medicine - An interactome-based approach to rare diseases

Zusammenfassung

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Recent advances in high-throughput technologies, such as genomics, proteomics and metabolomics, now allow us to study the molecular roots of human diseases at an unprecedented level of detail. At the same time, it has become apparent that increasing data alone will not suffice to truly understand disease phenomena in a holistic fashion. Despite having identified hundreds of implicated genes for most common diseases, many details of how exactly they contribute to the disease pathobiology remain in the dark. A major missing ingredient is that beyond identifying the perturbed components, we also need to understand the complex machinery in which they operate. Indeed, most diseases result from an interplay of multiple molecular components that interact with each other in intricate networks. The emerging field of 'network medicine' applies tools and concepts from network theory to systematically disentangle these networks.

One of the fundamental concepts of network medicine is to view diseases as perturbations within the 'interactome', i.e. the comprehensive network map of molecular components and their interactions. In a study of ~300 complex diseases we could recently show that the genes associated with a particular disease are localized in specific neighborhoods, or 'disease modules', within such an interactome (Menche et al., Science 2015). The overall ambition of this research project is to both deepen our fundamental understanding of the relationship between interactome perturbations and disease manifestations, and to convert conceptual insights into concrete computational methods, such as disease gene prioritization methods or diagnostic tools.

Rare diseases are the ideal starting point for this endeavor: First, close to 4000 rare diseases have a well-described genetic origin, thus offering the opportunity to conduct large-scale analyses and uncover general principles that are common to many diseases. Second, rare diseases include a wide range of disease phenomena, from specific syndromes with well-characterized, often monogenic origins, to heterogeneous phenotypes with complex genetic associations. This allows us to systematically explore the full spectrum of disease associated interactome perturbations, from single, highly detrimental mutations to hundreds of variations with small contribution. Third, rare diseases provide a promising entry point to translate conceptual insights from network medicine into concrete precision medicine applications. Compared to complex diseases, the molecular basis of specific phenotypes can often be pinpointed more precisely in rare diseases, thus considerably simplifying the first step towards using the molecular characteristics of an individual patient to tailor a personalized treatment.

Wissenschaftliche Disziplinen:
106044 - Systems biology (50%) | 102004 - Bioinformatics (30%) | 305907 - Medical statistics (15%) | 103029 - Statistical physics (5%)

Keywords:
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VRG leader:	Jörg Menche
Institution:	CeMM - Research Center for Molecular Medicine GmbH of the Austrian Academy of Sciences
Proponent:	Giulio Superti-Furga
Institution:	CeMM - Research Center for Molecular Medicine GmbH of the Austrian Academy of Sciences

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Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter
https://archiv.wwtf.at/programmes/vienna_research_groups/VRG15-005