SFB 680

MOLECULAR BASIS OF
EVOLUTIONARY INNOVATIONS

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Impact of natural genetic variation on molecular phenotypes

The concept of quantitative trait loci (QTL) has been widely used to identify and describe polymorphic genomic regions impacting on physiological traits such as body size or blood pressure. During the last ten years this concept has been extended to molecular traits (like gene expression) being affected by QTL - thus giving rise to 'expression QTL' or eQTL.
I will introduce new methods for identifying such QTL that are capable of dealing with non-linear (epistatic) interactions between loci. Such multi-locus models significantly improve the QTL mappings and biological insights. Whereas the impact of cellular context on expression levels in general is well established, much less is known about the cell-state specificity of eQTL. Based on murine mRNA expression data from four stages of hematopoiesis and 14 related cellular traits we have analysed to what extend eQTL depend on the cell type and we have developed a unified framework distinguishing static, conditional and dynamic eQTL. Detailed analysis of these different eQTL types revealed that they affect functionally distinct types of genes.
An obvious next step is the extension of this concept to other molecular traits such as protein concentration (i.e. pQTL), which requires precise measurement of the same peptides over a large number of samples. Using a combination of shotgun- and targeted proteomics techniques we performed such a pQTL study over a set of 78 *S. cerevisiae* strains. The analysis revealed a complex relationship between independent genetic loci, impacting the levels of related proteins. The very high precision of the proteomics measurements enabled us to detect a surprisingly large number of epistatic interactions affecting protein levels. Further analysis of molecular pathways suggested that selective pressure favors the acquisition of sets of polymorphisms that adapt protein levels while maintaining the stoichiometry of functionally related pathway members.

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Institute for Genetics, Zülpicher Str. 47a, New Seminar Room, Ground Floor

Host: Johannes Berg and Michael Lässig

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