Molecular Logic Gates and Network Medicine

Directionality in protein signalling networks is due to modulated protein-protein interactions and is fundamental for proper signal progression and response to external and internal cues. This property is in part enabled by linear motifs embedding post-translational modification sites. These serve as recognition sites, guiding phosphorylation by kinases and subsequent binding of modular domains (e.g. SH2 and BRCT). Characterisation of such modification-modulated interactions on a proteome-wide scale requires extensive computational and experimental analysis. In my talk I will review our latest advances in methods for unravelling phosphorylation mediated cellular interaction networks. In particular I will discuss how the combination of quantitative mass-spectrometric technologies and computational algorithms (NetworKIN **[1]** and NetPhorest **[2]**) together are enhancing mapping of these largely uncharted dynamic networks. By combining quantitative measurements of phosphorylation events with computational approaches I will discuss how systems level models will help to decipher complex diseases through the ability to predict cellular systems trajectories. Recently, we have utilised these algorithms in combination with quantitative genetic screens to model the regulatory networks surrounding JNK kinase in Drosophila **[3]**. I will show how this new integrative approach is crucial for gaining new insight into phosphorylation driven molecular gating and cellular decision processes..

1: Linding et al., Cell 127, 2007.
2: Miller et al., Science Signaling, 1, 2nd September, 2008.
3: Bakal, Linding, Llise et al., Science, October, 2008.