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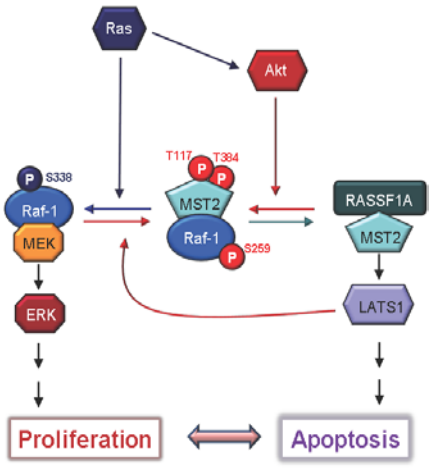
The advent of modern -omics technologies has revolutionised biology and has led us to view biological processes as interconnected networks rather than as assemblies of isolated molecules. This paradigm shift has instigated efforts to analyse cellular networks through computational models, which in turn has revealed new insights into the mechanisms of fundamental biological processes and their malfunctioning in disease states. However, the translation of the computational modelling of cellular networks into medical applications remains limited. In my lab, we ask the following questions: "How can we harness network biology and modelling to better understand diseases such as cancer? And can we turn network modelling into new diagnostic and therapeutic applications?". We propose to address these using integrated systems approaches, which combine predictive computational network modelling with cutting-edge experimental technologies. Our main focus is to exploit developed and tested mathematical models of cancer-related signalling networks to rationally: (i) understand the mechanism of drug resistance which arise from network structures; (ii) find effective anti-cancer drug combinations which either avoid or overcome developed drug resistance; and (iii) design therapies tailored to patients' mutational profiles. This model-based approach is applicable to multiple signalling pathways and cancer types.

Research Projects

1. **Predictive modelling of the mTOR network to discover novel therapies**
2. **Systems analysis of the ErbB interaction network in Breast Cancer (Collaboration with Professor Roger Daly)**
3. **Mathematical modelling to understand network dynamics and cell-fate decisions**



Protein interactions coordinate cellular life/death decisions through Raf-1 and MST2/Hippo signalling.

Selected significant publications:

1. Varusai TM, Kolch W, Kholodenko BK and **Nguyen LK***. 2015. Protein-protein interactions generate hidden feedback and feed-forward loops to trigger bistable switches, oscillations and biphasic dose-responses. *Molecular Biosystems* (in press) (* Correspondence)
2. **Nguyen LK***, Degasperi A, Cotter P & Kholodenko BK. 2015. DYVIPAC: an integrated analysis and visualisation framework to probe multi-dimensional biological networks. *Scientific Reports 5*, Article number: 12569 doi:10.1038/srep12569 (*Correspondence)
3. Romano D, **Nguyen LK***, Matallanas D, Halasz M, Doherty C, Kholodenko BN, Kolch W. 2014. Protein interaction switches coordinate oncogenic and apoptotic signaling. *Nature Cell Biology* doi: 10.1038/ncb2986. *Lead modeller.
4. **Nguyen LK**, Cavadas MAS, Scholz CC, Fitzpatrick SF, Bruning U, Cummins EP, Tambuwala MT, Manresa MC, Kholodenko BN, Taylor CT, & Cheong A. 2013. A dynamic model of the hypoxia-inducible factor (HIF) network. *Journal of Cell Science*. doi: 10.1242/jcs.119974. Epub 2013 Feb 6. (Most read paper of JCS, February 2013).
5. **Nguyen LK**, Muñoz-García J, Maccario H, Ciechanover A, Kolch W & Kholodenko BK. 2011. Switches, excitable responses and oscillations in the Ring1B/Bmi1 ubiquitination system. *PLoS Computational Biology* 7(12): p. e1002317. (Highlighted in the Conway Research Focus)