"Network-based approaches to study human context-specific cell signalling"

Evangelia Petsalaki, EMBL-EBI, Hinxton, UK

It is well established that signalling responses happen through complex networks. However, most signalling research still uses linear pathways as the ground truth. Moreover, signalling responses are highly dependent on context, such as tissue type, genetic background etc and therefore these static pathways are not always suitable. There is also a high bias in the literature towards kinases and pathways for which reagents and prior knowledge is readily available. This leaves a huge dark space in our understanding of cell signalling and significantly hinders



studies of its general principles. In my group we combine mathematical approaches with network inference to study of the principles underpinning the context-specific regulation of human cell signalling.

In the first part of this talk I will present various network-based methods and approaches that we have developed in the group to extract active network signatures from omics datasets and to study condition-specific signalling networks and their relation to phenotype.

For the second part I will present 2 ongoing projects to showcase the use of our tools to study fundamental biological questions. The first one focuses on the effect of different tissue contexts on signalling network rewiring downstream cancer driver gene mutations in cancer. The second one showcases use of integrative omics and network analysis to gain insight into melanoma drug resistance mechanisms and the role of cell state in regulating signalling responses.

Bio sketch

I am originally from Athens Greece, where I also completed my undergraduate degree in Biology at the University of Athens, with a thesis on using neural networks for the prediction of protein subcellular location. I then moved to the EMBL in Heidelberg, where under the supervision of Rob Russell I did a PhD (2009) on structural bioinformatics predicting peptide binding on protein structures. My postdoc was done under the supervision of Tony Pawson and Fritz Roth where I worked on a diverse array of projects from Rho signalling, proteomics, phosphoproteomics to yeast genetics. Since 2017 I am a group leader at the EMBL-EBI and my group focuses on the study of the principles underpinning context specific cell signalling responses in humans, mainly using network-based approaches.