

Focus on : computational methods to study the function and evolution of PTMs

A potential motivation for the review could be a call to arms to the computational biology community to develop approaches to study the function and evolution of PTMs. One way to introduce the problem as a story could be draw an analogy to the recent past where we face a similar challenge of having a lot of novel data of a type (genome sequences) and novel computational methods were needed to study these. From here you could introduce the problem that we face now of having these sets of PTMs from the mass-spectrometry experiments and the issues that are needed to study them.

Evolution of PTM regulators (not the origin)

- Example of the evolution of the tyrosine kinase family
 - Research: <http://www.sciencemag.org/content/325/5948/1686.abstract>
 - Research: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2443182/>
 - Essay: [http://www.cell.com/abstract/S0092-8674\(10\)00954-2](http://www.cell.com/abstract/S0092-8674(10)00954-2)
- This section can include the methods to predict binding specificity of the regulators
 - See slides for references to Netphorest, Predikin
- There is no study of the conservation of the binding specificity of the regulators across species. You could discuss why it is expected that the binding specificity of the regulators should tend to be conserved. Changing it would affect all the targets simultaneously. You can make the analogy to the study of transcription factor binding specificity. There is at least one example of a study of a transcription factor that changed specificity (can you find one?). This tells us that kinases or other regulators could also have different specificity in different species.

Evolution of PTM sites/interactions

- Comparing PTM positions across species
 - There are many papers that have studied this. Some look only at the conservation of the amino-acid residue while others look at the conservation of the modification state.
 - Research <http://www.sciencemag.org/content/325/5948/1682>
 - Research <http://www.sciencedirect.com/science/article/pii/S0168952509000535>
 - Research <http://www.sciencedirect.com/science/article/pii/S0092867412007064>
 - There are many more, but overall they point in the same direction that the sites are not very conserved. There is not much novelty from the methods perspective when thinking about the conservation of the sites.
- Predicting and comparing enzyme interactions
 - Research <http://www.sciencedirect.com/science/article/pii/S0092867407007271>
 - Research <http://stke.sciencemag.org/cgi/content/full/sigtrans;2/81/ra39>
 - The prediction of kinase interactions using computational methods has been reviewed in 2009 <http://onlinelibrary.wiley.com/doi/10.1002/pmic.200900266/full> but try to find more recent prediction papers. Mention also articles and databases on datasets that can be used as gold positives for the training sets.

Functional PTMs

- Different approaches used to predict functionally important PTMs - This is the most recent direction of this field. There are not many articles on this and more methods are needed.
 - Research [http://www.cell.com/structure/abstract/S0969-2126\(11\)00334-0](http://www.cell.com/structure/abstract/S0969-2126(11)00334-0)
 - Research <http://www.sciencedirect.com/science/article/pii/S0092867412007064>
 - Research <http://www.nature.com/msb/journal/v8/n1/full/msb201231.html>