SLiMErich: computational assessment of protein-protein interaction data as a source of domain-motif interactions

INTRODUCTION

Many important cellular processes involve protein-protein interactions (PPIs) mediated by a Short Linear Motif (SLiM) in one protein interacting with a globular domain in another. Despite their significance, these domain-motif interactions (DMIs) are typically low affinity, which makes them challenging to identify by classical experimental approaches, such as affinity pulldown mass spectrometry (AP-MS) and yeast two-hybrid (Y2H).

DMIs are thought to be underrepresented in PPI networks as a result. A number of computational methods now exist to predict SLIMs and/or DMIs from experimental interaction data but it is yet to be established how effective different PPI detection methods are for capturing these low affinity SLiM-mediated interactions.

SLiMErich

Here, we introduce a new computational pipeline (SLiMErich) to assess how well a given source of PPI data captures DMIs and thus, by inference, how useful that data should be for SLiM discovery.

SLiMErich interrogates a PPI network for pairs of interacting proteins in which the first protein is known or predicted to interact with the second protein via a DMI. Permutation tests compare the number of known/predicted DMIs to the expected distribution if the two sets of proteins are randomly associated. This provides an estimate of DMI enrichment within the data and the false positive rate for individual DMIs.

CASE STUDY

As a case study, we detect significant DMI enrichment in a high-throughput Y2H human PPI study. SLiMErich analysis supports Y2H data as a source of DMIs, but highlights the high false positive rates associated with naïve DMI prediction.

WHERE TO GET SLiMErich

SLiMErich is available as an R Shiny app. The code is open source and available via a GNU GPL v3 license at: https://github.com/slimsuite/SLiMEnrich. A web server implementation is available at: http://shiny.slimsuite.unsw.edu.au/SLiMEnrich/.