Project outline

The project outline is guided by the research questions of the project. The first part to look at in the PhD is to how the genetic connections are rearranged during the consecutives deletions that occurred on the evolutionary trajectory.

Question 1: How can we quantified the re-organization of the genetic interaction/epistasis dynamics of network along this evolutionary trajectory?

- Ideas about the role of BRE5 as minihub that has more than 40% interactors that are common to the interactors of BEM1,BEM3,NRP1,BEM2. However, no direct connection/linkage/interaction is registered for BEM3,NRP1. There is just registered direct genetic interactions with BEM1, and BEM2. The type of the interaction is negative, e.g. the double mutation is deletirous.

    - Hypothesis: Upon BEM1 deletion, the interaction between BEM3 and NRP1, is based on the common interactions with BRE5. This idea is based on the amount of interactors genes shared between them. Bre5 interactors share nearly 60% with Nrp1 interactors (so far studied). Bre5 is the highest connected to Nrp1, from all BEM1 negative interactions. In addition, BRE5 interactors share 40% with BEM3 interactors. Hence, BRE5 should be a negative interactor of the bem1bem3 background. And NRP1 should be a direct genetic interactor of BEM3 in the bem1 background (**how to proof experimentally this?**).
    - Ideas to proof the hypothesis:
    - Find that BRE5 is a negative interactor in bem1bem3 background (SATAY).
    - Find that NRP1 is a positive interactor in the bem1bem3 background (control check in SATAY)

- Ideas about the role of CLA4, ACT1 and CDC3 as minihubs that couple BEM1,BEM3,NRP1 and BEM2 together. They are the only common interactors they have. These genes are very important for establishment and maintenance of the polarity in budding yeast.

    - BRE5 only interacts directly with ACT1 and CDC3.
    - The idea is that upon Bem1 deletion the evolution happens by transforming the subnetworks connected to the hubs of the system, that is, CLA4, ACT1, and CDC3. Is a similar idea of what was found out about HSP90 in this paper.
    - However this does not answer why such evolutionary trajectory is reproducible, because the fact that BEM3, NRP1 and BEM2 are connected by those genes it doesn mean that they are the only genes the mini hubs shared in common.

Question 2:Can we understand/make sense of the accessibility/reproducibility of this evolutionary pathway assuming a linkage model, among genetic interactors?

Question 3: Can we elucidate potential recovery evolutionary/mutational pathways from a genetic interaction network of a sick organism?