Evolutionary history of clathrin-mediated endocytosis and the eisosome

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I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

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Abstract

Endocytosis is both an ancient and a diverse feature of the eukaryotic cell. Studying how it evolved can provide insight into the nature of the last common eukaryotic ancestor, and the diversification of eukaryotes into the known extant lineages. In this thesis, I present two studies on the evolution of endocytosis. In the first part of the thesis I report results from a large-scale, phylogenetic and comparative genomic study of clathrin-mediated endocytosis (CME). The CME pathway has been studied to a great level of detail in yeast to mammal model organisms. Several protein families have now been identified as part of the complex set of protein-protein and protein-lipid interactions which mediate endocytosis. To investigate how such complexity evolved, first, I defined the modular nature of the CME interactome (CME-I) by literature review, and then I carried out a systematic phylogenetic and protein domain architecture analysis of the proteins involved. These data were used to construct a model of the evolution of the CME-I network, and to map the expansion of the network's complexity to the eukaryotic tree of life. In the second part of the thesis, I present results from evolutionary and functional studies of the eisosome, a protein complex which has been proposed to regulate the spatial distribution of endocytosis in *S. cerevisiae*. The phylogeny of eisosomes components Pil1 and Lsp1 reported here, suggests that eisosomes are likely to have originated at the base of the fungi, and then diversified significantly via multiple gene duplications. I thus studied the localisation and function of Pil1 and Lsp1 homologues in *Magnaporthe oryzae* to investigate the role of eisosomes in filamentous fungi. Results suggests that eisosomes are linked with septal formation and integrity in *M. oryzae*, and that the septal specific Pil2 paralogue was lost in budding yeasts. Together, the data presented in this thesis describe the evolutionary history of a complex biological system, but also highlights the problem of asymmetry in the understanding of endocytic diversity in the eukaryotes.

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