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Designing novel kinases using evolutionary sequence analysis AREEZ MODY, JOAN WEINER, LAKSHMAN IYER, SHARAD RA-MANATHAN, Bauer Center for Genomics at Harvard University — Cellular pathways with new functions are thought to arise from the duplication and divergence of proteins in existing pathways. The MAP kinase pathways in eukaryotes provide one example of this. These pathways consist of the MAP kinase proteins which are responsible for evoking the correct response to external stimuli. In the yeast Saccharomyces cerevisiae these pathways detect pheromones, osmolar stresses and nutrient levels, leading the cell into dramatic changes of morphology. Despite being homologous to each other, the MAP kinase proteins show specificity of function. We investigate the nature of the amino acid sequences conferring this specificity. To this end, we i) search the sequences of similar proteins in other Eukaryote species, ii) make a study of simple theoretical models exploring the constraints felt by these protein segments and iii) experimentally construct, a large suite of hybrid proteins made of segments taken from the homologous proteins. These are then expressed in Yeast cells to see what function they are able to perform. Particularly we also ask whether it is possible to design a new kinase protein possessing new function and specificity.

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