Nature Reviews Genetics | AOP, published online 11 May 2010; doi:10.1038/nrg2801

SIGNALLING

Making new connections

> recombining domains from proteins in the budding yeast mating pathway leads to diversity in pathway response dynamics

In signalling networks, protein domains usually have a catalytic function or have a role in the regulation or localization of a protein, and it has been suggested that the reorganization of domains during evolution leads to new signalling activities. Peisajovich *et al*. present data in support of this theory by showing that recombining domains from proteins in the budding yeast mating pathway leads to diversity in pathway-response dynamics and changes in mating phenotype.

The authors used the domains of the 11 proteins in the mating pathway to construct a library of 66 recombinant proteins. Chimeric proteins representing all possible recombinations of domain-containing amino-terminal and carboxy-terminal portions were made, and each was transformed into yeast expressing endogenous mating pathway genes. Mating pathway activation, as judged by the expression level of GFP driven by a mating-responsive promoter, revealed that domain recombination results in a wide range of dynamic responses, with variants preventing or strengthening pathway activation. By contrast, duplicate domains have little effect on pathway activation. Co-expression of analogous, unlinked C-terminal and N-terminal portions also has limited effect on the pathway, so the observed variations must depend on domain recombination.

Domain recombination produces yeast strains with altered mating efficiency: yeast strains expressing domain-recombination variants that strengthen mating pathway activation mated more efficiently than wild-type yeast, whereas those expressing recombinants that weaken pathway activation mated poorly.

How do recombination variants alter the mating response? Analysis of the ten recombination variants that most markedly change yeast behaviour revealed that seven created new links between the different signalling complexes, whereas only three created links in an individual functional complex. Thus, new behaviours might arise when key signalling domains change their complex formation or their localization.

Recombining catalytic domains with different regulatory domains therefore results in the novel regulation or localization of the catalytic domain and distinct changes in signalling behaviour and phenotype, and might play a part in the evolution of signalling networks.

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ORIGINAL RESEARCH PAPER Peisajovich, S. G., Garbarino, J. E., Wei, P. & Lim, W. A. Rapid diversification of cell signaling phenotypes by modular domain recombination. *Science* **328**, 368–372 (2010)

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