URLS

Reed Wickner's laboratory: **http://www.niddk.nih.gov/intram/people/wickner/ure3.htm**

PRIONS

Prions help themselves

Protein-based inheritance with infectious proteins known as prions usually involves the prion forming an amyloid or aggregated form. But theoretically, any protein whose altered form is essential for its own alteration — that is, acts on itself — and can be transmitted, could be a prion. Now, reporting in *Genes and Devlopment*, Roberts and Wickner have identified a new type of prion in the yeast *Saccharomyces cerevisiae* — called [β] — that is infectious, curable, and necessary for sporulation.

Yeast protease B (PrB) is a serine protease that is derived from an inactive precursor (zymogen). The PrB zymogen is activated by cleavage with two proteases, Protease A (PrA) and PrB itself. In the absence of PrA, PrB is essential for its own activation. PrB also activates carboxypeptidase Y (CpY). So, the activity of PrB can be determined by monitoring the activity of carboxypeptidase Y — even in isolated colonies — using a colorimetric plate assay. The authors took advantage of several factors. First, PrB expression can be switched on and off using selective growth conditions. Second, the genetics of *S. cerevisiae* are powerful and it is possible to knockout genes easily. Third, using a process called cytoduction, the cytoplasm of a donor cell can be transferred to a recipient cell. This is biologically relevant because yeast viruses can be transmitted using this method.

When PrA is absent (A^-) CpY remains active as long as cells have active PrB (also known as [β]). Transmission of [β] by cytoduction, to a strain deleted for PrA and cured of [β] converted the phenotype of the recipient to CpY^+, which demonstrated infectivity. If the donor strain contained an inactive immature form of PrB — which can't self-cleave — it wasn't possible to convert the phenotype of recipients by cytoduction. Active PrB [β] can be reversibly cured, and overexpression of PrB led to increased frequency of [β] arising *de novo*. Presence of [β] correlated with survival from starvation and was necessary for sporulation.

These experiments show that potentially any self-modifying protein can be a prion, as long as there is a mechanism of transmission, and the modified form of the protein is necessary for its own modification.

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References and links

ORIGINAL RESEARCH PAPER Roberts, B. T, & Wickner, R. B. Heritable activity: a prion that propagates by covalent autoactivation. *Genes Dev.* 2003 (doi:10.1101/gad.1115803).