Introduction

Prions are proteins which can adopt various forms of aggregation and folding which affect the phenotype of the ‘host’ organism and are heritable or infectious. Commonly cited models are the neurodegenerative diseases in mammals linked to the prion forms of the PrP protein expressed in the brain (Prusiner 2013, review), in *E. coli*, a protein, *curli*, which is excreted and helps in the formation of biofilms and in the yeast *Saccharomyces cerevisiae*, the *[PSI]+* prion, which is an aggregate of the polypeptide chain termination factor Sup35/eRF3 (Tuite et al. 2015, review). In *S. cerevisiae*, the prion-associated phenotypes are stable over thousands of cell generations, while PrP-based infections are essentially incurable.

Most, if not all prions so far identified consist of amyloid fibres in which the individual proteins, unlike the native form, are rich in β-sheet. The phenotype which is most commonly used to identify *[PSI]+* strains of yeast arises through a deficiency in chain termination at nonsense codons. The indicator read-through phenotype is an alleviation of nonsense mutations in vitro or in vivo in either the *ADE1* or the *ADE2* gene (Cox 1965; Tuite et al. 1983). Such mutations cause a red pigment to accumulate in cells; the *[PSI]+* prion prevents that and colonies of *[PSI]+* *ade1-14* mutants, for example, are white (Fig. 1). From the earliest days of its discovery (Cox 1965), the colour difference between *[PSI]+* and *[psi]−* strains has allowed conditions in which the inheritance of the prion is rendered unstable, to be readily identified.

Both inheritance and infection of prions are the consequence of the ability of amyloid fibre to template the addition and refolding of monomeric protein to the growing fibres with fragmentation increasing their numbers.
The remodeling and addition of molecules to an aggregate can occur spontaneously, but is greatly enhanced by pre-existing remodeled molecules. The new additions adopt the form of the model template, and fragmentation promotes an exponential increase in amount of amyloid from a pool of monomer both in vitro and in vivo.

A number of factors have been found to affect the stability of inheritance of prions. The stability of \( [\text{PSI}^+] \) is affected by environmental stress (e.g. Singh et al. 1979; Tuite et al. 1981; Newnam et al. 2011) or by mutations in either the \( \text{SUP35} \) or the \( \text{HSP104} \) gene (Young and Cox 1971; Doel et al. 1994; DePace et al. 1998) or by manipulation of gene expression (Chernoff et al. 1995; Glover and Lum 2009; Helsen and Glover 2012a, b; Chernova et al. 2017; Ness et al. 2017). Some of the variant forms of the prion amyloid also show an inherent instability during cell division (Uptain et al. 2001). The degree of instability can range from total loss of the prion (often referred to as ‘curing’) to stochastic random loss characteristically giving rise to red sectors on white \( [\text{PSI}^+] \) colonies. The involvement of Hsp104 is because this chaperone is required for the fragmentation of amyloid fibres of nearly all yeast prions so far identified, including the Sup35p \( [\text{PSI}^+] \) prion.

The Hsp104 ‘curing’ paradox

Recently, we provided evidence that definitively supports one of two theories which have been offered for a long-running paradox surrounding the inheritance of \( [\text{PSI}^+] \) (Ness et al. 2017). The paradox is as follows: the AAA+ disaggregase Hsp104 is essential for \( [\text{PSI}^+] \) inheritance and blocking the ATPase activity of Hsp104 using guanidine hydrochloride (GdnHCl) allows the prion to be diluted out during cell division due to the loss of fragmentation by this disaggregase (Eaglestone et al. 2000; Byrne et al. 2007). But \( [\text{PSI}^+] \) can also be eliminated from cells by elevating the levels of the same enzyme (Chernoff et al. 1995). The most straightforward explanation for this oddity, first offered by Paushkin et al. (1996), was that over-expression caused an increase in the disaggregase activity of the enzyme such that the amyloid aggregates of the prion form of Sup35 were resolved into its constituent monomers in their native form. This would result in the restoration of normal polypeptide chain termination activity to Sup35 and abolishing both the read-through of nonsense codons characteristic of the presence of \( [\text{PSI}^+] \) and the templating activity of the prion form of the protein on which its inheritance depends. Yet this
hypothesis has now been challenged by our new findings (Ness et al. 2017).

We show that there is no significant degradation of Sup35 \([PSI^+]\) high molecular weight (HMW) aggregates into lower molecular weight forms when Hsp104 is over-expressed. Rather what happens in many cell divisions is that the genetic units of prion inheritance, entities we call propagons (Cox et al. 2003), are partitioned unequally prior to cells dividing. Retention by the mother cell is such that in about 10% of divisions per generation in our strains and conditions, a daughter cell, and always the daughter cell, segregates without any prions and is \([psi^-]\) (Figs. 1, 3) (Ness et al. 2017). By contrast, the over-expression of an ATPase-negative mutant of Hsp104 (Hsp104\(^{2KT}\)) in a \([PSI^+]\) cell leads to the competitive inhibition of the wild type ATPase and the resulting prion loss mimics quantitatively the kinetics of GdnHCl-induced \([PSI^+]\) curing (Fig. 2) (Ness et al. 2017). However, this mode of curing by Hsp104\(^{2KT}\) over-expression, as with GdnHCl-induced curing, results from dilution out of propagons during cell division (Byrne et al. 2007) with a halving in the number of propagons in each generation (Cox et al. 2003; Ness et al. 2017). Nevertheless, the consequences for prion inheritance of over-expression of this mutant differs dramatically from GdnHCl inhibition of Hsp104, in that from the very earliest stages of over-expression red sectors start to appear on the mature colonies growing from \([PSI^+]\) cells after plating on standard growth medium relieves the over-expression (Fig. 1c). This is a clear indication that over-expression of the mutant Hsp104 induces a change which is inherited through several generations but only expressed once over-expression is relieved.

There are genetic differences as well as differences in molecular events between the two \([PSI^+]\) ‘curing’ regimes mediated by wild type and mutant Hsp104, respectively. These are first, that the N-terminal domain of Hsp104 is dispensable for the propagation of all yeast prions, but is required for curing by over-expression (Hung and Masison 2006). Second, the loss of the Hsp90 co-chaperones Sti1 and Cpr7 interferes neither with the propagation of \([PSI^+]\) nor with the curing of \([PSI^+]\) by growth in GdnHCl, but loss of either or both does almost abolish the curing by wild type Hsp104 over-expression (Moosavi et al. 2010; Reidy and Masison 2010). Third, an Hsp104 binding site in the M-region of Sup35 allows binding without the cooperation of Hsp70 or Sis1 (Helsen and Glover 2012a, b, Winkler et al. 2012a; Frederick et al. 2014) and deletion of residues 131–140 in the M region of Sup35 eliminates curing by over-expression, but has no other effect on \([PSI^+]\) propagation (Helsen and Glover 2012a, b) and curing by inhibition of Hsp104 ATPase proceeds normally.

**Fig. 2** Two modes of \([PSI^+]\) elimination involving Hsp104. Elimination of \([PSI^+]\) by over-expression of Hsp104 (empty square) shows very different kinetics to elimination by inhibition of Hsp104 ATPase by adding 5 mM guanidine hydrochloride to the medium (empty circle). In this experiment Hsp104 over-expression was driven from the \(GAL1,10\) promoter
and are observed in the absence of over-expression of Hsp104. These aggregates involve Hsp104 associated with Hsp70s and are observed in the absence of over-expression of Hsp104. In a $[PSI^+] \times [PSI^+]$ cross, some of the PNM-induced elimination of $[PSI^+]$ occurs during the growth of the diploid culture following mating and before sporulation, leading to the $4:0$ segregation of $[psi^-]:[PSI^+]$ spore cultures (Young and Cox 1971) (Fig. 4a). However, if the switch to sporulation-inducing growth conditions occurs 4 h after the zygote forms and before it can resume growth after mating, more than 90% of the propagons are eliminated in the course of sporulation itself. This

Hsp104: Sup35 interactions

These genetic differences correlate with different binding regimes of Hsp104 with the Sup35 amyloid substrate: “productive” but labile, leading to prion aggregate fragmentation, presumably common to all Hsp104-dependent yeast prions and “non-productive” and stable, dependent, in Sup35, on Sup35M-domain residues 131–140.

The productive interaction involves Hsp104 being recruited to the substrate by Hsp40 (Sis1)/Hsp70 (Ssa1) chaperones (Tipton et al. 2008; Winkler et al. 2012b; Lee et al. 2013) leading to polymer fragmentation. The second, non-productive binding regime in the M-region of Sup35 allows binding without the cooperation of Hsp70 or Hsp40 but does involve the two Hsp90s, Cpr7 and Sti1 (Helsen and Glover 2012a, b; Winkler et al. 2012a; Frederick et al. 2014). Saarikangas and Barral 2015, have described replicative age-related mother cell retention of, among other proteins, Sup35 $[PSI^+]$ aggregates. The aggregates involve Hsp104 associated with Hsp70s and are observed in the absence of over-expression of Hsp104. Instability of $[PSI^+]$ is not observed in these conditions, nor is malpartition. It may be that the association of Sup35 with these objects is the labile one described by Frederick et al. (2014), allowing normal partition and becomes stable with over-expression when the binding involves Hsp90s and not Hsp70s.

Hsp104 has also, apparently two different roles: disaggregation of toxic and misfolded proteins, particularly those resulting from heat-shock, and anchoring misfolded proteins to the actin cytoskeleton. The latter role is associated with cell ageing and involves lantrunculin-sensitive anchoring to the actin cytoskeleton of ageing mother cells as part of the rejuvenation of daughter cells (Tessarz et al. 2009; Helsen and Glover 2012a, b). Ness et al. (2017) propose this latter activity is also likely to be responsible for $[PSI^+]$ loss induced by over-expression of Hsp104, an activity which is unique to this one prion out of the half-dozen which have been checked.

Inheritance of $[PSI^+]$ propagons in zygotes and ascis

Hsp104 also has effects, few of which have been reported, on the propagation of the $[PSI^+]$ prion in sporulation. These effects have been revealed by dominant mutations of Hsp104 which were the first mutants isolated in this gene in 1968 by Hamish Young (Young and Cox 1971). We now call such mutants “PNM” (“Psi No More”) and the two PNM loci identified by Young in his original screen are the HSP104 gene (PNM1; Cox, BS, Kerry KM, unpublished) and the SUP35 gene (PNM2; Doel et al. 1994). PNM mutants can prevent the inheritance of $[PSI^+]$ by spores as shown by the observation that when either PNM1 $[psi^-]$ or PNM2 $[psi^-]$ mutants are mated with a $[PSI^+]$ strain the diploids are $[psi^-]$ and so are all the meiotic products i.e. haploid spores, after sporulation (Fig. 4a). This is not a universal effect because some conformational variants of $[PSI^+]$ are not eliminated by PNM1 mutations (Derkatch et al. 1999) consistent with the observation of Frederick et al. (2014) that different conformational variants of Sup35 show differing degrees of Hsp70-independent interaction with Hsp104.

![Partition at 5.7 Generations](https://example.com/image)

**Fig. 3** The distribution of $[PSI^+]$ propagons between mothers and daughters following over-expression of Hsp104. After 5.7 generations post induction of elevated levels of Hsp104, propagon numbers were counted by the single-cell method of Cox et al. (2003) and the numbers in daughter cells are plotted against those in their mothers. The dotted line box indicates the limits of such plots in various control and $t_0$ populations, and the dashed regression lines are the observed limits of the proportion of propagons segregating to daughter cells in these populations. The average value of this proportion is 0.4, the approximate ratio of the volumes of mother and daughter cells at cytokinesis (Byrne et al. 2009). The extreme ratios observed in control and $t_0$ divisions were 0.57 and 0.33. The points below the lower regression are the result of retention of propagons in mother cells. These points indicating divisions where the daughters were $[psi^-]$ (no popagons) are highlighted.
Hsp104 and transmission of \([PSI]^+\) propagons in sporulation

The cross discussed above (Table 1) involved a PNM allele of \(SUP35\) (i.e. \(PNM2^{G58R}\)) not \(HSP104\) which leaves open the question whether the elimination of \([PSI]^+\) in this cross is due to an unusual sensitivity of the mutant protein to Hsp104 disaggregate. However, we find that dominant \(PNM1\) mutants of Hsp104 totally lacking ATPase activity give results either quantitatively indistinguishable from those in Table 1, or are even more severe in terms of reduction of propagon numbers (Cox, BS unpublished data: see below).

Loss of \([PSI]^+\) in the \(PNM2^{G58R} [psi^-] \times [PSI]^+\) would not appear to be an amyloid disaggregation problem, but a propagon segregation problem. Nevertheless, in the absence of any perturbation of Hsp104 function by mutation or environment, all the empirical evidence is consistent with a random distribution of \([PSI]^+\) propagons in both vegetative (mitotic) and sporulation (meiotic) divisions (Table 1; Byrne et al. 2009). Mutations or environmental disturbance may nevertheless affect inheritance in either.

The role of Hsp104 in sporulation has not been explored very extensively although sporulation occurs normally in diploids homozygous for a \(\Delta hsp104\) deletion (e.g. Ünal et al. 2011). The possibility remains that, without being essential Hsp104 nevertheless has a role which is important for the distribution of \([PSI]^+\) propagons and perhaps other organelles to spores (see Suda et al. 2007). The possibility that a link between these observations and the rejuvenation which accompanies spore formation (Ünal and Amon 2011; Ünal et al. 2011) is tantalizing. To explore this we followed the fate of GFP-decorated propagons in sporulation in \(PNM1-1/+ [psi^-]\) diploids. This diploid segregated an average of seven propagons to spores in a total of 10 tetrads analysed. In spite of a starting cytoplasm replete with diffuse GFP and GFP-decorated punctate spots before the arrest of vegetative division and also for 24 h after the induction of meiosis (Fig. 5a, b), by the time sporulation was complete after four days, ascii showed no fluorescence within the four spores and only weak diffuse fluorescence outside them (Fig. 5c). Once returned to growth medium, GFP fluorescence reappeared in the two spores in every ascus to which the Sup35::GFP fusion gene segregated, mostly without the evidence of Sup35::GFP-decorated aggregates (Fig. 5d) and there was minimal evidence of GFP-decorated aggregates inherited from the zygoties in which these ascospores formed. In the presence of the dominant \(PNM1-1\) mutation in these sporulating zygoties we estimate that at most only 10% of the Sup35, whether aggregated or not, was dispersed to the spores. What we see is Mendelian inheritance of autonomous new synthesis of

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**Fig. 4** A Analysis of the meiotic segregants arising from a \(PNM1-1 [psi^-] \times [PSI]^+\) strain. Each tetrad (numbered 1–8) gives rise to four haploid spore-generated colonies (labelled a–d). All of the haploid spores are red \([psi^+]\). B Dominance of the \(PNM1-1\) allele of Hsp104 measured by survival of heat shock treatment is illustrated. NB the \(x\) axis is on a log scale. The survival of WT Hsp104 in the presence of 3 mM guanidine HCl is shown for comparison. The \(PNM1-1\) allele has the following four mutations: F118L, I338T, G619D, G706D (Jones KM, unpublished data) of which the last three are found in the ATPase domains of the enzyme.

effect is illustrated by Fig. 5 and the data in Table 1. (N. B. that the data in this table are taken from a \(PNM2^{G58R} [psi^-] \times [PSI]^+\) mating: data from \([psi^-] \times [PNM1]\) crosses are not shown but are exactly comparable). Zygotes formed by crossing a \(PNM1.1 [psi^-]\) strain with a ‘strong’ variant of \([PSI]^+\) 4 h after zygote formation, results in decoration of the propagons from the \([PSI]^+\) parent with Sup35p from the \([psi^-]\) cell (e.g. Fig. 5a; Satpute-Krishnan et al. 2009) and an increase in the number of propagons per cell consistent with the increased cell volume of the zygote (Table 1a, b). Analysis of propagon numbers in five tetrads from these zygotes showed a random distribution of 252 propagons per spore with no loss compared with the propagons’ numbers (Table 1c). By contrast, when the \([psi^-]\) parent in the cross was replaced with a \(PNM2^{G58R} [psi^-]\) strain and the same sporulation regime applied (Table 1d), 60% of the spores had no propagons with the total number of propagons in the 20 spores scored being 4% of the total number of propagons scored in the five tetrads with the wild-type \([psi^-]\) diploid. It should be noted that half the spores analysed in this cross would carry the \(PNM2\) gene so any propagons they inherited would not be detectable by the assay we employ. Figure 5c, d appear to corroborate exactly these genetic data, including the 2:2 segregation of the PNM genes involved, apparent on germination.
this GFP-linked essential protein in the germinating spores, very little of which decorates any Sup35 aggregates.

Degradation, disaggregation or malpartition?

Another question we raise in our new study (Ness et al. 2017) is that of the source of instability of the [PSI+] prion that is commonly observed in [PSI+] variants, PNM2(SUP35) mutants and heterozygotes formed between them and with strains expressing wild type Sup35, and also in partially dominant PNM1(HSP104) mutants. Such prion instability characteristically appears as sectoring in colonies growing on normal growth medium (Fig. 1c) and the implication is that the instability is associated with malpartition rather than degradation. No doubt having very low numbers of large propagons would contribute to the spectrum of instability, but interaction with Hsp104 in rejuvenation mode may be a common feature (Verges et al. 2011).

What is not certain is that any form of intrinsic or induced instability of Sup35/[PSI+] prions is due to significant degradation or disaggregation of the amyloid form. Disaggregation can be observed in vitro (Shorter and Lindquist 2004) albeit with molar ratios of Hsp104:Sup35.
polymer that are far in excess of what may be observed in vivo, but until now (i.e. Ness et al. 2017) has not been directly assayed in vivo.

One of the epidemiological myths about the mammalian PrPSc prion is that it is indestructible by normal physical or chemical methods. For example, sterilizing surgical instruments is not sufficient to quell iatrogenic prion infection, nor is cooking; resistance to proteases has been used as a means of identifying amyloid and Alper et al. (1967) could not kill the infectious scrapie agent by ionizing radiation or UV. The thermodynamic facts are that an amyloid fibre exists in an entropy pit and relatively large amounts of energy input are required to get it out (Eichner and Radford 2011). Fragmentation by Hsp104 with the 12 ATPase sites in the hexamolecular collar is achieved by merely extracting a single molecule from within the fibre (Glover and Lum 2009). In spite of several published claims to the contrary, there has been no direct demonstration of in vivo degradation of PrPSc Sup35 amyloid aggregates. This leaves us with the need to find other explanations for the appearance of prion-free cells.

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References

Alper T, Cramp WA, Haig DA, Clarke MC (1967) Does the agent of scrapie replicate without nucleic acid? Nature 214:764–766

Byrne LJ, Cox BS, Cole DJ, Ridout MS, Morgan BJ, Tuite MF (2007) Cell division is essential for elimination of the yeast [PSI+] prion by guanidine hydrochloride. Proc Natl Acad Sci USA 104:11688–11693

Byrne LJ, Cole DJ, Cox BS, Ridout MS, Morgan BJ, Tuite MF (2009) The number and transmission of [PSI+] prion seeds (propagons) in the yeast Saccharomyces cerevisiae. PLoS ONE 4:e4670

Chernova TA, Wilkinson KD, Chernoff YO (2017) Prions, chaperones, and protein aggregation: an ethanol story. FEBS Lett 591:1354–1362

Chernoff YO, Lindquist SL, Ono B, Inge-Vechtomov SG, Liebman SW (1999) The role of the chaperone protein Hsp104 in propagation of the yeast prion-like factor [psi+]. Science 286:880–884

Chernoova TA, Wilkinson KD, Chernoff YO (2017) Prions, chaperones, and protein aggregation in yeast. Cold Spring Harb Perspect Biol 9:a023663

Cox BS (1965) [PSI], a cytoplasmic suppressor of super-suppressors in yeast. Heredity 20:505–521

Cox BS, Ness F, Tuite MF (2003) Analysis of the generation and segregation of propagons: entities that propagate the [PSI+] prion in yeast. Genetics 163:23–33

De Pace AH, Santos A, Hillner P, Weissman JS (1998) A critical role for amino-terminal glutamine/asparagine repeats in the formation and propagation of a yeast prion. Cell 93:1241–1252

Derkatch IL, Bradley ME, Zhou P, Liebman SW (1999) The PNM2 mutation in the prion protein domain of SUP35 has distinct effects on different variants of the [PSI+] prion in yeast. Curr Genet 35:59–67

Doel SM, McCready SJ, Nierras CR, Cox BS (1994) The dominant PNM2- mutation which eliminates the Ψ factor of Saccharomyces cerevisiae is the result of a missense mutation in the SUP35 gene. Genetics 137:659–670

Eaglestone SS, Ruddock LW, Cox BS, Tuite MF (2000) Guanidine hydrochloride blocks a critical step in the propagation of the prion-like determinant [PSI+] of Saccharomyces cerevisiae. Proc Natl Acad Sci USA 97:240–244

Eichner T, Radford SE (2011) A diversity of assembly mechanisms of a generic amyloid fold. Mol Cell 43:8–18

Frederick KK, Debelouchina GT, Kayatekin C, Dominy Y, Jacobsen SE (2006) N-terminal domain of yeast Hsp104 is the result of a missense mutation in the SUP35 gene. Proc Natl Acad Sci USA 103:19388–19393

Helsen CW, Glover JR (2009) Remodeling of protein aggregates by Hsp104. Protein Pept Lett 16:587–597

Helsen CW, Gloor JR (2012a) Insight into molecular basis of curing of [PSI+] prion by overexpression of 104-kDa heat shock protein (Hsp104). J Biol Chem 287:542–556

Helsen CW, Gloor JR (2012b) A new perspective on Hsp104-mediated propagation and curing of the yeast prion [PSI+]. Proc Natl Acad Sci USA 109:2324–2329

Hung GC, Massion DC (2006) N-terminal domain of yeast Hsp104 chaperone is dispensable for thermostolerance and prion propagation but necessary for curing prions by Hsp104 overexpression. Genetics 173:611–620

Lee J, Kim JH, Biter AB, Sielaff B, Lee S, Tsai FT (2013) Heat shock protein (Hsp) 70 is an activator of the Hsp104 motor. Proc Natl Acad Sci USA 110:8513–8518

Moosavi B, Wongwigmarn J, Tuite MF (2010) Hsp70/Hsp90 co-chaperones are required for efficient Hsp104-mediated elimination of the yeast [PSI+] prion but not for prion propagation. Yeast 27:167–179

Ness F, Cox BS, Wongwigmarn J, Naemi WR, Tuite MF (2017) Over-expression of the molecular chaperone Hsp104 in Saccharomyces cerevisiae results in the malpartition of [PSI+] propagons. Molec Microbiol. 104:125–143

Newnam GP, Birchmore JL, Chernoff YO (2011) Destabilization and recovery of a yeast prion after mild heat shock. J Mol Biol 408:432–448

Paushkin SV, Kushnirenko VV, Smirnov VN, Ter-Avanesyan MD (1996) Propagation of the yeast prion-like [psi+] determinant is mediated by oligomerization of the SUP35-encoded polypeptide chain release factor. EMBO J 15:3127–3134

Prusiner SB (2013) Biology and genetics of prions causing neurodegeneration. Annu Rev Genet. 47:601–623

Reidy M, Massion D (2010) St11 regulation of Hsp70 and Hsp90 is critical for curing of Saccharomyces cerevisiae [PSI+] prions by Hsp104. Mol Cell Biol 30:3542–3552

Saarikangas J, Barral Y (2015) Protein aggregates are associated with replicative aging without compromising protein quality control. eLife 4:e06197

Satpute-Krishnan P, Langseth SX, Serro TR (2009) Hsp104-dependent remodeling of prion complexes mediates protein-only inheritance. PLoS Biol 5:e24

Shorter J, Lindquist S (2004) Hsp104 catalyzes formation and elimination of self-replicating Sup35 prion conformers. Science 304:1793–1797

Singh A, Helms C, Sherman F (1979) Mutation of the non-Mendelian suppressor, Ψ+, in yeast by hypertonic media. Proc Natl Acad Sci USA 76:1952–1956

Suda Y, Nakaneshi H, Matheson EM, Neiman A (2007) Alternative modes of organelar segregation during sporulation in Saccharomyces cerevisiae. Eur Cell 6:2009–2017

Tessarz P, Schwarz M, Mogk A, Bukau B (2009) The yeast AAA+ chaperone Hsp104 is part of a network that links the actin cytoskeleton with the inheritance of damaged proteins. Mol Cell Biol 29:3738–3745

Tipton KA, Varges KJ, Weissman JS (2008) In vivo monitoring of the prion replication cycle reveals a critical role for Sis1 in delivering substrates to Hsp104. Mol Cell 32:584–591

Tuite MF, Mundy CR, Cox BS (1981) Agents that cause a high frequency of genetic change from [psi+] to [psi−] in Saccharomyces cerevisiae. Genetics 98:691–711

Tuite MF, Cox BS, McLaughlin CS (1983) In vitro nonsense suppression in [psi+] and [psi−] cell-free lysates of Saccharomyces cerevisiae. Proc Natl Acad Sci USA 80:2824–2828

Tuite MF, Stanforth GL, Cox BS (2015) [PSI+] turns 50. Prion.

Uptain SM (2001) Strains of [PSI+] are distinguished by their efficiencies of prion-mediated conformational conversion. EMBO J 20:6236–6245

Verges KJ, Smith MH, Toyama BH, Weissman JS (2011) Strain conformation, primary structure and the propagation of the yeast prion [PSI+]. Nat Struct Mol Biol 18:493–499

Winkler J, Tyedmers J, Bukau B, Mogk A (2012a) Chaperone networks in protein disaggregation and prion propagation. J Struct Biol 179:152–160

Winkler J, Tyedmers J, Bukau B, Mogk A (2012b) Hsp70 targets Hsp100 chaperones to substrates for protein disaggregation and prion fragmentation. J Cell Biol 198:387–404

Young CSH, Cox BS (1971) Extrachromosomal elements in a supersuppression system of yeast. 1. A nuclear gene controlling the inheritance of the extrachromosomal elements. Heredity 26:413–422