While the results above are consistent with a role for Blm10 in promoting proteasome function, note that genetic analysis of proteasomal assembly and function pathways can be difficult to interpret. For example, Ump1 is needed for normal growth during the proteolytic stress associated with elevated temperature as revealed by weak growth at 37°, but an *ump1*-Δ mutant was more resistant than a WT strain to a different proteolytic stress, the presence of a low level of canavanine (compare rows 1 and 5 in the canavanine 1.5 at 30° panel). Rpn4 is a transcription factor that upregulates proteasome gene expression under conditions of proteolytic stress (Mannhaupt et al., 1999; Xie and Varshavsky, 2001), but an *rpn4*-Δ mutant grows normally at 37°, is sensitive to 4NQO, and in our tests is more resistant than WT to canavanine at 30° but more sensitive than WT to canavanine at 37°. Unlike the *pre4*-Δ*CT* or *ump1*-Δ strains, the *rpn4*-Δ mutant is sensitive to the protein synthesis inhibitor cycloheximide (Cyh). Loss of Blm10 suppressed this defect and the 4NQO sensitivity, but enhanced the defect in growth observed for the *rpn4*-Δ strain on canavanine at 37°. Schmidt et al. (2005) found that *rpn4*-Δ caused slight sensitivity to canavanine and that *rpn4*-Δ *blm10*-Δ double mutants had a slight synthetic growth defect both on rich medium and on canavanine. These results differ from ours, possibly due to strain background differences. Alternatively, as we have found that *blm10*-Δ mutants lose mitochondrial function at a high frequency, perhaps some of the variation among different experiments can be accounted for by clonal variation. That is, different cultures will have different retention of mitochondrial function due to the stochastic nature of the loss, contributing to phenotypic variation among cultures in a given assay even when comparing different clones of the same strain.

Together these results are consistent with a role for Blm10 in a proteasome-dependent process, but they illustrate the difficulty of interpreting genetic effects when examining a factor like the proteasome that directly or indirectly alters many facets of a broad range of physiologically important processes.