

(E) *S. cerevisiae* Blm10 sequence. Secondary structures (above) colored as in Figure 1. HEAT repeat helices are labeled 1A for helix A of HEAT repeat 1, etc. Residues disordered in the structure are indicated with a dashed line. Residues that approach the proteasome within 4.0 Å are marked with a square below; contact to $\alpha 1$ blue, $\alpha 2$ cyan, $\alpha 3$ green, $\alpha 4$ magenta, $\alpha 5$ orange, $\alpha 6$ red, $\alpha 7$ gray. Residues identical in *S. cerevisiae* Blm10 and human PA200 are underlined. Blm10 residues conserved in an alignment of 46 related sequences are shown on a yellow background. Conservation is defined according to the ESPript consensus (Gouet et al., 1999) from the automatic alignment, with a few residues also defined as conserved because simple manual adjustment of gaps aligns residues that appear to be structurally important.

Proteasome residues have been highly conserved throughout evolution, especially on the α -subunit surface, with 82/112 (73%) of the proteasome residues that contact Blm10 being identical in *S. cerevisiae* and human. In contrast, the Blm10 sequence is much more divergent, with only 162/2143 (8%) of the residues conserved in the alignment indicated here. The conservation is somewhat higher at the proteasome interface, especially for residues that contact proteasome $\alpha 5$ and $\alpha 6$ subunits, where 17/62 (27%) of Blm10 residues contacting these subunits are conserved.