Abstract

26S proteasomes are protease complexes in the nucleo- and cytoplasm. They are responsible for selective degradation of short-lived proteins which regulate nearly all cellular processes.
The proteolytically active core complex, the 20S proteasome, is faced by two regulatory 19S complexes. 20S proteasomes consist of alpha and beta subunits which are stacked in four rings with alpha(1-7) beta(1-7) beta(1-7) alpha(1-7) configuration. The mature 20S proteasome is formed by dimerisation of two precursor complexes, which consist of an alpha(1-7) ring and beta subunit precursors. During precursor complex dimerisation the beta subunit proproteins are processed by an autocatalytic reaction which yields the active site residues inside the proteolytic chamber. A small protein, named Ump1, is associated with precursor complexes and accompanies the maturation process. Burried inside the proteolytic chamber Ump1 becomes the first substrate of the matured 20S proteasome.
In yeast, an eukaryotic model organism, the majority of proteasomes localizes to the nucleus and around the nuclear membrane suggesting that proteasomal proteolysis is mainly required in this subcellular compartment.
Nuclear import of 26S proteasomes occurs via precursor complexes of the 20S proteasome and subcomplexes of the regulatory 19S complex. Thus, nuclear 26S proteasomes are most likely assembled in the nucleus. The proteasomal subcomplexes are recognized by the classical nuclear localization receptor, karyopherin / importin alpha / beta. Classical nuclear localization signals are present in proteasomal subunits. A subunit of the 19S base subcomplex harbours an essential nuclear localization sequence which is crucial for nuclear 26S proteasome function.
Furthermore, the nuclear high molecular mass protein Blm3 (recently renamed Blm10) was found to be associated with late intermediates of 20S proteasome precursor complexes suggesting that Blm3 regulates late steps in nuclear 20S proteasome maturation.
The impact of Blm3 and related proteins on 26S proteasome assembly is currently under investigation.