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THE BINDING ACTIVITY OF THE CHAPERONE BIP IN THE PLANT ENDOPLASMIC RETICULUM AND ITS ROLE IN THE SYNTHESIS OF SECRETORY PROTEINS

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The binding protein (BiP) is a member of the heat shock 70 chaperone family and a major resident of the endoplasmic reticulum (ER). BiP has been found in ATP-sensitive transient association with the newly synthesized forms of many secretory proteins and in more prolonged association with structurally defective polypeptides. Numerous experiments support a model in which BiP avoids improper interactions that can lead to irreversible misfolding and at the same time contributes to ER retention of not-yet mature proteins and targeting of permanently defective proteins for degradation, thus being a major actor of protein quality control within the ER. In vitro studies using random synthetic peptides indicate that BiP has affinity for sequences enriched in hydrophobic amino acids and thus exposed on the surface of proteins only before the tertiary and quaternary structures have been acquired. An algorithm based on these studies has been developed and used to predict BiP binding sites in secretory proteins. Along the sequence of the vacuolar protein phaseolin (the major storage protein of common bean) we have mapped a short domain that promotes in vivo interactions with BiP both in phaseolin and when added to reporter proteins. Consistently with the results of the above mentioned in vitro experiments with synthetic peptides and the model of BiP activity, this domain has an unusually high content of putative BiP binding sites as predicted by the BiP algorithm and is directly involved in phaseolin trimerization. However, by expressing these and other chimeric proteins in transgenic plants, we have found that mutated proteins that will eventually be degraded by quality control, or accumulate in large amounts in the ER or are delivered to the vacuole can have unusually extensive interactions with BiP when compared to wild type counterparts, suggesting that other interactions play a role in determining the final fate. Possibly, the selection of one destiny over the other depends on the degree of overall structural defects of the protein and the ability to form very large complexes.

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