UNCONVENTIONAL SECRETION OF A-CRYSTALLIN B REQUIRES THE AUTOPHAGIC PATHWAY AND IS CONTROLLED BY PHOSPHORYLATION OF ITS SERINE 59 RESIDUE

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α-Crystallin B (CRYAB or HspB5) is a chaperone member of the small heat-shock protein family that prevents aggregation of many cytosolic client proteins by means of its ATP-independent holdase activity. Surprisingly, several reports show that CRYAB exerts a protective role also extracellularly, and it has been recently demonstrated that CRYAB is secreted from human retinal pigment epithelial cells by an unconventional secretion pathway that involves multi-vesicular bodies. Here we show that autophagy is crucial for this unconventional secretion pathway and that phosphorylation at serine 59 residue regulates CRYAB secretion by inhibiting its recruitment to the autophagosomes. In addition, we found that autophagosomes containing CRYAB are not able to fuse with lysosomes. Therefore, CRYAB is capable to highjack and divert autophagosomes toward the exocytic pathway, inhibiting their canonical route leading to the lysosomal compartment.