

Potential dual function of PQ-loop proteins such as cystinosin

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Zhang *et al.* (1) demonstrate convincingly that cystinosin has a dual function. In addition to its low-molecular-weight solute transport, it participates in small GTPase-regulated vesicle trafficking and lysosomal localization of LAMP2A, a protein regulating chaperone-mediated autophagy. If cystinosin is absent or impaired, LAMP2A is mislocalized. Such a protein-trafficking function has been suggested previously, based on a bioinformatics analysis (2). Cystinosin belongs to a diverse family of homologous proteins named PQ-loop (2). Some of the members have been shown to be solute transporters, *e.g.* plant SWEETs (3); others have been shown to be protein cargo receptors in vesicle trafficking, *e.g.* KDEL receptors (4). The molecular functions of many of them, *e.g.* MPDU1 and CLPT1L, have not yet been found despite their involvement in important biological processes. The cargo-trafficking function has been described for mammalian SWEET1, alias RAG1AP1 (5), although not noticed when its solute transport was later discovered (3). The most recent discovery of this dual function in cystinosin (1) suggests that it could be a general property of

many other family members and should always be considered when investigating these important proteins. It could turn out to be particularly relevant for KDEL receptors that show several activities independent of their receptor function (4).

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