

Public Abstract

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The Role of the AP-1 Adaptor Complex in Trafficking between the Trans-Golgi Network and Endosomal System

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In *Saccharomyces cerevisiae* it is generally accepted that there are two routes for trafficking of proteins from the trans-Golgi network (TGN) to the vacuole. One involves direct transport from the TGN to the vacuole. The second involves transport from the TGN to the prevacuolar compartment (PVC) via GGA coated vesicles, followed by PVC to vacuole transport. We propose that there is a third route. This route entails transit from the TGN to the early endosome (EE), followed by delivery to the PVC and vacuole.

In support of an alternative route, the processing kinetics of A(F→A)-ALP are not affected by mutations in the GGA proteins. This is in contrast to proteins that use the GGA pathway, as their delivery to the vacuole is significantly slowed when GGA function is ablated. Further support of an EE itinerary is the observation that A(F→A)-ALP colocalizes with the lipophilic dye, FM4-64 at a time when the dye is associated with the EE. Disruption of the AP-1 vesicle coat complex leads to an accelerated processing of A(F→A)-ALP. Appending the region of A(F→A)-ALP that interacts with AP-1 to Cps1p delays its progress to the vacuole. These results are consistent with a model in which A(F→A)-ALP passes through the EE in transit to the vacuole. A(F→A)-ALP physically interacts with AP-1, and this interaction delays its delivery to the vacuole. Data presented in this thesis suggests that in *Saccharomyces cerevisiae* AP-1 functions as a retrieval mechanism from the EE to the TGN.