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Peroxisome homeostasis

Peroxisomes are eukaryotic organelles that perform many metabolic functions, including fatty acid oxidation. Enzymes within peroxisomes are imported post-translationally and are guided through the import process by a cycling receptor; in mammals this protein is Pex5. The import process involves the ubiquitination of Pex5 on the peroxisome membrane. Maintenance of peroxisome numbers requires balance between proliferation and degradation. A receptor for degradation of peroxisomes uses ubiquitin to accumulate on peroxisomes – could the ubiquitin involved in protein import also play a role in peroxisome degradation? To address this question we have developed stochastic computational models of the Pex5 cycle at the peroxisome membrane and use them to track the ubiquitin involved in the Pex5 import cycle. Recently, a model of export-driven import of cargo proteins was proposed, where Pex5 removal from the membrane is coupled to the translocation of the cargo across the membrane. We modeled conventional, uncoupled import and a newly proposed model of coupled export-driven import of cargo proteins. Both uncoupled and directly coupled import resulted in the peroxisomal Pex5 and ubiquitin both increasing as the amount of protein cargo increased, the opposite of the expected behaviour if the ubiquitin involved in import is also participating in degradation. However, with protein translocation cooperatively coupled to Pex5 export we find the opposite trend of decreasing ubiquitin levels with increasing protein cargo. This natural buildup of ubiquitin at low protein cargo levels suggests that ubiquitin could play a dual role in both peroxisome protein import and peroxisome degradation.