Abstract: Accurate knowledge of the intracellular location of proteins is important for numerous areas of biomedical research including assessing fidelity of putative protein-protein interactions, modeling cellular processes at a system-wide level and investigating metabolic and disease pathways. Many proteins have not been localized, or have been incompletely localized, partly because most studies do not account for entire subcellular distribution. Thus, proteins are frequently assigned to one organelle while a significant fraction may reside elsewhere. As a step towards a comprehensive cellular map, we used subcellular fractionation with classic balance sheet analysis and isobaric labeling/quantitative mass spectrometry to assign locations to >6000 rat liver proteins. We provide quantitative data and error estimates describing the distribution of each protein among the eight major cellular compartments: nucleus, mitochondria, lysosomes, peroxisomes, endoplasmic reticulum, Golgi, plasma membrane and cytoplasm. Accounting for total intracellular distribution improves quality of organelle assignments and assigns proteins with multiple locations. We also demonstrate the utility of this approach in identification of candidate disease genes underlying previously unsolved human hereditary disorders.

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