TITLE

Stepping forward in unraveling the role of PMP34 in mammalian peroxisome biology

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ABSTRACT

Peroxisomes are central characters in cellular redox maintenance and signaling. However, there are still many gaps in our knowledge about the molecular mechanisms underlying peroxisome-mediated redox signaling events. In this context, Peroxisomal Membrane Protein 34 (PMP34) is a particularly interesting protein, as it is the only known peroxisomal member of the mitochondrial solute carrier family 25 and its function and ligand specificity are still uncertain, although it has recently being implicated in the metabolism of phytol.

To investigate the potential role of human PMP34 in peroxisomal redox regulation, a PMP34-deficient Flp-In 293 T-REx cell line was generated by CRISPR/Cas9 technology. In this work, we monitored how inactivation of PMP34 may affect important redox parameters (e.g., GSSG/GSH ratio, H_2O_2 levels, and NAD^+/NADH ratio) in the cytosol, mitochondria, and peroxisomes by employing targeted variants of genetically encoded ratiometric fluorescent sensors (e.g., roGFP2, roGFP2-ORP1, and SoNar). In addition, we explored the potential involvement of PMP34 in H_2O_2 permeation across the peroxisomal membrane, as well as the importance of this protein for maintaining mitochondrial health.

Our data point to a role for PMP34 in peroxisomal redox regulation but rule out the hypothesis that this protein is essential for H_2O_2 channeling. Although the *bona fide* role of PMP34 in mammalian peroxisomes is not yet clear, our work is a step forward into its elucidation and may provide new insights in the redox biology field.

ACKNOWLEDGMENTS

This work has received funding from the European Union's Horizon 2020 research and innovation programme (Marie Skłodowska-Curie grant agreement No 812968) and the Research Foundation – Flanders (Research projects G095315N and G091819N). C.L. is supported by a postdoctoral fellowship of the Research Foundation – Flanders (1213620N), and H.L. is supported by the China Scholarship Council (201906790005).