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AREA OF EXPERTISE:	Cell Biology
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DATE OF DISPUTATION:	6th of September 2018

DISSERTATION TITLE: *Novel observations of Rab7a as a key regulator of endosomal maturation and cellular homeostasis*

Mammalian cells are divided into different organelles that have unique and vital functions for the cell. All of these membrane-bound organelles have specific membrane proteins that define their function. The family of Rab proteins, constitute one of this membrane-associated proteins, and are involved in the regulation of intracellular transport. The PhD candidate Duarte Mateus studied one of these proteins, Rab7a. This protein is found on endosomes, vesicles that internalize external cargo which can be sorted to other compartments or degraded. The recruitment of Rab7a to endosomes has been the focus of intense debate because it occurs in parallel to the displacement of an upstream endosomal Rab protein – Rab5. The molecular mechanism of this "Rab switch" has been previously described. However, in this thesis, the candidate has described an additional mechanism of Rab5 displacement and Rab7a recruitment, consisting of fission and fusion of vesicles, respectively. Furthermore, the candidate has described the temporal link between this switch and the sorting of endosomal cargo, showing that these two events are mutual checkpoints, where the inhibition of one leads to the incompletion of the other.

Additionally, the candidate revealed a new function for Rab7a on the maintenance of cellular homeostasis. The candidate discovered that the absence of Rab7a leads to the onset of cellular stress, identified through a phenotypical alteration in the endoplasmic reticulum (ER), which leads to downstream traffic defects.

The work of the candidate contributes to a deeper understanding of the central role of Rab7a in the eukaryotic cell. In particular, it expands on the canonical role of Rab7a in the "Rab

switch" during endosomal maturation and cargo sorting. Furthermore, the work explores organelle interactions, in particular the Rab7a-containing endosomes and the ER. Finally, this work advances the understanding of endosomal trafficking, which is important for cellular homeostasis.