**Introduction**

- The Anaphase Promoting Complex/Cyclosome (APC/C) is an E3 ubiquitin ligase involved in cell cycle progression by targeting cell-cycle regulators for degradation.
- It is conserved from yeast to humans and relies on two adaptor proteins, Cdc20 and Cdh1, which identify its substrates due to the presence of recognition motifs.
- In humans, Cdh1 recognizes a broader set of substrates than Cdc20, including proteins from nonmitotic processes such as glycolysis and mitochondrial fission (Drp1).
- Previous work from the group suggest Cdh1 may target additional mitochondrial proteins in *S. cerevisiae*.

**Aim:** Identify APC/C-Cdh1 mitochondrial targets in *S. cerevisiae* and determine its role in mitochondrial function and cell cycle progression.

**Results**

**Identification of altered mitochondrial proteins in the absence of Cdh1 points to an increase in respiratory metabolism**

![Figure 1](image1.png)

Figure 1. (A) Proteome analysis of mitochondrial extracts in the absence of CDH1. Up-regulated proteins (p-value=0.05) and down-regulated proteins (p-value = 0.05). (B) Gene ontology-term enrichment analysis on biological processes made for statically changed proteins using STRING v11.0

The most represented biological processes in up-regulated proteins (putative Cdh1 substrates) are the Krebs cycle, respiratory chain (including proteins from all the respiratory complexes) and mitochondrial fission (including Dnm1/Drp1). Down-regulated proteins include mostly unrelated proteins.

**Mitochondrial respiration is increased in cells lacking Cdh1**

![Figure 2](image2.png)

Figure 2. Interaction network map built using STRING v11.0 and based on 58 up-regulated proteins (A) and 105 down-regulated proteins (B) detected in *S. cerevisiae* cdh1Δ. Proteins are shown as nodes and the existence of interactions between them are represented by edges. Edge thickness indicates the strength of the different interactions.

**Further Work**

- Identification of the transcription factors (TF) involved in the cdh1Δ-increase in mitochondrial respiration;
- Determination of the TFs as APC/C-Cdh1 targets by recognition motif validation; evaluate its role in cell cycle progression.
- Establish a novel role for the APC/C-Cdh1 in the regulation of mitochondrial function.

**Acknowledgements**

This work was funded by PCT-Porto for a Ciência e a Tecnologia, under the projects IF/00891/2015/CP1393/CT0044 and UIDB/04551/2020 and through PhD grants attributed to AIL (SFRH/BDE/137901/2018).

**References**