

# Compartmentalized synthesis of triacylglycerol at the inner nuclear membrane

Antonio D. Barbosa<sup>1</sup>, Koini Lim<sup>2</sup>, Muriel Mari<sup>3</sup>, James R. Edgar<sup>1</sup>, Lihi Gal<sup>4</sup>, Peter Sterk<sup>1</sup>, Benjamin J. Jenkins<sup>5</sup>, Albert Koulman<sup>5</sup>, David Savage<sup>2</sup>, Maya Schuldiner<sup>4</sup>, Fulvio Reggiori<sup>3</sup>, Philip A. Wigge<sup>6</sup>, Symeon Siniosoglou<sup>1\*</sup>

<sup>1</sup>Cambridge Institute for Medical Research, University of Cambridge, Cambridge CB2 0XY, UK

<sup>2</sup>Metabolic Research Laboratories, Wellcome Trust-Medical Research Council Institute of Metabolic Science, University of Cambridge, Cambridge CB2 0QQ, UK

<sup>3</sup>Department of Cell Biology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands.

<sup>4</sup>Department of Molecular Genetics, Weizmann Institute of Science, Rehovot 7610001, Israel.

<sup>5</sup>NIHR BRC Core Metabolomics and Lipidomics Laboratory and University of Cambridge Metabolic Research Laboratories, Wellcome Trust-Medical Research Council Institute of Metabolic Science, Cambridge CB2 0QQ, UK.

<sup>6</sup>Sainsbury Laboratory, University of Cambridge, Cambridge CB2 1LR, UK.

\* **Corresponding author:** ss560@cam.ac.uk

Cells dynamically adjust organelle organization in response to growth and environmental cues. This requires the regulation of synthesis of phospholipids, the building blocks of organelle membranes. Fatty acids (FAs) are essential components of phospholipids, but also of triacylglycerols (TGs) that enable energy storage in lipid droplets (LDs). Phospholipid and TG synthesis mainly take place at the endoplasmic reticulum membrane. How cells control the allocation of FAs between phospholipids, for membrane growth, and TG, for energy storage, remains unclear. We will present evidence of a lipid remodeling pathway operating at a subdomain of the inner nuclear membrane to regulate nuclear structure. We find that this pathway results in the synthesis of TG at the inner nuclear membrane in response to cell-cycle and nutrient signals and its compartmentalization is critical for nuclear integrity. Finally, we will present evidence supporting the presence of a mechanism that exports nuclear TG to the cytoplasmic side of the nuclear membrane.