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## Cholesterol-Enriched Diet Provokes Pathological Alterations in Kidneys with Traits Typical of Lysosomal Storage Diseases

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Obesity represents a growing public-health problem. Besides being a major risk factor for the onset of diabetes and cardiovascular diseases, obesity has been associated with the onset of chronic kidney diseases (CKD) and end-stage renal diseases (ESRD). Emerging evidence indicates a lipid-mediated effect in initiating renal dysfunction/injury. However, the cellular mechanisms connecting obesity/dyslipidaemia with CKD/ESRD remain largely unclear.

We found that upon over nutrition with a cholesterol-rich Western-type diet (WD), renal proximal tubular epithelial cells (PTEC) become target sites of lipid deposition and display giant vacuoles of lysosomal/autophagosomal origin harbouring oxidized lipoproteins and concentric membrane layer structures. These organelles are reminiscent of multi lamellar bodies (MLBs) found in lysosomal storage diseases (LSD). In fact, similarly to LSD traits, lipidomics and proteomics showed that MLBs function as intracellular lipid storage sites and are likely to be secreted into urine by lipid-overloaded PTEC. In addition, the tubular intralysosomal lipid storage is accompanied by inflammation, fibrosis, tubular damage and dysfunction and a tubular cell transcriptional reprogramming to increase lysosomal degradation.

Collectively, our data show that renal epithelial cells actively respond to over nutrition and participate in the management of lipid overload by generating MLBs. Our study emphasizes the role of renal cells in lipid handling and the importance of healthy lysosomes in the maintenance of kidney wellbeing.

### Biography:

Dr. Elena Rampanelli After graduating in Medical Biotechnology from the University of Bologna, Italy, she obtained her PhD degree at the University of Amsterdam, The Netherlands. After her PhD, Dr. Rampanelli worked as postdoc at the University Hospital of Regensburg (UKR), Germany; subsequently, she worked at the Academic

Medical Center of Amsterdam (AMC), The Netherlands, and later at the UNC Lineberger Comprehensive Cancer Center, University of North Carolina (UNC), US. She recently returned to The Netherlands to join the Amsterdam University Medical Center (AUMC).