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## Renal dysfunction and metabolic syndrome: The chicken or the egg?

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The impact of diet-induced obesity, dyslipidemia and hypertension (metabolic syndrome, MetS) on kidney health and function is now emerging. Despite epidemiologic analyses show that MetS/dyslipidemia puts patients at higher risk for chronic kidney diseases (CKD), a causal relationship between dyslipidemia and renal dysfunction has not been completely elucidated. In our latest work, we aim to unravel the effects of high-fat diet (HFD) on renal physiology and the direct impact of LDL (low density lipoproteins) on cultured renal tubular epithelial cells (TEC). Our data show that LDL overload leads to TEC damage by inducing phospholipidosis, mitochondrial damage and apoptosis and causes alterations in the plasmatic membrane composition. These effects associate with impaired absorptive functions, decreased ATP levels and defective cellular responses to growth factors in terms of signaling and proliferation. Low-grade inflammation is a hallmark of MetS. Soon after LDL exposure, TEC start secreting TNF- $\alpha$  and IL-1 $\beta$  and display increased intracellular levels of active caspase-1 which is required for the cleavage of pro-IL-1 $\beta$ . The maturation of both caspase-1 and IL-1 $\beta$  indicates the activation of the NLRP3 inflammasome which is a multimeric danger-sensing complex implicated in the onset of obesity-induced inflammation and MetS. Interestingly, absence of a fully active NLRP3 inflammasome (shRNA/sgRNA) reduces the rate of LDL-induced phospholipidosis in cultured TEC. Accordingly; lack of NLRP3 attenuates the HFD-induced cholesterol and phospholipid accumulation in proximal tubules in mice. In conclusion, our research offers insight into the molecular processes at play in renal tubular cells during metabolic overloading and shed light on the role of NLRP3 in renal lipid metabolism.

## Biography

Elena Rampanelli has completed her Medical Biotechnology studies at the University of Bologna (Italy). Before starting her PhD, she carried out Scientific Research at the Rizzoli Orthopedic Institute in Bologna (Italy) and at the Queensland Institute of Medical Research in Brisbane (Australia). Between 2008 and 2013, she worked as a PhD student at the Academic Medical Hospital of Amsterdam (Netherlands). She then carried out her first Post-doctorate at the Institute of Clinical Chemistry and Laboratory Medicine of the University Hospital of Regensburg (Germany). She is currently conducting her Postdoctoral Research at the Academic Medical Hospital in Amsterdam, Netherlands.

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