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Interplay between metabolic signals and regulation of gene expression in activated macrophages: Focus on the ACLY / NF-kB axis

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A metabolic reprogramming drives a proinflammatory phenotype in macrophages activated by pathogen-associated molecular patterns like lipopolysaccharide or lipoteichoic acid. Changes in gene expression also represent a hallmark of induced macrophages. Both metabolic and gene regulation shifts aim to support cell's function; although the relationships between them remain poorly explored. In recent years, we demonstrated that the metabolic enzyme ATP citrate lyase (ACLY), the producer of citrate-derived acetyl-coenzyme and oxaloacetate, plays a pivotal role in producing critical inflammatory mediators such as reactive reactive oxygen species, nitric oxide and prostaglandin E2, whose levels lowered after treatments with ACLY inhibitors or during ACLY gene silencing. Newly, through immunocytochemistry and cytosol–nucleus fractionation, we observed a short-term ACLY nuclear translocation. By means of protein immuno-precipitation, the role of nuclear ACLY in NF-kB acetylation has been proved in human PBMC-derived macrophages. Markedly, septic patients - with sepsis in the early hyper inflammatory phase -showed ACLY-mediated NF-kB acetylation. By inducing NF-kB full activation, ACLY-mediated NF-κB acetylation drives the expression levels of proinflammatory genes, including SLC25A1 which encodes the mitochondrial citrate carrier—and ACLY, thus promoting a proinflammatory loop.

Speaker Biography

Vittoria Infantino has completed her PhD in "Cell Biochemistry and Pharmacology" from the University of Bari (Italy), studying mechanisms of transcriptional regulation. She further focused on this topic in postdoctoral studies. She is currently an Assistant Professor in Cellular Biology at University of Basilicata, Italy. Her research is focused on the relationship between gene regulation and metabolism in physiological and pathological conditions, with particular interest in cancer and inflammatory diseases. To deepen these topics, she worked as visiting scientist at the research group headed by Prof. Luke O'Neill, Trinity College Dublin, in 2016. She has published more than 50 papers in international peer-review journals.

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