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Global and unique translational regulation suggests a novel regulatory mechanism of the inflammatory response to LPS in macrophages

Hiroaki Sako[1], Katsuhiko Suzuki[2]
[1]Graduate School of Sport Sciences, Waseda University, Japan
[2]Faculty of Sport Sciences, Waseda University, Japan

Once organisms encounter bacterial infections, rapid cellular response is critical to initiate the inflammatory response. A widely used model of acute inflammation, lipopolysaccharide (LPS)-stimulated macrophage, dramatically shifts the cellular conditions toward sophisticated pro-inflammatory status. This is exemplified by the phosphorylation and the activation of pro-inflammatory signaling cascades and related transcription factors, such as Mitogen-Activated Protein Kinase (MAPK), Inhibitor of κB (IκB), Nuclear Factor of κ light polypeptide gene enhancer in B cells (NFκB), Activator Protein 1 (AP-1), and Interferon Regulatory Factor (IRF) as well as the increased synthesis of chemokines and cytokines. To provide a comprehensive perspective of these complex mechanisms, global analyses have recently been conducted focusing on phosphoproteomics, transcriptomics, and epigenomics. However, the importance of global translational regulation in the inflammatory response is still poorly understood. Here we used recently developed ribosome profiling based on high-throughput RNA sequencing (RNA-Seq) and conducted a genome-wide translational analysis of the early inflammatory response to LPS (30min) in RAW264 macrophages. The result showed unique translational dynamics, independent to the pro-inflammatory transcriptome regulation. We provide evidence that global translational regulation, especially down regulation, has a potential role in triggering and/or modulating the early inflammatory response of macrophages to LPS. This implies a possibility that global translational regulation is one of the critical regulatory mechanisms underlying in the exercise-induced pro-/anti-inflammatory responses.