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LECT2 association with macrophage-mediated killing of *Helicobacter pylori* by activating NF-κB and nitric oxide production

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ABSTRACT. *Helicobacter pylori* employs unique methods to colonize the stomach, which induces chronic inflammation. It is also able to avoid eradication by macrophages and other immune cells. Leukocyte cell-derived chemotaxin 2 (LECT2), a multi-functional cytokine involved in many pathological conditions, has recently been shown to activate macrophages via the CD209a receptor. Therefore, we aimed to investigate the effects of LECT2 on *H. pylori*-infected macrophages. Macrophages were treated with recombinant LECT2, and both their ability to kill *H. pylori* and produce nitric oxide were analyzed. Western blot was performed to determine nuclear translocation and protein phosphorylation of p65, a subunit of nuclear factor (NF)-κB.

Transfection experiments were performed to analyze the signaling pathway of LECT2 in macrophages. We found that treatment with LECT2 enhanced *H. pylori* killing and nitric oxide production in macrophages. In addition, DNA-binding activity and nuclear translocation of p65 were up-regulated by LECT2 treatment. Furthermore, we found that NF-κB activation by LECT2 was mediated by Raf-1 in macrophages, and Raf-1 phosphorylation was specifically altered in response to LECT2. Moreover, LECT2 induced Ser28 phosphorylation in the intracellular domain of CD209a. CD209a Ser28 phosphorylation was required for LECT2-induced Raf-1 and NF-κB activation in RAW264.7 macrophages. Our study showed that the effects of LECT2 on *H. pylori* killing and nitric oxide production were dependent on CD209a phosphorylation, Raf-1, and NF-κB activation. Together, these results demonstrate for the first time that exposure to LECT2 can modulate specific intracellular mechanisms downstream of CD209a to enhance *H. pylori* killing and nitric oxide production in macrophages.

Key words: LECT2; CD209a; Macrophages; *Helicobacter pylori*; Bacterial killing; NF-κB