Contribution of mTOR to Oxidative/Nitrosative Stress via NADPH Oxidase System Activation in Zymosan-Induced Systemic Inflammation in Rats

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Abstract : We hypothesized that mTOR inhibition may prevent the multiple organ failures following severe multiple tissue injury associated with increased NADPH oxidase system activity occur in zymosan-induced systemic inflammation. Therefore, we investigated the role of mTOR in oxidative/nitrosative stress associated with increase in NADPH oxidase activity in zymosan-induced systemic inflammation model in rats. Male Wistar rats received saline (4 ml/kg, i.p.) and zymosan (500 mg/kg, i.p.) at time 0. Saline, or zymosan-treated rats were given rapamycin (1 mg/kg, i.p.) 1 h after saline or zymosan injections. Rats were sacrified 4 h after zymosan challenge and kidney, heart, thoracic aorta, and superior mesenteric artery were collected. NADPH oxidase activity, p22phox, gp91phox, and p47phox protein expression and nitrotyrosine levels were measured in tissue samples. Zymosan administration caused an increase in NADPH oxidase activity, p22phox, gp91phox protein expression and nitrotyrosine levels in kidney, heart, thoracic aorta, and superior mesenteric artery. These changes caused by zymosan reversed by rapamycin, a selective mTOR inhibitor. Rapamycin alone had no effect on the parameters measured. Our results demonstrated that zymosan-induced oxidative/nitrosative stress presumably due to enhanced activity of NADPH oxidase, expression of p22phox, gp91phox, and p47phox and production of peroxynitrite were mediated by mTOR. [This work was financially supported by Research Foundation of Mersin University (2016-2-AP3-1900)].

Keywords : oxidative stress, mTOR, nitrosative stress, zymosan

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