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МЕТИЛОФИОПОГОНАНОН А ИНГИБИРУЕТ LPS/АТР-ИНДУЦИРОВАННЫЙ ПИРОПТОЗ МАКРОФАГОВ ЧЕРЕЗ ПУТЬ ROS/NLRP3¹

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Как побочный продукт митохондриального дыхания или метаболизма активные формы кислорода (ROS) могут действовать как сигнальные молекулы для активации инфламмосомы NLRP3 (NLR family pyrin domain containing 3), тем самым индуцируя иммунный ответ. NLRP3 инфламмосома действует как сенсор различных опасных сигналов и играет центральную роль в контроле возникновения пироптоза. Пироптоз макрофагов тесно связан с атеросклерозом, артритом, фиброзом легких и другими воспалительными заболеваниями. Метилофиопогонанон А (МО-А) — основной гомоизофлавоноид, входящий в состав китайского лекарственного растения *Ophiopogonis Radix* и проявляющий антиоксидантную активность. Однако неясно, может ли МО-А ослаблять пироптоз макрофагов путем ингибирования окислительного стресса. Нами показано, что МО-А усиливает активность супероксиддисмутазы и каталазы, ингибирует образование ROS, снижает активацию NLRP3-инфламмосомы и высвобождение лактатдегидрогеназы, а также подавляет пироптоз в макрофагах, индуцированный липополисахаридами (LPS) и аденозинтрифосфатом (АТР). Эти эффекты могут быть отменены активатором ROS — пероксидом водорода (H₂O₂). Таким образом, МО-А может ингибировать пироптоз макрофагов через путь ROS/NLRP3 и, следовательно, рассматриваться в качестве кандидата для разработки противовоспалительного лекарственного средства.

Ключевые слова: инфламмосома NLRP3, пироптоз, макрофаги, активные формы кислорода, метилофиопогонанон А

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Methylophiopogonanone A Inhibits LPS/ATP-Induced Macrophage Pyroptosis via ROS/NLRP3 Pathway

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As a byproduct of mitochondrial respiration or metabolism, reactive oxygen species (ROS) can act as a signaling molecule to activate NLR family pyrin domain containing 3 (NLRP3) inflammasome, thereby triggering immune response. NLRP3 inflammasome acts as a sensor of various danger signals and is central to

the control of pyroptosis occurrence. Macrophage pyroptosis is closely related to atherosclerosis, arthritis, pulmonary fibrosis and other inflammatory diseases. Methylophiopogonanone A (MO-A) is a main homo-isoflavonoid in Chinese herb *Ophiopogonis Radix*, which has antioxidant effect. However, it is not clear whether MO-A can alleviate macrophage pyroptosis by inhibiting oxidative stress. Here we have shown that MO-A increases the activities of superoxide dismutase (SOD) and catalase (CAT), inhibits the production of ROS, reduces the activation of NLRP3 inflammasome and the release of lactate dehydrogenase (LDH), and inhibits pyroptosis in macrophages induced by lipopolysaccharides (LPS) and adenosine triphosphate (ATP). These effects can be reversed by the ROS promoter hydrogen peroxide (H_2O_2). Therefore, MO-A can inhibit macrophage pyroptosis through the ROS/NLRP3 pathway and may be considered as a candidate drug for the treatment of inflammatory diseases.

Keywords: NLRP3 inflammasome, pyroptosis, macrophages, ROS, methylophiopogonanone A