Granulomatous inflammation in inbred mice of different strains: a comparative study

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Comparative investigation of the time-course of formation, persistence and involution of granulomatous inflammation induced by different doses of fibrogenic particles (carbon dioxide) or by non-fibrogenic ones (zymosan) in the liver, lungs and subcutaneous space was carried out in inbred mouse strains C3H/F, BALB/c, CBA/Lac, C57BR and C57Bl/6 which differ substantially in 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMG-CoA reductase) inducibility. It was demonstrated, that interstrain differences in granulomagenic and in fibrogenic response correlated with myelopoietic activity in bone marrow and were of regular character, being stable irrespective of the granulomagenesis localization, of the nature of inflammatory agent, or of the dose or the route of administration of the agent. The ability of macrophages of different strains of mice to produce pro- (GM-CSF, TNFα, NО) and anti-inflammatory (IL-10, TGFβ1) mediators and cytokines was studied. A clear concurrency between strain-specific mononuclear phagocyte system responsiveness, the level of granulomatous and fibrogenic response on one hand, and the strain-specific inducibility of 3-hydroxy-3-methyl-glutaryl-CoA reductase, a key enzyme of mevalonate pathway, on the other, was established. A possible important role of mevalonate pathway response in regulation of macrophage responsiveness in inflammation is hypothesized. (Cytokines and Inflammation. 2013. Vol. 12. № 1–2. P. 26–33.)

Key words: granulomatous inflammation, macrophages, 3-hydroxy-3-methyl-glutaryl-CoA reductase.