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WAS基因缺陷小鼠巨细胞病毒急性感染模型的建立

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Title: Establishment of WASp-deficient mice model of acute murine cytomegalovirus infection and infection characteristics

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摘要:

目的　用小鼠巨细胞病毒（murine cytomegalovirus, MCMV）Smith株建立WAS基因缺陷小鼠（129S6/SvEvTac-Was^{tm1Sbs}/J）全身播散型感染模型并观察感染特点。方法　同窝内简单随机法选取实验组小鼠（129S6/SvEvTac）WASp-/-（雌雄各半），感染对照组小鼠（129S1/SvImNJ）WASp+/+ 6只，雌雄各半，6～8周龄。腹腔内接种0.2 mL小鼠巨细胞病毒悬液1×10^{5}PFU；另设6只129S6小鼠为空白对照组。各组分别接种MCMV 9 d后处死小鼠，取小鼠唾液腺分离病毒，RT-PCR检测小鼠主要脏器组织中MCMV gB基因，HE病理染色观察小鼠脏器病理损害，流式细胞术检测WAS基因缺陷小鼠脾脏MCMV特异性细胞毒性T细胞（CTL）比例。　结果　与对照组野生型小鼠相比，实验组WASp-/-小鼠MCMV感染后一般状况差，体质量下降，活动少，耸毛反应明显，有死亡（1/6）。感染后第9天，实验组和感染对照组小鼠唾液腺均分离出巨细胞病毒，主要脏器心、肝、肺、肾和唾液腺中MCMV gB基因RT-PCR检测结果为阳性。实验组小鼠肺内MCMV gB基因mRNA含量显著高于对照组小鼠（P<0.05），空白对照组未检测出病毒。MCMV感染后主要脏器出现明显病理损害，其中肺部病理损害严重。流式细胞术检测结果显示WAS基因缺陷小鼠脾脏MCMV CTL比率与对照组比较无统计学差异（P=0.26）。　结论　腹腔注射MCMV 1×10^{5}PFU成功建立成年WAS基因缺陷小鼠急性感染模型，观察到较对照组野生型小鼠更明显的、较重的急性感染反应；肺为感

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染主要靶器官之一；初次感染后脾脏MCMV CTL比例无明显变化。

Abstract: Objective To establish a WASp-deficient mouse (129S6/SvEvTac-Was^{tm1Sbs}/J) model of induced systemic infection with murine cytomegalovirus (MCMV) and investigate the infection characteristics. Methods WAS-null mice were randomly chosen as model group and blank control group respectively (*n*=6 for each group). They were infected with 1×10^5PFU MCMV (0.2 mL) by intra-peritoneal administration. WASp+/+ mice were used as infection control (*n*=6). All experimental mice were under closely observation and sacrificed in 9 d after the intraperitoneal injection. Tissue samples were collected under aseptic conditions from each experimental mouse. Salivary glands were taken for virus separation and titer test. The histological changes of the main visceral organs and tissues were examined after HE staining, and the mRNA expression of MCMV gB was detected by RT-PCR. Flow cytometry was used to detect the percentage of MCMV cytotoxic T lymphocytes (CTLs) in splenic lymphocytes from model group and infection control group. Results Compared with WASp+/+ mice infection control, the general condition of infected mice in WASp-/- infection groups was getting worse after the infection in terms of body weight reduction, lack of movement, more piloerection, with a mortality of 1/6. In 9 d after infection, cytomegalovirus was found in the salivary glands of both infection groups, and MCMV gB mRNA was positive in the heart, liver, lung, kidney and salivary glands, with the expression level significant higher in the WASp-/- infection group than in WASp+/+ infection control (*P*<0.05). No MCMV mRNA was detected in mice without the infection. Histopathological injury was found in the livers, kidneys, lungs and hearts, and the lung was the critical target organ. The proportion of MCMV CTLs in splenic lymphocytes had no significant difference among these groups (*P*=0.26). Conclusion An acute virus-infection model is established for the first time by intra-peritoneal injection of 1×10^5 PFU MCMV in adult WASp-/- mice. More obvious and severe manifestations of acute infection are observed in WASp-deficient mice than in wide type, with lung as the critical target organ. There is no obvious change in the proportion of MCMV CTLs after the primary infection between the deficient and wild type mice.

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