



Title	Functional analysis of natural resistance-associated macrophage protein (Nramp) in the pathway of nitric oxide synthesis in mice
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by two stimulatory proteins, the cleavage and polyadenylation specificity factor (CPSF) and PABII. Northern blot analysis of *Pabp3* revealed a single transcript of approximately 1.2kb only in testis. To determine if *Pabp3* is differentially expressed in specific testicular cell lineages, northern blot analysis was performed in testis from normal and germ cell-deficient *W/W<sup>V</sup>* mutant mice, and also the different stages of post-natal development in normal mice. As a result, *Pabp3* was expressed only in the adult

testis. *Pabp3* protein was detected in the nucleus in a specific period (from late pachyten spermatocytes to step 9 round spermatid) by immunohistochemistry. *Pabp3* function is unclear in the mouse testis, but these results suggest that *Pabp3* is involved in specific spermatogenic cell differentiation.

It was demonstrated in this study that *Pabp3* locus mapped at centromeric position with  $4.2 \pm 2.9\text{cM}$  apart from *Ctla1* on mouse chromosome 14.

#### Functional analysis of natural resistance-associated macrophage protein (Nramp) in the pathway of nitric oxide synthesis in mice

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The ability of a host to resist infection with a wide range of viral, bacteria, and parasitic pathogens is strongly influenced by a lot of genetic factors. The *Bcg/Ity/Lsh* gene on mouse Chromosome 1 regulates priming/activation of macrophage for antimicrobial and tumoricidal activity. A candidate gene expressed in macrophages has been identified as the natural resistance-associated macrophage protein (Nramp) by positional cloning and full-length sequence analysis. Macrophages are concerned with antimicrobial activity by numerous cytokine-induced nitric oxide productions.

In this study, the following experiments were performed to reveal the relationship between Nramp and NO production by macrophages. The production of NO by macrophages from *Nramp<sup>r</sup>* mice (*Nramp<sup>r</sup>* macrophage) was much larger than that from *Nramp<sup>s</sup>* mice (*Nramp<sup>s</sup>* macrophage), in the case of activations with IFN- $\gamma$ , LPS+IFN- $\gamma$ , IL-1 $\beta$ , TNF-

$\alpha$  and L-Mannose. No significant difference between the expressions of Nramp mRNA in the cytokine-activated *Nramp<sup>r</sup>* and *Nramp<sup>s</sup>* macrophages was determined by Northern blot analysis. In order to examine the cause of different NO production between *Nramp<sup>r</sup>* and *Nramp<sup>s</sup>* macrophages, both *Nramp<sup>r</sup>* and *Nramp<sup>s</sup>* macrophages were activated by LPS, IFN- $\gamma$ , LPS+IFN- $\gamma$ . After activation, the levels of iNOS mRNA were detected by Northern blot analysis. It was noted that high levels of iNOS mRNA were found in the *Nramp<sup>r</sup>* macrophages activated by IFN- $\gamma$ , LPS+IFN- $\gamma$ . Under these same conditions, high levels of iNOS mRNA were not seen in the *Nramp<sup>s</sup>* macrophages. In the analysis of uptake of L-arginine by *Nramp<sup>r</sup>* and *Nramp<sup>s</sup>* macrophages, no significant relationship between the uptake of L-arginine and the NO production was observed in both macrophage types.

These results suggested that the antimicrobial activity controlled by Nramp was depen-

dent on the amount of NO production by macrophages. Additionally, it was emphasized that the macrophages from Nramp<sup>r</sup> mice was activated by even in a small amount of cytokines, followed to induce the expression of iNOS mRNA via IFN- $\gamma$  activation, produce a large amount of

NO, and finally suppress the growth of intracellular pathogens. The process which Nramp generates the NO production in a signal transduction would be concerned with the activation by IFN- $\gamma$ .

### Molecular biological and histological analyses of Fas receptor-Fas ligand system in the testis of mice

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Although numerous studies have been reported on the cell surface receptor (FasR) and its ligand (FasL) which are mediators of apoptosis in the immune system, little is known about their role outside of the lymphoid system. Recently it has been shown that both FasR and FasL are expressed in several nonlymphoid tissues, such as testis.

In the present study, to find out the function of the FasL-FasR system in testis, the relationship between FasR or FasL expression and the distribution of apoptotic signal were investigated by molecular biological and histological techniques using normal and lpr mutant mice which had a leaky mutation in FasR. Both FasR and FasL mRNA were detected in the testis from normal mice by Northern hybridization and RT-PCR. FasR expression was observed on the cell surfaces of spermatogonia, spermatocytes

and round-spermatids, but not on elongating spermatids by in situ hybridization and immunohistochemistry. Whereas, FasL expression was restricted to Sertoli cells. In the testis from lpr mice, it was noted by Northern hybridization and immunohistochemistry that FasR expression was reduced compared with that from normal mice.

Although an apparent difference of FasR expression in testis was detected between the normal and lpr mice, TUNEL method revealed that the apoptotic cells were localized to the stage12 of spermatogenesis in testis of both normal and lpr mice.

These results suggest that the FasL-FasR system plays a minor role in the regulation of physiological cell turnover within the testis. Additionally, it may be suggested that FasL in Sertoli cells of the testis involves in the defense mechanisms against FasR-bearing T cells.