**Short communication**

The role of hepatic lectins and the activity of the mononuclear phagocyte system in systemic *Listeria monocytogenes* infection in Balb/c mice*

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**Abstract.** Hepatic lectin blocking experiments with D-galactose in Balb/c mice showed that parenchymal liver cells are obviously not involved in *Listeria monocytogenes* infection (strain SLCC 4013, $5 \times 10^4$ cells i.v.). Using the bacterial immunomodifier *Propionibacterium avidum* KP-40 the importance of an activated mononuclear phagocyte system in the early stage of *Listeria* infection could be demonstrated.

*Listeria monocytogenes* is a facultative intracellular bacterium which parasitizes host phagocytes [3, 4, 8]. Virulent strains induce in mice acute systemic infections which primarily affect reticulo-endothelial organs [4, 8, 9]. The mononuclear phagocyte system (MPS) is surely the major mediator of natural antilisterial resistance [2, 8, 10, 12]. The role of NK cells, granulocytes and hepatocyte membrane receptors (hepatic lectins) in *Listeria* infection is not yet clear [1, 2, 8, 10].

In this report we discuss the blocking of hepatic lectins by systemic D-galactose treatment as well as the effect of activated MPS in the very early stage of systemic *Listeria* infection using a murine model [4, 5, 6] and *Propionibacterium avidum* KP-40, a very potent MPS activator. To initiate acute systemic infection the highly *Listeria*-sensitive Balb/c mouse strain [2, 8, 12] is used as well as a rather high challenge dose ($5 \times 10^6$ cells i.v.) of the virulent *L. monocytogenes* strain SLCC 4013 [6].

Inbred male Balb/c mice, 8–12 weeks old, weighing 20–22 g, were received from the Central Institute for Experimental Animals, Hannover, FRG. Whole cells of immunomodifier *P. avidum* KP-40 were heat inactivated, lyophilized and suspended in PBS (1 mg/0.1 ml) [6, 11].

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Table 1. Bacterial load per gram of liver and kidney 24 h after intravenous infection of Balb/c mice with $5 \times 10^6$ viable cells of *L. monocytogenes* SLCC 4013

<table>
<thead>
<tr>
<th>Balb/c mice (each group n = 5)</th>
<th>$\log_{10} L. monocytogenes/g$ organ weight (± SD)</th>
<th>Liver</th>
<th>%</th>
<th>Kidney</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>9.50 (± 0.71)</td>
<td>100</td>
<td>6.60 (± 0.51)</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>5.84 (± 0.90)*</td>
<td>61.5</td>
<td>1.97 (± 0.38)**</td>
<td>29.8</td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td>9.02 (± 0.93)</td>
<td>94.9</td>
<td>6.74 (± 0.10)</td>
<td>102.1</td>
<td></td>
</tr>
</tbody>
</table>

Group I, control; group II, *P. avidum* treated; group III, D-galactose treated (hepatic lectins blocked)
SD, standard deviation
* $P < 0.01$; ** $P < 0.001$ (both significant according to Student's t-test)

Balb/c mice (five animals in each group) were intravenously infected with $5 \times 10^6$ viable cells of *L. monocytogenes* strain SLCC 4013. As shown in the table, this infection caused heavy organ colonization of liver and kidney (group I, control). MPS activation by *P. avidum* KP-40 (1 mg i.p. 7 days before challenge, group II) increased nonspecific resistance to *Listeria*: bacterial counts per gram of liver and kidney (determined 24 h after challenge by plating) were significantly lower than in controls (Table 1). Moreover, survival time (recorded 6 days after challenge) of stimulated mice was considerably better: all control animals ($n = 10$) died within 36 h after infection, whereas six of 10 *P. avidum*-treated mice survived.

Animals in group III received D-galactose (Serva GmbH, Heidelberg, FRG) 1 h prior to infection and at 12-h intervals after infection (2 mg/g body weight i.p.). This blocking of hepatic lectins by systemic D-galactose treatment [1] did not protect Balb/c mice from liver colonization.

Administration of *Propionibacteria* induces a marked enlargement of spleen, liver and lymph nodes, dependent on enhanced proliferation and stimulation of macrophages, histiocytes and hemopoietic cells [11]. We were able to demonstrate that this MPS activation is a strain-specific property rather than species- or genus-related [7]. Therefore in earlier experiments we used the following two biological response modifiers (BRM): *P. granulosum* KP-45 and *P. avidum* KP-40. The two strains have similar activities, but preparations of *P. avidum* KP-40 proved to be more stable and better standardizable.

Previous studies [6] had already demonstrated the importance of MPS for the nonspecific antilisterial resistance, using less *Listeria*-sensitive NMRI mice, a lower challenge dose ($10^3$ cells i.v.) and *P. granulosum* KP-45 as BRM. The data of this report fully confirm this using a much higher challenge dose, the more *Listeria*-sensitive Balb/c mice and *P. avidum* KP-40 as BRM. Activated MPS is very beneficial at least in the early stage of systemic *Listeria* infection.

The blocking of hepatocyte membrane receptors (hepatic lectins) by systemic D-galactose treatment did not show any remarkable effects. *L. monocytogenes* resides within reticuloendothelial cells and seems not to be able to colonize parenchymae liver