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Mit Gesunden Infizieren

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H. J. Girschick · H. I. Huppertz · H. Rüssmann
V. Krenn · H. KarchIntracellular persistence of *Borrelia burgdorferi* in human synovial cells

Abstract: Morph. changes to include - *ausgefaltet, abwärts*
to fold - *falten, Zusammenklappen*
Confocal -
to re-isolate - *Wiederherstellen*
to engulf - *verschlucken*
at least - *wenigstens*

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Abstract To investigate if *Borrelia burgdorferi* can persist in resident joint cells, an infection model using cell cultures of human synovial cells was established and compared to the interaction of *Borrelia burgdorferi* and human macrophages. *Borrelia burgdorferi* were found attached to the cell surface or folded into the cell membrane of synovial cells analysed by transmission electron and confocal laser scanning microscopy. In contrast to macrophages, morphologically intact *Borrelia burgdorferi* were found in the cytosol of synovial cells without engulfment by cell membrane folds or phagosomes. *Borrelia burgdorferi* were isolated from parallel cultures. Treatment with ceftriaxone eradicated extracellular *Borrelia burgdorferi*, but spirochetes were reisolated after lysis of the synovial cells. *Borrelia burgdorferi* persisted inside synovial cells for at least 8 weeks. These data suggested that *Borrelia burgdorferi* might be able to persist within resident joint cells in vivo.

Key words *Borrelia burgdorferi* · Synovial cells · Intracellular persistence

Introduction

Lyme borreliosis transmitted by a tick bite is caused by the spirochete *Borrelia burgdorferi*. Clinical manifestations include erythema migrans, meningoradiculoneuritis and

arthritis [1]. Lyme arthritis usually begins several months after the infection [2]. Lyme arthritis is treated by antibiotics, but approximately 25% of patients have ongoing arthritis after one or two antibiotic treatments [2, 3].

Although the aetiology of Lyme arthritis is known, the pathogenesis is far from clear. Several pathogenic aspects have been discussed including B- and T-cell responses against *Borrelia burgdorferi* [4, 5], autoimmune mechanisms [6] and phagocytosis of persisting spirochetes [2, 7]. Two patterns of phagocytosis have been described: (1) Conventional phagocytosis, leading to the enclosure and degradation of *Borrelia burgdorferi* inside the phagosomes; (2) coiling phagocytosis by which spirochetes are enrolled by coiled pseudopods [8] and degraded inside the cytosol in the absence of phagosomes [9]. However, although their isolation and recultivation from joint fluid has rarely been successful [10], *Borrelia burgdorferi* can be detected in the joint by a variety of methods, even after antibiotic treatment [11–14]. Thus, chronic Lyme arthritis might be due to a persistent infection.

To investigate a possible long-term persistence of *Borrelia burgdorferi* in the joint, we established an in vitro model for human Lyme arthritis using non-phagocytic resident joint cells. A long-lasting cytosolic persistence of viable *Borrelia burgdorferi* in human synovial cells was demonstrated in vitro. This might be a key mechanism for *Borrelia burgdorferi* to escape from phagocytosis and antibiotic treatment.

H. J. Girschick · H. I. Huppertz (✉)
Children's Hospital, University of Würzburg, Josef-Schneider-Str. 2,
D-97080 Würzburg, Germany
Fax: +49-931-201-2242; email: Huppertz@rzbox.uni-wuerzburg.de

H. Rüssmann¹ · H. Karch
Institute of Hygiene and Microbiology, University of Würzburg,
Würzburg, Germany

V. Krenn
Institute of Pathology, University of Würzburg, Würzburg, Germany

Present address:

¹ Department of Molecular Genetics and Microbiology, SUNY at
Stony Brook, New York, USA

Material and methods

Cells

Human synovial cells (SC) were prepared from normal human joint tissue by tryptic digestion [15], and maintained in culture and passaged as described [16]. Cells were characterized by indirect immunoperoxidase staining of cytospin preparations using the following monoclonal mouse antibodies diluted in 0.5% bovine albumin (see also Table 1): anti-HLA-B, Camibody at 1:100 (Bethesda Research Laboratories, Neu-Isenburg, Germany); anti-HLA-DR antibody at 1:2000 (Becton-Dickinson, Heidelberg, Germany); KI-M8 antibody