Immunocompetence of Schwann Cells

G. Meyer Zu Hörste, MD; W. Hu, MD; Hans-P. Hartung, MD; H. C. Lehmann, MD; B. C. Kieseier, MD

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2621 Superior Dr NW Rochester, MN 55901

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ABSTRACT: Schwann cells are the myelinating glial cells of the peripheral nervous system that support and ensheath axons with myelin to enable rapid saltatory signal propagation in the axon. Immunocompetence, however, has only recently been recognized as an important feature of Schwann cells. An autoimmune response against components of the peripheral nervous system triggers disabling inflammatory neuropathies in patients and corresponding animal models. The immune system participates in nerve damage and disease manifestation even in non-inflammatory hereditary neuropathies. A growing body of evidence suggests that Schwann cells may modulate local immune responses by recognizing and presenting antigens and may also influence and terminate nerve inflammation by secreting cytokines. This review summarizes current knowledge on the interaction of Schwann cells with the immune system, which is involved in diseases of the peripheral nervous system.

THE IMMUNOCOMPETENCE OF SCHWANN CELLS

GERD MEYER ZU HÖRSTE, MD, WEI HU, MD, HANS-PETER HARTUNG, MD, HELMAR C. LEHMANN, MD, and BERND C. KIESEIER, MD

Department of Neurology, Heinrich-Heine-University, Moorenstrasse 5, 40225 Düsseldorf, Germany

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Schwann cells myelinate and support axons of the peripheral nervous system (PNS) and they can become targets of a primary and secondary immune response. We review pathogenetic concepts and models of immune reactions in the PNS and elaborate on specific immune functions of Schwann cells in greater detail.

Human inflammatory neuropathies are caused by an immune response mounted against still incompletely characterized autoantigens within the PNS. The clinical picture ranges from Guillain–Barré syndrome (GBS) to chronic inflammatory demyelinating polyneuropathy (CIDP). Different subforms and distinct regional variants have been defined.

Depending on the primary target of the autoimmune reaction, acute inflammatory neuropathies are classified either as the most common acute inflammatory demyelinating polyneuropathy (AIDP) or as the less frequent acute motor (and sensory) axonal neuropathies (AMAN and AMSAN, respectively). Miller Fisher syndrome (MFS) denotes the acute regional variant involving predominantly cranial nerves. Multifocal motor neuropathy (MMN) is a multifocal variant of CIDP involving mainly motor fibers.

A consistent model of how these disorders develop has been established for certain subforms. Even under normal conditions, there may be autoreactive T lymphocytes recognizing peripheral nerve antigens in the systemic immune compartment, but their continuous suppression ensures self-tolerance. During a minor infectious disease these lymphocytes become activated upon encountering microbial epitopes. The hallmark finding that microbial epitopes can resemble endogenous peripheral nerve antigens has been termed “molecular mimicry.” Autoreactive T lymphocytes stimulate B cells to produce autoantibodies, which in turn can block nerve conduction, activate complement, and facilitate a macrophage attack in the peripheral nerve. Activated T cells transgress the blood–nerve barrier and provoke local inflammation by proinflammatory cytokines. Attracted macro...
phages act as antigen-presenting cells, release toxic mediators, and directly damage myelinating Schwann cells and axons. Long-term disability is mainly determined by the degree of axonal degeneration. The immune response may eventually be terminated by increased T-cell apoptosis, as demonstrated in animal models of inflammatory neuropathies.

PATHOMECHANISMS OF AUTOIMMUNE DISORDERS OF THE PNS

The pathological hallmark of the demyelinating subtypes of inflammatory neuropathies is the infiltration of the PNS by lymphocytes and macrophages, which results in multifocal demyelination, predominantly around blood vessels. Macrophages actively strip off myelin lamellae from axons, induce vesicular disruption of the myelin sheath, and phagocytose both intact and damaged myelin, as shown by electron microscopy. Macrophages, numerous as resident cells in the endoneurium, represent the predominant cell population in the inflamed PNS, and they reside in spinal roots as well as in more distal segments of the affected nerves.

Pathological studies suggest that the early invasion of the PNS by leukocytes is crucial in the pathogenesis of inflammatory demyelination. Circulating autoreactive T cells need to be activated in the periphery in order to cross the blood–nerve barrier and incite a local inflammatory response. Breakdown of the blood–nerve barrier is one of the earliest morphologically demonstrable events in lesion development in the animal model of demyelinating GBS.

It remains elusive how the cascade of autoimmune responses targeting PNS structures is ignited. One pathogenic mechanism of special relevance to autoimmune neuropathies is “molecular mimicry.” In a proportion of patients with GBS, epitopes shared between the enteropathogen Campylobacter jejuni, cytomegalovirus, or Haemophilus influenzae and nerve fibers have been identified as targets for aberrant cross-reactive B-cell responses. In a recent study, antibody responses to the ganglioside GM1 were linked to axonal and motor injury, as seen in one clinical variant of GBS and in an experimental model induced in rabbits by active immunization with this glycoconjugate. This provides a conclusive pathomechanism of axonal subtypes of GBS.

Despite long-term efforts, no such conclusive mechanistic models have been confirmed in the demyelinating GBS subtypes. Myelin protein–like structures have not been proven to exist in microbes. Antibodies against various components of the myelin sheath are found in only a fraction of demyelinating GBS patients and even in some healthy subjects. There may be several explanations for this observation. First, myelin components may not be the target of the immune response in demyelinating GBS. Second, antibodies against myelin components are important, but may not be the main orchestrators of the immune response in demyelinating GBS. A primarily cellular immune response may not be controlled sufficiently by screening for antibodies.

Thus, it is impossible to prove that an animal model of demyelinating GBS actually reflects human disease, because the definite immunopathogenetic mechanisms and target antigens of this disease in humans still have not been identified. From a pathological, electrophysiological, and clinical point of view, myelin-induced experimental autoimmune neuritis (EAN) is a good model of acute demyelinating GBS. Furthermore, plasma exchange and intravenous immunoglobulins, the clinical mainstays of human GBS therapy, are effective in myelin-induced EAN.

GBS should be defined as an organ-specific immune-mediated disorder emerging from a synergistic interaction of cell-mediated and humoral immune responses to still incompletely characterized peripheral nerve antigens. Schwann cells represent one of the major targets in immune-mediated disorders of the PNS.

ANIMAL MODELS OF INFLAMMATORY NEUROPATHIES

Many features of human inflammatory neuropathies are accurately recapitulated in EAN, an animal model of GBS that has greatly extended our knowledge of the underlying pathological mechanisms. Table 1 provides an overview of the available animal models. These models are explained in what follows.

A variety of antigens can induce immunological responses against peripheral nerves in different species, including rats, mice, rabbits, monkeys, and guinea pigs (Table 1). Immunization with Schwann-cell or myelin components generates demyelinating neuropathy models, whereas axonal components elicit axonal damage representing axonal GBS subtypes (Table 1). In the most widely used GBS model, Lewis rats are immunized with peripheral myelin homogenates, myelin proteins, or derived peptides to develop EAN (Table 1). Like entire myelin homogenates, the major myelin adhesion molecule P0, and the fatty acid–binding protein P2, and their immunogenic peptides, elicit marked im-
munological responses. Less severe forms of rat EAN are triggered by peripheral myelin protein of 22 kDa.\(^{28,59}\) Alternatively, transfer of stimulated T lymphocytes that are reactive toward various myelin antigens, including myelin proteins P2,\(^{98}\) P0,\(^{68}\) and derived peptides, evokes adoptive transfer EAN in host animals (Table 1). Adoptive transfer of lymphocytes that are reactive against myelin-associated glycoprotein (MAG) generates mild peripheral nerve inflammation.\(^{129}\)

Unlike rats, mice were generally thought not to be susceptible to immunization with peripheral myelin, but recent studies have challenged this view. Although myelin protein P2 induced only subclinical EAN in SJL mice, extended immunization protocols have allowed the induction of severe EAN by myelin homogenates in this strain (Table 1).\(^{14}\) Adoptive transfer EAN in BALB/c mice identified myelin basic protein (MBP) as an alternative neuritogenic antigen. The number of regulatory T cells differs between mouse strains,\(^{17}\) which might explain their differential autoimmune susceptibility, and a similar concept might be relevant for human autoimmune diseases.\(^{22}\) Generation of active EAN by two different P0 peptides, P0(180–199)\(^{137}\) and P0(106–125),\(^{81}\) together with pertussis toxin adjuvant in C57/B6 mice, has recently been reported. This protocol might enable the study of peripheral nerve inflammation in genetically modified animals, which are mostly generated on this background, allowing us to further extend our knowledge of inflammatory neuropathies.

The present data clearly highlight the fact that immunization with myelin components derived from Schwann cells as the cellular source can be used to induce an immune response against the PNS.

### Table 1. Animal models of inflammatory neuropathies.

<table>
<thead>
<tr>
<th>Animal model</th>
<th>Transfer</th>
<th>Possible antigens</th>
<th>Description</th>
<th>Reference nos.</th>
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<tr>
<td>Rat</td>
<td>Active</td>
<td>PNS myelin, P0, P2, P0(180–199), P2(53–78), P2(57–81)</td>
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<tr>
<td>Lewis</td>
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<td>CIDP-like chronic relapsing, not robust</td>
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<td>BN, SD, BUF, Wistar</td>
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</tr>
<tr>
<td>Dark Agouti</td>
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<td>PNS myelin</td>
<td>CIDP-like relapsing</td>
<td>46</td>
</tr>
<tr>
<td>Lewis</td>
<td>AT</td>
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<td>Rapid-onset EAN, CIDP-like relapsing if transferred repeatedly</td>
<td>76, 64</td>
</tr>
<tr>
<td>Mouse</td>
<td>C57/B6</td>
<td>Active P0(180–199), P0(106–125) + PTx</td>
<td>Varying effectiveness reported</td>
<td>81, 137</td>
</tr>
<tr>
<td>SJL</td>
<td>Active</td>
<td>P2</td>
<td>Mild course EAN</td>
<td>121, 14</td>
</tr>
<tr>
<td></td>
<td>Active</td>
<td>Myelin + PTx (+IL-12)</td>
<td>Severe course EAN</td>
<td>2</td>
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<tr>
<td>BALB/c</td>
<td>AT</td>
<td>MBP</td>
<td>Peripheral and central demyelination</td>
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<td>B7-2 (^{+})</td>
<td>Spontaneous</td>
<td>—</td>
<td>Spontaneous autoimmune neuropathy</td>
<td>CIDP-like</td>
</tr>
<tr>
<td>Rabbit</td>
<td>Rabbit</td>
<td>Active PNS myelin, P2 galactocerebroside</td>
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<tr>
<td>Rabbit (axonal)</td>
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<td>Acute motor axonal neuropathy</td>
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<tr>
<td>Other</td>
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<td>Active PNS myelin</td>
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<tr>
<td></td>
<td>Monkey</td>
<td>Active PNS myelin, P2</td>
<td>Spontaneous autoimmune neuropathy</td>
<td>109</td>
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</tbody>
</table>

PNS, peripheral nervous system; EAN, experimental autoimmune neuritis; CIDP, chronic inflammatory neuropathy; P0, myelin protein zero; P2, myelin protein 2; PMP22, peripheral myelin protein of 22 kDa; BN, Brown–Norway rats; SD, Sprague–Dawley rats; BUF, Buffalo rats; MAG, myelin-associated glycoprotein; MBP, myelin basic protein; PTx, pertussis toxin; AT, adoptive transfer.

### SECONDARY IMMUNE REACTIONS IN NON-INFLAMMATORY HEREDITARY NEUROPATHIES

Even hereditary disorders of the peripheral nervous system trigger immune responses in the peripheral nerve. These responses have been suggested to be an important determinant of disease manifestation.

Charcot–Marie–Tooth (CMT) disease, clinically termed hereditary motor and sensory neuropathy (HMSN), is the most common inherited peripheral neuropathy. Animal models of many subtypes of...
CMT have been generated and have vastly extended our knowledge of the underlying disease mechanisms. In the more frequent demyelinating CMT forms, a genetic defect results in progressive destruction of myelin sheaths and secondary axonal loss. One may easily conceive that such genetically determined defects of myelination can trigger a secondary immune response. Indeed, infiltration of lymphocytes and macrophages has been demonstrated in peripheral nerves of some human CMT patients, and corresponding animal models.

Apart from this secondary immune response, however, a series of experimental studies have suggested immune cells as a primary cause for disease manifestation in genetically determined neuropathies. Mouse models of CMT subtypes CMT1B and CMTX were crossbred with mouse strains lacking functional T lymphocytes or with impaired macrophage function. Surprisingly, immune deficiency ameliorated mild, chronic demyelination in these models of inherited neuropathies. Impairment of immune function was achieved by abolishing functional T lymphocytes in mouse strains carrying null mutations of the recombination activating gene-1 (Rag-1) or the T-cell-receptor α-subunit gene.

Macrophage function was impeded in mice lacking functional genes of macrophage colony stimulating factor and adhesion protein sialoadhesin preferentially expressed in macrophages. Demyelination in the Rag-1-deficient CMT1B model could be reconstituted by transfer of wild-type bone marrow, which excludes Schwann-cell intrinsic effects of Rag-1 deficiency.

This effect, however, has not been shown in the most common CMT subtype, 1A, and, in contrast to its effect on mild demyelination, immune deficiency was found to aggravate early-onset severe dysmyelination. Furthermore, myelinating cell cultures generated from a CMT1A animal model develop defects of myelination despite the obvious absence of immune cells in such a model. The efficacy of an anti-inflammatory treatment in CMT remains controversial.

One possible explanation for the increased immune reaction in the CMT1B animal model may be reduced intrathymic induction of tolerance. A heterozygous knockout of the myelin protein zero (P0) gene determines this CMT subtype and this reduction in gene dose was demonstrated to increase T-cell reactivity to a P0 peptide. Genetically determined P0 deficiency in mice abolishes tolerance and causes the P0 protein to be recognized as a foreign antigen, which further supports autoimmune mechanisms in hereditary neuropathies.

Finally, we have learned that macrophages and lymphocytes are required for myelin loss in models of at least certain forms of hereditary neuropathies. This raises the question of how immune cells “sense” the defectiveness of the myelin sheath and why they participate in its gradual destruction. Increased immunogenity due to altered protein composition or mechanical instability of the myelin sheath has been suggested. Molecules required for antigen presentation could communicate this information from Schwann cells to immune cells and one may speculate that a myelin protein mutant Schwann cell would not demyelinate if it lacked the molecules required for antigen processing and presentation.

We have described the intimate interaction between myelinating Schwann cells and immune cells and its importance for various peripheral nerve disorders. In what follows, we specifically elaborate on the expanding recognition of Schwann cells as immunocompetent cells that form part of the local immune circuitry within the peripheral nerve. The present data suggest that the entire spectrum of an immune response can be displayed by Schwann cells, which includes recognition of antigens; presentation of antigens; mounting of an immune response; and, finally, terminating the immune response within the inflamed peripheral nerve (Fig. 1).

**ANTIGEN RECOGNITION BY SCHWANN CELLS**

Two types of responses to invading organisms can take place in the mammalian immune system: an acute response launched within hours and a delayed response occurring within days. The immediately responding system is called the innate immune system, and it evolves stereotypically and at the same intensity regardless of how often the infectious agent is encountered. The strategy of the innate immune response is not to recognize every possible antigen, but rather to focus on a few highly conserved structures present in large groups of microorganisms. These structures are referred to as pathogen-associated molecular patterns, and the corresponding receptors of the innate immune system are called pattern-recognition receptors. Examples of pathogen-associated molecular patterns are bacterial lipopolysaccharide (LPS), peptidoglycan, and bacterial DNA. Although chemically quite distinct, these molecules display common features, They are only produced by microbial pathogens and not by their host. They generally represent invariant structures shared by large classes of pathogens, and they are usually relevant for the survival or pathogenicity of microorganisms.
The family of toll-like receptors (TLRs) belongs to the group of pattern-recognition receptors that recognize specific conserved components of microbes, such as LPS, and that have been implicated to play a critical role in various inflammatory disorders. To date, 11 TLRs have been identified in humans and 7 in rats. LPS, a major component of the outer membrane of gram-negative bacteria, which appears to be a relevant antigen triggering immune-mediated demyelination of the PNS, is recognized by TLR-4.

TLRs are usually found on antigen-presenting cells, such as dendritic cells. TLR-2 has been shown to be expressed constitutively on primary human and rat Schwann cells and has been invoked as a target receptor for Mycobacterium leprae. Under inflammatory conditions, expression of various TLRs, especially TLR-4, is inducible on rat Schwann cells in vitro. Selective stimulation of TLR-4 on Schwann cells with LPS has been shown to elicit the production of various inflammatory mediators such as chemokines, protease inhibitors, and growth factors. Thus, in aggregate, these findings suggest that Schwann cells can detect LPS fragments and may act as a link between innate and acquired immunity via TLR-4 activation in the inflamed PNS. Recent studies have also revealed that inflammatory Schwann-cell activation can be induced via TLR-2 and TLR-3.

**SCHWANN CELLS AS FACULTATIVE ANTIGEN-PRESENTING CELLS**

The task of displaying the antigens of cell-associated microbes for recognition by T lymphocytes is performed by specific molecules that are encoded by genes comprising the major histocompatibility complex (MHC). The physiological function of MHC molecules is the presentation of peptides to T cells.
Two types of MHC gene products can be distinguished, class I MHC molecules and class II MHC molecules, which differ functionally. Each MHC molecule consists of an extracellular peptide-binding cleft or groove and a pair of immunoglobulin-like domains, containing binding sites for the T-cell surface markers CD4 and CD8. By transmembrane domains, MHC molecules are anchored to the cell surface. MHC molecules exhibit a broad specificity for peptide binding, whereas the fine specificity of antigen recognition resides mostly in the T-cell receptor. In general, endogenous cytotoxic peptides are presented via MHC class I molecules to CD8+ T cells, whereas mainly exogenously derived peptides generated in vesicles are bound to MHC class II molecules and recognized by CD4+ T lymphocytes. The two classes of MHC molecules are expressed differentially on cells. All nucleated cells exhibit MHC class I molecules, although hematopoietic cells express them at the highest densities. MHC class II molecules, in contrast, are normally only expressed on professional antigen-presenting cells, such as macrophages, dendritic cells, and B lymphocytes. The levels of both class I and II molecules can be markedly upregulated by cytokines, particularly interferon-γ and tumor necrosis factor (TNF)-α. Macrophages are the predominant professional antigen-presenting cells in EAN. These macrophages in EAN shift from resident endoneurial in the early disease stages to a hematopoietic origin in later stages.

Apart from such professional antigen-presenting cells, other cell types may acquire the ability to process and present antigens in inflammatory conditions, thus representing facultative antigen-presenting cells. Human and rat Schwann cells in vitro constitutively express low levels of MHC class I but not MHC class II. Significant numbers of MHC class II molecules can be detected on Schwann cells in the presence of activated T lymphocytes upon stimulation with the proinflammatory cytokine interferon-γ, which can be synergistically increased by the addition of TNF-α. Moreover, a number of molecules that are prominent in the intracellular processing cascade of peptides prone to MHC presentation can be visualized in Schwann cells in vitro and in vivo (Meyer zu Hörste and Kieseier, unpublished observations). In human nerve biopsies from patients with GBS and its chronic variant CIDP, Schwann cells stained positive for MHC class II, suggesting that these cells may indeed act as facultative antigen-presenting cells in immune-mediated disorders of the PNS. Antigen-presenting cells are characterized by their ability to phagocytose exogenous antigen and its degradation to antigenic peptides, which can be expressed in the cleft of the MHC molecule. Schwann cells in vitro have been shown to present foreign and exogenous antigens, such as MBP, to antigen-specific syngeneic T-cell lines. Moreover, the presentation of endogenous antigen, such as the myelin component P2, by Schwann cells via MHC class II can restimulate resting antigen-specific CD4+ T-cell lines.

Non-endogenous antigen can also be presented by Schwann cells, which may be of special relevance in leprosy. On a global scale, leprosy is one of the major causes of peripheral neuropathy, with sensory loss being its foremost symptom. Neuropathy in leprosy mainly affects pain and temperature sensation from small cutaneous nerves, resulting in painless injury and mutilation. The causal agent of the disease, Mycobacterium leprae, shows a remarkable preference for invading and proliferating in non-mylinating Schwann cells. Schwann cells present M. leprae-derived antigens to lymphocytes in an MHC II-dependent manner, whereas CD8+ lymphocytes lyse M. leprae-infected Schwann cells in vitro. A different study showed M. leprae-derived antigen presentation by Schwann cells to CD4+ lymphocytes. This MHC II-mediated interaction resulted in Schwann-cell destruction. Thus, apart from other mechanisms described, antigen presentation by Schwann cells evolves as an important mechanism of nerve damage in this infectious neuropathy.

For optimal T-cell activation and differentiation to occur, at least two distinct signals delivered during the interaction with an antigen-presenting cell are required. These include antigen-specific signaling via MHC and signaling through costimulatory molecules. If the T cell does not receive adequate costimulation, it is rendered anergic or undergoes apoptosis. Thus, the costimulation signal is central to T-cell activation and survival. Recent data suggest that BB-1, a member of the family of costimulatory molecules, can be detected on non-mylinating Schwann cells and appears to be upregulated on myelinating Schwann cells in nerve biopsies from CIDP patients. This further indicates that Schwann cells possess the cellular components required to act as facultative antigen-presenting cells in the inflamed PNS.
cells actively control the local T-cell response within the peripheral nerve by acting as facultative antigen-presenting cells.

**SCHWANN CELLS AS REGULATORS OF AN AUTOIMMUNE RESPONSE**

For a long time, cytokines, as mediators of an immune response within the peripheral nerve, were considered to be the exclusive product of inflammatory cells. Nowadays, there is a large body of evidence implying that Schwann cells can produce and secrete a wide variety of cytokines, which could act as immunomodulators. Interleukin (IL)-1, a cytokine relevant in the initiation of an immune response, can be produced by cultured Schwann cells. Other proinflammatory cytokines, such as IL-6, TNF-α, TNF-β, and transforming growth factor-β, are generated and released by Schwann cells. Schwann cells are able to regulate the production of proinflammatory cytokines, at least in part, in a specific autocrine manner, as shown for IL-1. The specific receptors for some of the cytokines, such as TNF receptor, are constitutively expressed on Schwann cells, rendering these cells susceptible to, for example, a TNF-α response. Other proinflammatory and immunoregulatory mediators, such as prostaglandin E2, thromboxane A2, and leukotriene C4, are synthesized in large amounts by Schwann cells, and may regulate the immune cascade within the inflamed PNS. Schwann cells include osteopontin, which is constitutively expressed and can be easily induced in Schwann cells, as well as glial cell line–derived neurotrophic factor, a known survival factor for neurons, and glial cell line–derived neurotrophic factor family receptor α-1, displayed on the surface of Schwann cells.

Nuclear transcription factor-κB (NF-κB) plays a pivotal role in the regulation of the host innate antimicrobial response. It governs the expression of many immunological mediators, including cytokines, their receptors, and components of their signal transduction. Recent studies have suggested that two NF-κB complexes, p65/p50 and p50/p50, can be activated and regulated in human Schwann cells under certain conditions. Interestingly, the natural inhibitor of NF-κB, IκB, can be detected in large amounts in Schwann cells. These observations further point to an active rather than a passive role for Schwann cells in the inflamed PNS. Apart from engaging such cellular factors, Schwann cells can modulate local immune reactivity by humoral mechanisms. One pathway may operate through the production and release of nitric oxide (NO), a multipotential mediator with neurotoxic and immunosuppressive properties. Schwann cells are endowed with inducible nitrite oxide synthase, which is up-regulated after the stimulation with proinflammatory cytokines.

Taken together, a large number of pro- and anti-inflammatory mediators can be induced and released by Schwann cells. The extent to which these mediators have a significant impact on the clinical course of an immune-mediated disorder in the PNS clearly warrants further investigation.

In animal models of inflammatory diseases of the central nervous system, neurotrophic cytokines and neurotrophins have been suggested as important regulators of axonal degeneration and of resulting clinical impairment. Most interestingly, brain-derived neurotrophic factor (BDNF), originating from inflammatory cells, has been demonstrated to mediate neuroprotective effects, which emphasizes the concept of neuroprotective autoimmunity. Few studies, however, support a comparable concept in inflammatory diseases of the peripheral nervous system. Except for reduced urinary bladder weight as a possible indirect sign of reduced autonomic dysregulation, BDNF treatment did not significantly influence clinical disease manifestation in rat EAN.

**SCHWANN CELLS AS TERMINATORS OF THE AUTOIMMUNE RESPONSE**

In order to control the massive expansion of cellular and soluble immune mediators within the target tissue, certain mechanisms must operate with high fidelity to regulate the immune response. Once the target antigen has been eliminated or infection abated, the activated effector cells are no longer needed. When the antigenic stimulus is no longer present, the cells will succumb to programmed cell death or apoptosis.

The survival of lymphocytes depends on a delicate balance between death-promoting and death-inhibiting factors. Various mechanisms can induce apoptosis. It can, for example, be affected through the interaction of the cell surface receptor Fas on T cells with its ligand, FasL, a member of the TNF family. Schwann cells reveal surface expression of FasL after stimulation with proinflammatory cytokines in vitro. Functional analysis indicates that the interaction between Fas on T cells and FasL on Schwann cells promotes apoptosis of T lymphocytes. This raises the possibility that Schwann cells are...
important in terminating the immune response in the inflamed PNS.132

SCHWANN CELLS AS IMMUNOCOMPETENT CELLS

In summary, our current knowledge of the potential immunocompetence of Schwann cells suggests that these cells can induce an immune response within the peripheral nerve via pattern-recognition receptors, but can also trigger a T-cell response via the presentation of antigen fragments on MHC class II molecules in the context of costimulatory molecules. Through the release of immunomodulators, Schwann cells could regulate the immune reaction in situ and, by inducing apoptosis, appear even to terminate an ongoing immune response. This evidence collected in recent years indicates that the many functions of Schwann cells go far beyond forming the myelin sheath.

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