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ANNUAL REPORT 2008

It is a pleasure to present the 2008 annual report from the Danish Multiple Sclerosis Research Center (DMSC), Department of Neurology, The Neuroscience Center, Copenhagen University Hospital Rigshospitalet.
We have tried to give a short review of the clinical and research activities in DMSC during 2008. We hope that you will take pleasure in reading the annual report.

Morten Blinkenberg
Per Soelberg Sørensen,
Editors

A SHORT REVIEW OF 2008 IN THE DANISH MULTIPLE SCLEROSIS RESEARCH CENTER

Per Soelberg Sørensen
Professor
Director DMSC

The year 2008 brought along expansion in the Danish Multiple Sclerosis Research Center (DMSC) both of clinical activities and research. Currently the MS Clinic is providing care for more than 1700 patients, mainly from the capital region but also from all other parts of Zealand. The main reason for the continuing expansion of the activities in the MS Clinic has been the successful introduction of the new treatment natalizumab (Tysabri) that currently is the most effective treatment for relapsing-remitting MS.
The National Board of Health in Denmark has defined treatment with natalizumab (Tysabri) as a developing therapeutic activity and currently the treatment is offered at the 4 university hospitals: Copenhagen University Hospital; Odense University Hospital, Århus University Hospital and Aalborg University Hospital.
Approximately 250 patients are receiving treatment with natalizumab (Tysabri) every month at the MS Clinic, which has made heavy demands on the staff and the spatial planning in the MS Clinic.
In 2008 the Danish National Board of Health decided that a number of highly specialized tasks in treatment of MS should be concentrated at DMSC, Rigshospitalet. These tasks include treatment with strong immunosuppression (mitoxantrone and treosulphane) and treatment of severe spasticity with intrathecal Baclofen pumps. Further, it has been decided that treatment of children and adolescent patients with MS below the age of 18 in eastern Denmark should be treated at DMSC in close collaboration with the Neuropediatric Clinic at Rigshospitalet. Also the rare variants of MS, neuromyelitis optica (NMO) and acute disseminated encephalomyelitis in eastern Denmark should be referred to the DMSC.

The research activities can be grouped into 2 major fields: 1) Clinical research including neuroimaging and 2) neurogenetics, neuroimmunology and neuropathology.
The clinical research includes the search for and tests of new treatment for MS. DMSC has initiated and conducted a number of both single-center and multi-center clinical trials, and have participated in a large number of trials conducted by pharmaceutical companies. Neurogenetics, immunogenetics and neuroimmunology research are now interwined, and this major area has been the other big field of research for DMSC in 2008. We have been involved in the search for new genes conferring susceptibility to MS; we have looked into the immune system pathophysiology in MS and have been taking part in the search for biomarkers of disease activity and therapeutic response in blood and cerebrospinal fluid. DMSC has also contributed to new discoveries in the pathology of MS.

The research activities in the MS Research Unit and Neuroimmunology Laboratory have increased and the premises have been expanded. The main laboratory is still located in the Michaelsen Building 63, but in addition we have acquired a laboratory for cellular immunology research and flow cytometry in the basement of Building 93 where also samples belonging to our expanding Biobank are stored.

FACILITIES, ORGANIZATION AND STAFF

The MS Clinic is located within the Department of Neurology on the 8th floor of the main complex of Rigshospitalet at sections N2082 and N2084. The MS Clinic comprises a secretariat, offices for the professor and consultants, nurse's offices, three consultation rooms and a room for intravenous infusions, and a procedure room for invasive procedures.
The MS Research Unit and the Neuroimmunology Laboratory is located at the first floor in the Michaelsen Building 63, and recently DMSC has acquired a laboratory in the basement of Building 93, room 713. The facilities contain offices for the research staff and the Neuroimmunology Laboratory.

In 2008 the staff of DMSC consisted of:

***Director of DMSC**:*
Professor Per Soelberg Sørensen, MD, DMSc

***Senior physicians**:*
Morten Blinkenberg, MD, PhD, consultant
Annette Oturai, MD, PhD, consultant
Finn Sellebjerg, MD, DMSc, associate professor
Ana Voldsgaard, MD, staff specialist
Lars Pinborg, MD, DMSc, staff specialist

Neuropsychologist:
Chief neuropsychologist Agnete Jønsson

MS-nurses:
Anne Hansen, leading nurse
Merete Mogensen
Sidsel Walther Nielsen
Annette Husted Pedersen
Dorthe Stauning Rasmussen
Lene Almind

Research nurses:
Vibeke Jespersen
Joan Pietraszek

Physiotherapist:
Lis Albrechtsen

Medical social counselor:
Keld Nissen

Secretaries:
Malene Møllesøe
Maria Loizou Brændbjerg
Annette Larsen (scientific secretary)

PhD-students:
Dan Hesse
Stephan Bramow
Lars Börnsen
Jeppe Romme Christensen

Senior research fellows:
Poul Erik Hyldgaard Jensen, PhD, MSc (laboratory leader)
Helle Bach Søndergaard, PhD, MS (molecular biologist)

Junior research fellows:
Signe Limborg, MS (B. pharm.)
Marianne Ammitzbøll (pharmacy student)
Jan Christophersen (pharmacy student)

Laboratory technicians:
Joy Mendel-Hartvig (leading laboratory technician)
Marie Koefoed
Michael Kolbjørn Jensen
Anne Mette Hedegaard Nielsen

RESEARCH ACTIVITIES 2008

CLINICAL RESEARCH

Searching for new MS therapies
By Per Soelberg Sørensen

Clinical research group:
Per Soelberg Sørensen, Morten Blinkenberg, Finn Sellebjerg, Annette Oturai, Ana Voldsgaard, Lars Pinborg, Dan Hesse, Stephan Bramow, Lars Börnsen, Jeppe Romme Christensen, Vibeke Jespersen, Joan Pietraszek, Anne Hansen, Annette Larsen

Therapeutic trials
Two major clinical trials initiated and directed from DMSC were completed in 2008. The NORMIMS trial (principal investigator: Per Soelberg Sørensen) was a Scandinavian multi-center double-blind randomized placebo-controlled trial of five day monthly therapy with methylprednisolone tablets as add-on treatment to interferon-beta 1a subcutanously in relapsing-remitting MS patients, who have suffered a relapse during the last year on treatment with interferon-beta. Add-on therapy with methylprednisolone gave an impressive 62% reduction in the annualized relapse rate compared to add-on of placebo. Also the T2 lesion load was significantly lower in the methylprednisolone group, and other clinical and MRI outcomes showed strong trends towards the beneficial effect of methylprednisolone.
The MECOMBIN trial (principal investigator: Mads Ravnborg) was a multicenter double-blind randomized placebo-controlled trial of 3-day monthly therapy with methylprednisolone as add-on to treatment with interferon-beta 1a intramuscularly in relapsing-remitting MS. This large trial of more than 300 patients, who had never received interferon-beta before, did not meet the primary endpoint and only showed a strong trend towards a lower accumulation of permanent disability in patients treated with methylprednisolone. However, also the MECOMBIN trial showed a statistical significant reduction of 38% in the annual relapse rate in the methylprednisolone treated group. Also in this group many secondary endpoints showed a strong trend towards a beneficial effect of methylprednisolone.
Two other large combination trials have been initiated and directed from DMSC.
The SIMCOMBIN study (principal investigator: Per Soelberg Sørensen) is multi-center double-blind randomized placebo controlled trial of Simvastatin as add on treatment to interferon-beta

1a intramuscularly in de novo treated patients with relapsing-remitting MS. More than 300 patients have been included in the trial that will be completed in the spring 2010.
The RECYCLINE trial (principal investigator: Per Soelberg Sørensen) is a multi-center double-blind randomized placebo-controlled trial of Minocycline as add-on therapy to interferon-beta 1a subcutanously as de novo therapy for relapsing-remitting MS performed in the Nordic countries, France and Switzerland. Inclusion of the 320 planned patients will be terminated in August 2008, and the results will be available in late 2011.
Currently two single–center studies are planned and will start patient recruitment in 2009: One study will analyze the effect of erytropoietin (EPO) in patients with progressive forms of MS.
A placebo-controlled trial in relapsing-remitting MS will assess the beneficial effect of treatment with the eggs of the pig whipworm (Trichuris suis). In preliminary trials this treatment has shown beneficial effect in inflammatory bowel diseases and have been shown to safe in MS patients.

Neutralizing antibodies against biological therapies (interferon-β and natalizumab)
As a part of the Danish nationwide Interferon-beta Project all patients treated with interferon-beta have measurements of neutralizing antibodies (NAbs) against interferon-beta performed routinely. In a large series of published articles we have shown that NAbs abolish the in-vivo activity of interferon-beta, and decrease the therapeutic effect. We have published a study showing that neutralizing antibodies against interferon-beta may persist several years after discontinuation of interferon-beta therapy, and that it is impossible to remove NAbs when they have occurred, neither with monthly methylprednisolone treatment nor with the combination of methylprednisolone and azathioprine.
We have also shown that despite continuous interferon-beta therapy after some years NAbs may disappear, and in those patients the therapeutic effect of interferon-beta is restored.
Within the EU's Framework 6 Program DMSC has been one of five core centers in the NABINMS study (Neutralizing AntiBody of interferon-beta IN Multiple Sclerosis). At DMSC we have been responsible for a collaborative study in 4 centers of the correlation between NAbs and response to interferon-beta using prospectively collected data from population base cohorts from Denmark, Spain, The Netherlands and The Czech Republic. The study will run through 2009.
In the context of the NABINMS project we recently have concluded a study with Affymetrix gene chips showing that NAb positive patients, in whom the interferon-beta inducible molecule MxA could not be induced by interferon-beta, none of the more than 1000 genes that were calling in NAb negative patient after an interferon-beta injection were induced in NAb positive patients. The study clearly demonstrated that all interferon-beta bioactivity was exterminated in NAb positive patient without an in vivo MxA mRNA response after an interferon-beta injection.

NEUROIMMUNOLOGY

Studies of immune activation and MS therapy
By Finn Sellebjerg

Immunology group:

Finn Sellebjerg, Poul Erik H. Jensen, Helle Bach Søndergaard, Signe Limborg, Dan Hesse, Per Soelberg Sørensen, Joy Mendel-Hartvig, Marie Koefoed

In the past decade there has been considerable debate about the role of inflammation in the pathogenesis of MS. There is clear evidence that immunological processes are important in the relapsing-remitting phase of MS. The later, secondary progressive stage has, however, been considered to depend less on immunological processes and more on neurodegeneration due to previous, immune-mediated insults to the CNS. Furthermore, some have considered primary progressive MS to be a mainly degenerative disease with little evidence of a role of the immune system.

The view on the role of the immune system in MS is, however, rapidly changing. Clinical trials using monoclonal antibodies specifically targeting different immune cells or immune processes have strongly confirmed the notion that immunoinflammatory processes are important in the pathogenesis of relapsing-remitting MS. Furthermore, recent studies indicate that even in progressive MS patients, axonal degeneration is closely linked with ongoing inflammation. Nevertheless, progressive MS patients are less likely to respond to immunomodulatory and immunosuppressive treatment.

In relapsing-remitting MS the immune system is in a state of chronic activation. This activation can be detected even in patients who appear to be in clinical remission. The abnormal immune activation can be detected both in the T cells that are commonly assumed to be critical in the pathogenesis of MS and in other cell types, e.g. antigen-presenting cells such as dendritic cells and monocytes (J.R. Christensen, work in progress). B cells are also critically involved in the pathogenesis of MS, and treatment with B cell-depleting antibodies reduces disease activity in relapsing-remitting MS.

Recently completed studies from our laboratory using a combination of DNA array studies for large-scale mRNA analysis and real-time polymerase reaction (PCR) studies of selected cytokines and transcription factors have confirmed the generalized immune activation status of MS patients, and shown that this is associated with increased expression of molecules associated with T cell memory (F. Sellebjerg et al., manuscript in preparation). In untreated MS patients there is evidence of a protective effect of interleukin-10 induced by endogenous interferon-β; intriguingly interleukin-10 is also strongly induced by treatment with interleukin-10, and interleukin-10 expression can predict the response to treatment with interferon-β (D. Hesse et al., manuscripts in preparation). Ongoing studies are identifying the cellular source of different cytokines in subsets of blood cells from untreated MS patients and during immunomodulatory treatment.

We have collaborated with Chris Hedegaard and Claus Nielsen at the Institute for Inflammation Research at Copenhagen University Hospital, Rigshospitalet in studies of antigen-specific T cells from MS patients. These studies have shown increased activation of T cells reactive with the autoantigen myelin basic protein and increased production of proinflammatory cytokines, especially interleukin-17, in MS patients with disease activity (Hedegaard et al., 2008). We are currently using flow cytometry to study the cytokine production of antigen-specific T cells from MS patients (Figure 1) These studies, combined with studies of antigen-presenting cell activation, will provide further insight into how autoreactive T cells are involved in the pathogenesis of relapsing-remitting MS, and how they are affected by immunomodulatory treatment (L. Börnsen et al. and M. Nielsen et al., work in progress).

In chronic progressive MS systemic and intrathecal immune activation can be readily demonstrated, and the concentrations of a B cell chemoattracting molecule (CXL13) and a cytokine-like factor (osteopontin) are increased in cerebrospinal fluid both in relapsing-remitting and progressive MS patients (Sellebjerg et al., submitted and Börnsen et al., manuscript in preparation). The systemic immune activation in progressive MS is, however, different from what is observed in relapsing-remitting disease, and inflammation in progressive MS patients tends to be compartmentalized within the CNS. It is likely that the differences in immune activation and compartmentalization both contribute to the relative failure of current treatments for the primary and secondary progressive MS. Accordingly, treatments that interfere with systemic immune activation may be sufficient for the treatment of relapsing-remitting MS, where disease activity is initiated by systemic activation of pathogenic immune cells that have to migrate across the blood-brain barrier in order to enter the CNS and initiate

new lesions. In contrast, immune activation in progressive MS is much more profound throughout the CNS. This may be the result of the accumulation of activated immune cells during the disease course, and indicates that an effective treatment of progressive MS should also be effective at treating the intrathecal immune activation.
From 2008-2010 the Danish Multiple Sclerosis Society supports a focused effort aiming at understanding the pathogenesis of progressive MS and developing new treatments for progressive MS. As part of this effort, ongoing research projects at the DMSC aim at understanding basic pathogenic mechanisms in T cell activation, antigen presenting cell and regulatory T cell activation in progressive MS and how this is influenced by different experimental treatment regimens.
The patient samples for our studies are obtained from our MS clinic and from collaborations with other Danish MS Clinics. This is supported by a grant from the Danish Strategic Research Council to the project "Optimised Treatment and Monitoring of Multiple Sclerosis". This project aims at developing biomarkers that can identify MS patients more likely to respond to different immunomodulatory treatment and at developing new strategies for both the relapsing-remitting and the progressive phase of the disease. This is partly done in collaboration with other researchers, especially Claus Nielsen and coworkers at Institute for Inflammation Research at our institution and professor Tomas Olsson and coworkers at the Neuroimmunology Unit, Center for Molecular Medicine at Karolinska Hospital in Sweden).

Figure 1. Flow cytometry allows the study of many different parameters on single cells. The picture shows our eight-color flow cytometer and staff from our Neuroimmunology Laboratory. The application of flow cytometry with reagents labelled with up to eight different fluorochromes allows us to analyse the cytokine production of single, antigen-specific T cells, the activation state of individual circulating cells, or the effects on subsets of cells of different pharmacological agents ex vivo.

NEUROGENETICS

Identification of genes involved in Multiple Sclerosis
By Annette Oturai

Neurogenetics group:
Annette Oturai, Helle Bach Søndergaard, Finn Sellebjerg, Per Soelberg Sørensen
Laboratory technician: Anne Mette Hedegaard Nielsen

Genetic factors are important in the etiology of multiple sclerosis (MS). In family studies the concordance rate for monozygotic twins is 30%, for dizygotic twins 5% and for siblings 3,5%. When both parents are affected 7% of the children will develop MS. Identifying the involved genes is a complex challenge, because no single Medelian locus causes MS. Through decades scientists have worked to find gene variations tied to MS. Genome linkage screens have failed finding major genes except genes of the HLA-complex, where linkage to DR2 (HLADRB1*15) is strongest in Northern Europeans. The genetic influence in MS seems most likely to be caused by interaction of a limited number of susceptibility genes. A break-through took place in the summer 2007, when three new studies showed that the IL7R (receptor) and IL2R (receptor) genes are important risk genes of MS. Both genes are important for the T cell regulation, and thus the immune system. In all, the three studies included more than 14,000 people and constitutet the first replicated associations to MS apart from the HLA-DR2 association found back in 1973. The Wellcome Trust Case Control Consortium is presently investigating the largest set of MS cases and controls by more than 600.000 SNPs chips, the results are expected later this year. We are taking part in this large international genetic collaboration through our membership of the IMSGC (International Multiple Sclerosis Genetic Consortium).
For more than 13 years the MS Genetic Group at Rigshospitalet have collected DNA, and today we have DNA from more than 1000 Danish MS patients and 1200 controls; all kept in the "Danish Multiple Sclerosis Biobank" located at our department at Rigshospitalet. In order to increase the sample size for genetic testing we have participated in the "Nordic MS Genetic Group" since 1994, and today the Nordic material consists of 4000 MS cases and 4000 controls. Local research is focused on the candidate gene approaches and their biological effects especially the genetic influence on the differences in treatment response.

NEUROPATHOLOGY

Defining remyelination properties in progressive MS
By Per Soelberg Sorensen

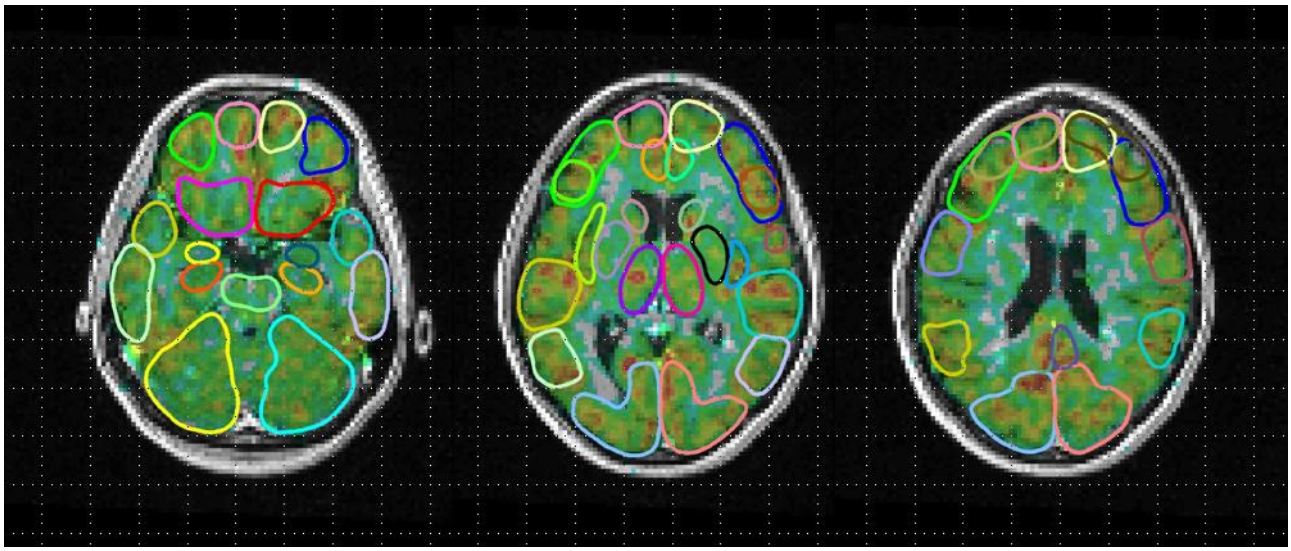
Neuropathology group:
Stephan Bramow, Per Soelberg Sørensen (Henning Laursen, Laboratory of Neuroimmunology)

In close collaboration with Dr. Henning Laursen, Laboratory of Neuropathology, Rigshospitalet and Hans Lassmann, Director of Institute for Brain Research in Vienna we have studied demyelination and remyelination properties in MS. We have shown that in a subset of patients extensive remyelination was found, not only in patients with relapsing-remitting MS but also in a subset of patients with progressive disease. We have studied biopsies from brain and spinal cord to characterize the dynamic evolution of inflammation and remyelinationin areas of active plaques, slowly expanding plaques and areas of remyelination. We have also shown that there is a close association between ongoing inflammation and neurodegeneration indicating that in patients in whom inflammation subsides there is no sign of ongoing acute axonal damage.

NEUROIMAGING
By Morten Blinkenberg

Neuroimaging group:
Morten Blinkenberg, Henrik Mathiesen, Per Soelberg Sørensen

PET
During the last decades, functional imaging has improved our understanding of the neurodegenerative processes in MS.
Former positron emission tomography (PET) studies, carried out in Danish Multiple Sclerosis Research Center, have shown that cerebral activation in MS patients, is severely reduced as a consequence of disease progression. We have also shown that several regions of importance for cognitive function is affected by MS, and that these changes correlate with neuropsychological measures, as well as MRI lesion burden.
Our current PET studies focuses on the early relapsing remitting phase of the disease and the corresponding changes in cerebral activation. Our hypothesis is, that changes in cerebral activation is present in very early disease, and affect neural networks of importance for cognitive function. We are currently analyzing data from a cross-sectional study, and a subgroup of these patients has also been followed prospectively, and awaits further analysis.



MRI

In collaboration with Danish Research Center for Magnetic Resonance we have initiated two functional imaging studies in 2007.

We have previously shown that measurements of MR Spectroscopy (MRS) correlate with cognitive dysfunction in MS. This cohort has now been re-evaluated and analyzed for longitudinal changes in MRS and cognitive function.

Another study focuses on the pathophysiological mechanisms underlying changes in cerebral activation in MS patients.

There is increasing evidence that the severity of the clinical manifestations of MS does not result simply from the extent of tissue destruction, rather it represents a complex balance between tissue damage, tissue repair and cortical reorganization.

Functional MRI (fMRI) provides information regarding the extent and nature of brain plasticity following MS-related structural injury, with the potential to limit the clinical manifestations of the disease. Functional connectivity MRI (fcMRI) is a new method of assessing neuronal connectivity in the human brain, by mapping brain regions with synchronous, regional fluctuations in cerebral blood oxygenation. fcMRI in combination with fMRI, may therefore detect functional alterations, that lead to neurological disability in MS.

Using this approach, we describe MRI changes in cerebral activation and neural connectivity during an acute MS relapse and following treatment with i.v. methylprednisolone. Furthermore, we describe functional activation and connectivity in a cross-sectional selection of MS patients with different stages of disease.

ROUTINE ANALYSES IN NEUROIMMUNOLOGY LABORATORY

By Poul Erik Hyldgaard Jensen

Neuroimmunology Laboratory group:
Poul Erik H. Jensen
Laboratory technicians: Joy Mendel-Hartvig, Marie Koefoed, Michael Kolbjørn Jensen, Anne Mette Hedegaard Nielsen

Diagnostic evaluations
The presence of oligoclonal IgG-bands in CSF are important for the diagnosis of Multiple sclerosis (MS). In 2008 we have analyzed 504 patient samples, using isoelectric focusing of CSF and corresponding plasma samples for the characterization of IgG bands.
In Myasthenia gravis (MG) autoantibodies against the acetylcholine receptor (AChR) may cause a diminished binding of ACh on muscular surfaces and thereby a reduced impulse transmission to the postsynaptic membrane of the neuromuscular endplate occurs. For diagnostic and therapeutic purposes, we measure the concentrations of these autoantibodies from patient serum samples, using a radio-immunoassay kit, and in 2008 we analyzed 1076 patient samples.

Measurement of neutralizing antibodies
Subgroups of MS patients, treated with IFN-β or Tysabri, generate neutralizing antibodies, which diminish the therapeutic effects. IFN-β molecules bind to leucocytes and a specific up-regulation of MxA mRNA in the cells occurs. Neutralizing antibodies may abolish this effect, and therefore we measure the MxA mRNA-expression as a biological response to treatment with IFN-ß. In 2008 we have analyzed 127 patient samples for MxA mRNA expression. Furthermore, we have screened 16 patient samples for IFN-ß binding antibodies using an ELISA-assay.
The action of Tysabri differs from IFN-β, since it blocks mononuclear cell binding to endothelial cells. In this way Tysabri inhibits mononuclear cells from entering the central nervous system. The generation of neutralizing antibodies to Tysabri in MS patients, block the biological effects of Tysabri. In 2008 we analyzed 756 blood samples for the presence of antibodies to Tysabri by ELISA.

SCIENTIFIC PUBLICATIONS 2007 - 2008

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SCIENTIFIC PRESENTATIONS AND ABSTRACTS 2008

Genes that are over-expressed in multiple sclerosis are not specifically regulated by treatment with interferon-beta
Sellebjerg F, Krakauer M, Ryder LP, Alsing I, Svejgaard A, **Sorensen PS**
Abstract at the 6th Annual Meeting of the American-Academy-of-Neurology, Chicago, USA, April 12-19, 2008
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Spontaneous MxA mRHA expression in multiple sclerosis is associated with IL10 mRNA expression and low MRI disease activity
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Therapeutic efficacy of natalizumab (Tysabri) in multiple sclerosis patients with high disease activity: A Danish Nationwide study
Danish MS Research Center, Rigshospitalet, Copenhagen, Department of Neurology, Aarhus University Hospital, and The University in Aalborg, Denmark
Oturai A, Petersen T, Koch-Henriksen N, **Jensen PEH**, **Sellebjerg F**, **Sorensen PS**
Abstract at World Congress on Multiple Sclerosis, Montreal, Canada, September 17-20, 2008

Evaluation of biomarkers for the response to interferon-β treatment in MS
Danish MS Research Center, Rigshospitalet, Copenhagen, Tissue Typing Laboratory, Department of Clinical Immunology, Rigshospitalet, Copenhagen, and Department of Neurology, Aalborg Hospital, Aalborg, Denmark
Jensen PEH, **Sellebjerg F**, Krakauer M, Ryder LP, Alsing I, **Hesse D**, Koch-Henriksen N, Svejgaard A, **Sorensen PS**
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Roed H, Christiansen M, Langkilde A, **Sellebjerg F**, Frederiksen J.
Poster presentation at the World Conference on Treatment and Research in Multiple Sclerosis, Montreal, Canada, September 17-20, 2008

HONORARY OFFICES
Per Soelberg Sorensen has held the following honorary offices:

A: National
Chairman of the Foundation for Research in Neurology, 1986-
Chairman of the Scientific Advisory Committee of the Danish MS Society, 2004-
Chairman of the Danish Multiple Sclerosis Group, 1996-

B: International
Executive Board Member of the European Charcot Foundation for Research in Multiple Sclerosis, 1994-
Member, Medical Advisory Board of the International Federation of Multiple Sclerosis Societies, 1998-
Member, US National Multiple Sclerosis Society Advisory Committee on Clinical Trials, 2000-
Chairman, Scientist Panel on Multiple Sclerosis, European Federation of Neurological Societies, 2003-
Chairman, Publication Committee, European Federation of Neurological Societies, 2003-

Finn Sellebjerg has held the following honorary offices:

A: National
Chairman, Danish Society for Research in Multiple Sclerosis (DAREMUS)

B: International
Finn Sellebjerg: member of European Federation of Neurological Societies scientist panel on demyelinating diseases.

Annette Oturai has held the following honorary offices:

A: National
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Member of the "Danish MS Biobank"
Board member of the "Torben Fogs and Erik Triers Fondation"

B: International

Member of "IMSGC" collaboration (International Multiple Sclerosis Genetic Consortium)

OTHER ACTIVITIES

Per Soelberg Sorensen has been a member of Editorial Boards:
European Journal of Neurology
Therapeutic Advances in Neurological Disorders

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Neuroimmunology Unit, Karolinska Hospital, Stockholm, Sweden (professor Tomas Olsson)
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