

ESF Exploratory Workshop on
MYELIN STRUCTURE AND ITS ROLE IN AUTOIMMUNITY

Potenza 5-8 June 2002

SCIENTIFIC REPORT

The workshop was held at the Giubileo Hotel, located in Rifreddo, close to Potenza at about 1200 m altitude and immediately adjacent to the forest of Rifreddo. The conference center was very pleasant, the meeting supporting staff (6 people) was excellent, as were the food and wine.

In total, 74 participants and 7 accompanying persons were registered and attended the meeting. Of the 74 participants, 54 were from Europe (39 from Italy, 7 from Germany, and one each from Finland, Sweden, England, Scotland, France, Spain, Switzerland, and Greece). Participants from other countries were from Canada (10), United States (6), Australia (2), Singapore (1), and Japan (1).

Other very distinguished colleagues were unable to be with us because of other commitments, family problems, or the strike at the Italian airports on June the 4th. Since they are not included in the final program, the organizers wish to thank them for their sincere interest in this meeting: *Henry Mac Farland, Hans-Peter Hartung, Cynthia Husted, Sandra Gliozzi, Kai Wucherpfennig, Edoardo Boncinelli, Roland Martin, Klaus-Armin Nave and Claudio Mastroianni*. All of these people were not only prepared to attend the meeting, but they were enthusiastic in their agreement that it is important to know how things are made and structured for the understanding of the mechanisms of assembly, function, and disruption in the physiopathology of myelin.

In accord with the objectives, the workshop brought together researchers whose interests were quite diverse ranging from biophysics, biochemistry, structural biology and bioinformatics, to neuroimmunology and therapy of multiple sclerosis. This diversity led to a number of discussions during the sessions, and to lively interactions during the session breaks and "free time", usually with wine or cappuccino. The sessions were highly focussed, with a good balance between basic and applied studies.

The presentation of the European Science Foundation (ESF) and of the Standing Committee for Life and Environmental Sciences (LESC) was given by George Harauz, after the introductory remarks by Paolo Riccio.

The scientific program of the meeting consisted of an Opening Lecture by Mario Moscarello on "Post Translational Modifications of MBP Suggest Novel Therapeutic Strategies", followed by 12 sessions over 4 days.

The first three sessions on the 1st day were educational tutorials:

1st day: June 5th

- 1st session: Composition and structure of CNS and PNS myelin; Multiple Sclerosis; Therapy of multiple sclerosis; nimal models.
- 2nd session: Physical techniques to determine native membrane and/or protein/peptide structures; Mass spectrometry; Crystallization of proteins.
- 3rd session: Assessment of myelinotoxic proteolytic activity; Molecular modeling; Bioinformatics.

Before dinner on the 1st day, all posters were put on display, and remained available for discussion throughout the conference. On the 2nd, 3rd, and 4th days, all sessions were scientific in nature. After dinner on the 2nd day, four young investigators presented their posters orally as well, having been selected for the special session. These individuals were Giulia Carlone (Bari), Ian Bates (Guelph), Corree Laule (Vancouver), and Maria Pagany (Martinsried).

The subsequent scientific sessions were as follows:

2nd day: June 6th

- 4th session: Myelin genes, structure and developmental origin; Myelin proteins
- 5th session: Structure of myelin proteins.
- 6th session: Myelin proteins and reconstituted systems.
- 7th session: Oral communications of young investigators.

3rd day: June 7th

- 8th-9th sessions: Factors influencing the formation, compaction and swelling of myelin; Myelinotoxic factors; Proteinases; Myelin breakdown; Remyelination; Myelin antigens.

4th day: June 8th

- 10th-11th sessions: Autoimmunity; Molecular mimicry.
- 12th session: Bioinformatics and molecular modeling; Data warehousing and databases.

Abstracts of all of the poster presentations and oral communications were all assembled into a booklet made available at the meeting.

Assessment of Results – Outcome and future contribution to the field.

The formula that the organizers had adopted for the meeting was excellent and highly successful in that it allowed strong and fruitful interactions between various disciplines, namely, biophysics, neuroimmunology, bioinformatics and clinical neurology. Not surprisingly, a number of participants expressed the desire to enlist the collaboration of colleagues so as to enlarge the breath of their work. There is no doubt that this conference will spread the seeds for future collaborations and thus it might be opportune to assess in the not too distant future, the potential outcome of these multidisciplinary research interactions. In planning a future meeting, effort should be made to attract many of the participants that were in Potenza, so as to assess the real achievements of the first meeting. Thoughts should also be given to who one can facilitate the interactions between disciplines that are perceived to be far apart such as biophysics and neuroimmunology. Indeed, some biophysicists and neuroimmunologists had, at times, some difficulty in understanding the presentations from the opposite fields. As this was the first such meeting, it was in some way to be expected, but will certainly be much better in the future. From this point of view, a following second meeting to be held in 2004 would be particularly appropriate. However, the possibility to organize such a symposium as part of the ISN meeting, in 2005, would have the added advantage of facilitating the participation of non-European scientists and enlarge the spectrum of knowledge in a particular field.

Given that the formula adopted at the Potenza meeting was rather new, it is somewhat difficult to objectively assess what we have missed? However, one can say that although there are in other meetings reports on structure, these are usually sporadic. The participation of our colleagues from the biophysics, physics, bioinformatics field in other myelin or general neurochemistry meetings is usually very limited and often confined to poster sessions. In the Potenza meeting the relationship between different fields was promoted. The topics were well chosen in definite fields and were organized in such way that structure was the 1st and the ultimate goal of a cycle of reports, starting from the myelin membrane and arriving to the peptides presented by the antigen presenting cells (APCs). Another important outcome of the meeting was the participation of postgraduate students as well as young scientists. Their exposure to good science as well as the possibility for them to meet more senior colleagues and discuss with them their research endeavors was for many a unique opportunity as well as a most valuable experience.

From comments made by both the junior as well as the more senior scientists, the meeting in Potenza was certainly very successful from the point of view of its organization, science and location. One can only hope that we will be able to meet again in the near future so as to share the wonderful experience of Potenza.

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Provincia di Potenza, Ospedale San Carlo Potenza, Crystal Research AB
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and under the patronage of

Società Italiana di Biochimica e Biologia Molecolare (SIB),
Società Italiana di Neurologia (SIN),
and Ordine Nazionale dei Biologi.

Honorary Chairs:

Henry McFarland, Mario Moscarello and Ernesto Quagliariello

Organizers:

Paolo Riccio and George Harauz

Scientific Advisory Committee:

Claude C.A. Bernard, Paolo Cavatorta, Kazuhiro Ikenaka, Dan Kirschner, Roland
Martin, Mario Moscarello, Robert Zand

1st Day - June 5th

Educational Sessions I-III

Opening events 75 min (10:00-11:30)

- Introductory remarks by *Paolo Riccio and George Harauz* (15 min)
- Presentation of the European Science Foundation (ESF) and of the Standing Committee for Life and Environmental Sciences (LESC) by *George Harauz* (15 min).

Post-translational modifications of MBP suggest novel therapeutic strategies.
Opening Lecture by *Mario Moscarello*, Toronto, Canada (30 min)

30 min discussion
15 min break

1.1. I Session 130 min (11:45-13:15)

Chairpersons: *GianLuigi Mancardi and Francesco Lolli*

Multiple sclerosis and other demyelinating diseases *GianLuigi Mancardi*, Genova, Italy (30 min)

Recent achievements in the therapy of multiple sclerosis *Maria Trojano*, Bari, Italy (30 min)

30 min discussion

Welcome Buffet (13.15)

1.2. II Session 105 min (14.15-16.00)

Chairpersons: *Robert Zand and Paolo Cavatorta*

Protein Identification by Mass Spectrometry, *Jordi Navarro*, Barcelona, Spain (30 min)

Protein Crystallization, *Jan Sedzik*, Huddinge, Sweden (30 min)

SAXS, SANS and Thin Solid Films, *Heinrich Haas*, Munich, Germany (30 min)

15 min discussion
15 min break

1.3. III Session 105 min (16.15-18.00)

Chairpersons:

Hans Berlet and Marcella Attimonelli

Assay of Matrix-metalloproteinases by zymography and ELISA, *Bernd Kieseier*,
Duesseldorf, Germany (30 min)

Molecular Modelling, *Eugenia Polverini*, Parma, Italy (30 min)

Bioinformatics: data retrieval and data warehousing, *Vladimir Brusic*, Singapore (30 min)
15 min discussion

Wine and soft drinks at the 1st POSTER SESSION (18:30-20:00)

Dinner (20:00)

21:30 POSTER SESSION

2nd Day - June 6th

Cell Biology, Biophysics & Biochemistry - Sessions IV-VI

2.1. Myelin genes, structure and developmental origin – Myelin proteins

90 min (08:45-10:15.)

Chairpersons: **Anthony Campagnoni & Kazuhiro Ikenaka**

Speakers:

Development of oligodendrocyte

Kazuhiro Ikenaka, Okazaki, Japan (25)

Multiple Functions of the Myelin Basic Protein Gene: Roles in the Immune and Nervous
Systems

Anthony Campagnoni, Los Angeles, CA (25)

An update on CNS/PNS myelin structure

Dan Kirschner, Boston, MA (25 min)

15 min discussion

15 min break

65 min (10:30-11:35)

Hierarchical Studies on Myelin P0: From Gene to Protein-Protein & Membrane-Membrane Interactions

Dan Kirschner, Boston, MA (20)

Glycolipid-Glycolipid and Protein-Protein Interactions in Myelin and Involvement in Transmembrane Signalling

Joan Boggs, Toronto, Canada (20)

The myelin-associated enzyme CNPase as a membrane anchor for tubulin

Maurizio Bifulco, Salerno, Italy (10)

15 min discussion

15 min break

2.2 Structure of myelin proteins 70 min (11.50-13.00)

Chairpersons: **Mario Moscarello & Dan Kirschner**

Speakers:

Increased Methylation and Decreased Phosphorylation in Myelin Basic Protein from Multiple Sclerosis Brain May Reflect an Important Role in the Etiology of MS

Robert Zand, Ann Arbor, MI (25)

MBP back home

Paolo Riccio, Potenza, Italy (15)

Why Is the Human Myelin-Associated Glycoprotein (MAG) so Unstable... Sometimes?

Anthony Heape, Oulu, Finland (15)

15 min discussion

Lunch: 13:30

2.3. Myelin proteins and reconstituted systems 110 min (15:15-17:05)

Chairpersons: **Joan Boggs & George Harauz**

Speakers:

Structural investigations of the 18.5 kDa isoform of myelin basic protein (MBP) in reconstituted protein:protein and protein:lipid systems.

George Harauz, Guelph, Canada (25)

Organized molecular assemblies from myelin basic protein and phospholipids at planar interfaces and in the bulk phase

Heinrich Haas, Munich, Germany (25)

Myelin basic protein-lipid complex: an atomic force microscopy study

Ranieri Rolandi, Genova, Italy (20)

Crystallomic of Myelin Membrane Proteins. I.

Jan Sedzik, Uppsala, Sweden (20)

20 min discussion

17:05-19:00 Free time /Excursion to Potenza

19:00-20:00 POSTER SESSION

20.00 Dinner

21.30-22.30 POSTER SESSION:

2.4. Oral Communications of Young Investigators

Chairpersons: **Fabrizio Mastronardi & Roberto Furlan**

Speakers: *Ian Bates, Giulia Carlone, Corrie Laule, Maria Pagany*

Social Events

3rd Day - June 7th

Myelin Breakdown

Session VII-VIII

3.1. Demyelination and Remyelination 90 + 30 = 120 min (8.45-10.45)

Chairpersons: **Naren Banik & Gianvito Martino**

Speakers:

Domain organization and ion channel clusters

Kazuhiro Ikenaka, Okazaki, Japan (10)

Immunopathogenesis of multiple sclerosis

Luca Massacesi, Firenze, Italy (10)

Calpain Upregulation Coincides with the Infiltration of Inflammatory Cells and Onset of Experimental Allergic Encephalomyelitis in Lewis Rats

Naren Banik, Charleston, SC (20)

Interferon-beta Treatment Inhibits Metalloproteinase Activity In Rat Microglia Cell Cultures

Grazia Liuzzi, Bari, Italy (15)

The Metal Affinity of myelin basic protein. Possible Functional Implications

Hans Berlet, Heidelberg, Germany (15)

Protecting Axons and Glia from Autoimmune Demyelination

Gianvito Martino, Milan, Italy (20)

30 min discussion

15 min break

3.1. Autoimmunity & myelin autoantigens 110+30 min (11.00-13.20)

Chairpersons: **Claude Bernard & Antonio Uccelli**

Speakers:

Molecular characterization of T and B cells responses in experimental autoimmune demyelination provoked by myelin oligodendrocyte glycoprotein

Claude Bernard, Melbourne, Australia (25)

Milk and mimicry: modulation of self-tolerance to the myelin oligodendrocyte glycoprotein (MOG)

Chris Linington, Munich, Germany (25)

MOG is critical for progressive demyelinating disease in mice

Sandra Amor, London, UK (20)

Immune responses to myelin antigens in marmoset EAE

Antonio Uccelli, Genova, Italy (20 min)

Antibodies directed against MOG induce demyelination in vitro : partial protection by PPAR- γ agonists

Jean-Marie Matthieu, Lousanne, Switzerland (20 min)

30 min discussion

Buffet

Half-day excursion to Matera or free time (14.30-20.00)

Gala Dinner (21.00)

Awards to Mario Moscarello and George Harauz

Tarantolata Dance

4th Day - June 8th

Molecular Mimicry & Bioinformatics
(a session dedicated to Marco Vergelli)

Sessions IX-XI

4.1 95 min (09:00-10:10)

Chairpersons: **Claude Bernard & Luca Massaccesi**

Speakers:

Commemoration of Marco Vergelli
Luca Massaccesi, Firenze, Italy (10)

AVIDITY REPERTOIRE OF ANTIGEN-SPECIFIC T-CELLS
Benedetta Mazzanti (10)

X-ray crystallography of TCR/MHC complexes.
How T cells recognize different antigens.
Massimo Degano, Milan, Italy (30)

20 min discussion

20 min break

4.2 90 min (10:30 –12:00)

Chairpersons: **Marco Salvetti & Graziano Pesole**

MBP 87-99 Epitope Conformation and Rational Design of Cyclic Analogues
John Matsoukas, Athens, Greece (10)

A Novel Algorithm to Measure the Probability of Mimicry with Self and Nonself
Proteomes May Predict Immunodominant Peptides

Graziano Pesole, Milan, Italy (10)

Analysis of MHC class II vs MHC class I human and microbial peptidomes.

Marcella Attimonelli, Bari, Italy (10)

Peptide propensity to ordered structure influences epitope selection by antigen presenting cells: consequences for self-nonsel self discrimination

Eugenia Polverini, Parma, Italy (10)

Self and Nonsel self in the Antigen Presenting Cells (APC) Perspective

Giovanni Ristori, Roma, Italy (10)

30 min discussion

10 min break (12:00-12:10)

4.3. 90 min (12:10 – 13:40)

Chairpersons: **Chris Linington & Marcella Attimonelli**

Speakers:

Post-Translational Modifications of Self Proteins in Autoimmunity.

Mark Mamula, New Haven, CT (25)

Prediction of Peptide Binding to MHC Molecules

Vladimir Brusic, Singapore(25)

IMGT (<http://imgt.cines.fr>) standardization and tools for the analysis of immunoglobulin and T cell receptor repertoires and 3D structures

Marie-Paule Lefranc, Montpellier, France(25)

15 min discussion

13:40 Buffet

Departures

The list of participants, some of the photos taken during the meeting, and the detailed final program may also be consulted on the web page of the workshop:

http://www2.unibas.it/utenti/riccio/Myelin_meeting_after.htm

The funds provided by the ESF were used to pay the registration fees of 32 European participants, including full board hospitality. Two airfares were also reimbursed. ESF funds also enabled the participation of young European scientists from Genova, Parma, Bari, and Munich. As for all other participants, the ESF funded people did not pay anything for the excursion to Matera and Potenza and the transfers between Rome, Naples or Bari airports and the Conference Center in Potenza. Some people also had the opportunity to visit Pompei.

In summary, it was a most enjoyable, very friendly conference, with excellent science presented in a pleasant location in a historical region of Europe.

Paolo Riccio
George Harauz