

tidis (Persson et al, *Nature: Structural Biology*, 2001). This enzyme is a key player in the synthesis of lipopolysaccharide in *Neisseria* species and this structure is the first to reveal interactions of the enzyme with both acceptor and donor sugars. This work is important from the perspective of basic biochemical characterization of this major class of enzymes and also because of the central role of lipopolysaccharides in bacterial pathogenesis.

d) Solution, for the first time, of the structure of a class D beta-lactamase - that of the enzyme from *Pseudomonas aeruginosa* (Paetzel et al, *Nature: Structural Biology*, 2000). This structure is revealed as a homo-dimer that has a novel catalytic mechanism and site for substrate binding. This structure should provide a template for the design of inhibitors and in this sense is vital because no clinically useful inhibitors of this class of beta-lactamases have yet been developed.

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## **Workshop On: Myelin Structure And Its Role In Autoimmunity**

**June 5-8, 2002, Hotel Giubileo, Rifreddo, Potenza, Italy**

**Sponsored by the International Society for Neurochemistry (ISN), the Italian Association of Neuroimmunology (AINI), and the Multiple Sclerosis Society of Canada.**

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### **OBJECTIVES OF THE WORKSHOP**

Myelin, the insulating sheath surrounding nerve axons, has proven to be one of the most difficult membrane systems to study. The reason is that myelin is the product of an intimate contact between two different cell types and because myelin has a compact multilamellar structure that limits the accessibility of its components. Indeed, the organisation of myelin at the molecular level and,

in particular, the high resolution structures of myelin proteins, remain to be clarified. There is also a significant lack of information regarding the putative functions of the various myelin proteins, since they do not seem to possess any detectable biological (viz., enzymatic) activity. However, deciphering myelin is very important in order to understand autoimmune demyelinating diseases, such as multiple sclerosis (MS) in the CNS. Amongst the candidate myelin autoantigens we have: MBP, the basic protein of myelin; PLP, the proteolipid; and more recently MOG, the glycoprotein of the myelin of the oligodendrocytes. Research on the structure of the myelin sheath has long been one of the main topics for the study of physiopathology of myelin. The myelin basic protein (MBP) was isolated and characterized by Eylar in 1969-1970. One important achievement was the finding in 1984 that MBP could be isolated in a form associated with the lipids originally present in the membrane. After a time of very active research on myelin structure, in particular in Canada and in the United States, this declined slowly. So far, the structures of MBP as well as other myelin proteins are still unknown.

In 1992, Ross Smith published a review in *J. Neurochem.* on the structure of MBP, in which he asserted that "further clarification of the structure and function of MBP may have to await development of more powerful techniques for studying proteins bound to large molecular aggregates, such as lipid bilayers". From the references reported in his review, it appears that research on MBP structure declined after the period 1984-1987.

Today, new and powerful techniques are available that were not at the time of Smith's review.

Funding from the European Union of a BIOMED project on "High resolution structure of myelin proteins" (1996-1999) gave a strong impetus to cooperation amongst seven European research groups active in Basel, Strasbourg, Bruxelles, Koeln and Potenza. At present, there is a fruitful cooperation between research centers studying myelin structure in Potenza, Bari, Parma, Rome, and Genoa, in Italy; Strasbourg and Grenoble in France; Uppsala in Sweden; Berlin in Germany; Campinas in Brasil; Boston in the USA; Toronto and Guelph in Canada; and Melbourne in Australia. Interesting results are now appearing regarding the crystallization of myelin proteins, their incorporation into lipid films, and the determination of their structures in solution both in the native and in the

unfolded forms. We expect that this workshop will help people to interact better, and aim for presentations that can be understood by researchers with different backgrounds.

In 1994, one of us, Paolo Riccio, organised and funded a workshop on "Proteases involved in demyelination and their origins" at the ESN (European Society for Neurochemistry) meeting in Jerusalem. He felt then that research on the involvement of proteolytic enzymes in demyelination was in a declining phase and had to be revitalised. It is now apparent in the literature that proteases, and in particular matrix metalloproteases, may have important roles in demyelinating diseases. Similarly, we want to provide new impetus to biochemical, biophysical, and molecular biological studies on the structure of myelin and myelin proteins. There is no doubt, indeed, that in order to understand the mechanisms of myelin breakdown, we have to know how the target of myelinotoxic factors is built up, how this target can be made more resistant to degradation, and what the roles are of autoantigens in their native form. Thus, we try to correlate the structure of myelin and myelin proteins/peptides with pathological events. Events involving cell/cell recognition, antibody/protein interaction, and protein/lipid association are revealing more and more the importance of protein structure and a possible role of molecular mimicry. New physical techniques and bioinformatics approaches have to be discussed in the context of myelin function.

The conference on Myelin Structure and Its Role in Autoimmunity could be considered a follow up of a very successful workshop that Paolo Riccio organised 11 years ago in Naples: Antigenic Properties of Myelin and the Role of Myelin in Pathology (Riccio P. and Dal Canto M.C. (1991) Conference Report, Naples, 22-23 October 1990. *J. Neuroimmunol.* **32**, 185-186).

On these grounds, the aims of this meeting are the following.

- 1) To gather together people who are interested in the architecture of the myelin sheath and, especially, the high resolution structures of myelin proteins.
- 2) To encourage the synthesis of different kinds of expertise in the fields of biophysics, biochemistry, molecular biology, neurology, neuroimmunology, and bioinformatics. Techniques such as SANS, SAXS, EXAFS, FITR, CD, AFM, Langmuir-Blodgett films, gravimetric analysis, mass spectroscopy, capillary

electrophoresis, zymography, electron and scanning probe microscopies, are specialised and not all well-understood by most researchers. On the other hand, some colleagues working on myelin proteins' structures may be so focussed that they may need to refresh their knowledge on what myelin as a whole really is.

- 3) To correlate the knowledge of myelin structure with its breakdown in demyelinating diseases, and to elucidate both how myelinotoxic factors can attack the myelin sheath and how myelin proteins can have a role in autoimmunity.
- 4) Finally, to describe in preliminary sessions selected techniques in biophysics, biochemistry, and bioinformatics, that would be of general interest to all attendees, but particularly young scientists, and provide them with a basis for understanding subsequent sessions and the literature.

#### **Information on the Location of the Workshop:**

##### **Hotel Giubileo, Potenza, Basilicata, Italy**

<http://Giubileohotel.cjb.net>

<http://www.directa.net/basilicata/potenza/hotels4/giubileo.html>

<http://www.italyguide.com/giubileo/giubileo.html>

<http://potenza.pandora.it/giubileo/igiubileo1.htm>

<http://potenza.pandora.it/giubileo/igiubileo3.htm>

The hotel (1200 m altitude), 12 km from Potenza, is situated in the green mountains surrounding Potenza.

Potenza, a town of about 75,000 inhabitants and the capital of Basilicata, is set between Bari and Naples in Southern Italy in the upper Basento Valley near the Appennino Lucano. Of antique pre-Roman origins, it has been conquered by different peoples in the course of the centuries, Lombardian, Swabian and Angevin. Today, Potenza has a vivacious cultural life and a small university with about 6,000 students.

Potenza can be reached by train or by car from Naples (170 km) or Rome (360 km), or by car from Bari (135-170 km), much more easily than Barga (Lucca), which is where Gordon Conferences on Myelin take place in Italy. Pompei (140 km), on the way to Naples, or the rupestrian churches and quarters of Matera (UNESCO monuments) (100 km), on the way to Bari, are also very interesting places to visit. <http://www.emmeti.it/Welcme/Basilicata/Potenza/index.uk.html>

## **PROPOSED STRUCTURE OF THE WORKSHOP**

### **Type of workshop : Scientific (75%) and educational (25%).**

Seven main sessions of about 150-250 min. each, platform presentations of 30 – 45 min. each:

- 1st session: Physical techniques to determine native membrane and/or protein structures;
- 2nd session: General aspects regarding structure and physiopathology of the myelin sheath;
- 3rd session: Reconstituted systems / Crystallography;
- 4th session: Recent achievements related to the structure of myelin proteins;
- 5th session: Factors influencing the formation, compaction and swelling of myelin. Myelinotoxic factors. Myelin breakdown.
- 6th session: The antigenic properties of myelin peptides. Molecular mimicry.
- 7th session: Bioinformatics and molecular modelling. Data warehousing and databases.

Estimated number of attendees: 80 in total.

40 posters with some posters selected for brief oral presentation. Other posters could be supported by Power Point presentation displayed on laptops.

### **Conference fees: 450 USD (full) and 300 USD (students).**

Registration fee includes participation in all sessions, lodging, full board and transportation from Bari and Naples Airports to the conference venue.