

## **SUMMER SCHOOL IN INFLAMMATORY MYOPATHIES, MYOSITIS**

**September 5-9<sup>th</sup> 2011, Sigtunahöjden, Sigtuna, Sweden**

### **Summary**

The course, Summer School, was arranged by the European myositis network (EuMyoNet), which is a European interdisciplinary research network launched in 2010 and supported by European Science Foundation (ESF) in order to support development of research in myositis and to create a platform for clinical multicenter clinical trials in myositis. The summer school was an international boarding course during five days. The hotel centre, Sigtunahöjden, Sigtuna (Stockholm), Sweden, was situated 15 minutes from the airport by car.

The overall aim of this summer school, a post-graduate course, was to cover scientific fields that are important in order to understand disease mechanisms and to develop novel therapies and to identify prognostic biomarkers in inflammatory myopathies, also known as myositis. Specific aim was to combine clinical research in myositis with epidemiological science and basic molecular science in muscle with a focus on immunology and physiology. Another aim was to facilitate interactions between participants from the different countries within the European network, EuMyoNet, and between students and teachers.

The course content was a combination of lectures, demonstrations, cases, group assignments, and students' own presentations to support interactive learning. The course was an international boarding course which enabled possibilities for deeper discussions between students and lecturers. This increased the knowledge of the students; increased their contacts and possibilities for future scientific collaborations.

### **Description of the scientific content and discussion at the event**

The course involved 26 teachers who were internationally recognized leading scientists in their fields. In total there were 34 participants; 31 were student participants within the course, all with an interest in myositis. These were PhD students and post docs, both with clinical and biological backgrounds. Five of these students were from countries outside EuMyoNet partnership (USA, Hungary, Spain) that wish for collaboration with EuMyoNet. One of these 31 students was also a patient representative from United Kingdom with an interest to start her own research in myositis. The other participants were one organizer, and two representatives from co-sponsoring companies attending one of the course days each.

The course took place in a small hotel outside Stockholm during five days with boarding. The structure of the course was based on lectures in the morning followed by problem oriented group discussions in the afternoon.

### **The course contents were divided into several main topics relevant for the inflammatory myopathies, myositis and were covered over five days, in chronological order:**

- Day 1 = Clinical phenotype: *Clinic - case demonstration, Outcome measures, Muscle pathology, Muscle physiology, Muscle atrophy.* Here the clinical and histopathological features of myositis and outcome measures in longitudinal studies were discussed. Molecular understanding of muscle physiology and normal muscle growth/atrophy was described.
- Day 2 = Immunology: *Innate immunity, Adaptive immunity, CD28 null T cells, Autoantibodies and clinical profiles, Autoantibodies - validation & methodology, Autoantigens & modifications.* A general introduction to the human immunity as well as to how the immune system interacts with muscle in inflammatory myopathies was given. We also learned how to identify novel autoantibodies, and which kind of modifications that can occur in an autoantigen, that could lead to an autoimmune response by creating autoantibodies. Autoantibodies in myositis have shown to be strongly related to specific clinical phenotypes which have challenged the classification criteria of myositis.
- Day 3 = Genetics, ethics & animal models: *Genetics in Rheumatoid Arthritis, Genetics in myositis, Ethics in research and Animal models in myositis.* What can we learn from other

autoimmune diseases? It was discussed that the etiology of autoimmune diseases is unknown, but scientific data support an interplay between genetic and environmental/lifestyle factors contributing to the onset of the diseases. An example of such support is that in i.e. rheumatoid arthritis (RA), an interaction between HLA-DR shared epitope (SE) and smoking has been demonstrated in patients developing the most severe form of RA, which is characterized by the presence of antibodies directed against citrullinated proteins (anti-CCP+ RA) [1]. In parallel, the strongest genetic risk factor in myositis is HLA-DR3 [2]. According to preliminary data from a newly formed European case-only multi-center study (n=600 patients) there is an association between smoking, HLA-DR3 and anti-Jo-1 positive myositis [3]. A big difference between RA and myositis, is that myositis is a rare disease for which in particular genetic studies require multicenter networking to be enabled. The ethics in clinical research with a focus on international collaboration using clinical cohorts and biobanks was discussed. We also learned how animal models can contribute to understand the human myositis disease.

- Day 4 = Epidemiology: *Registries, Euromyositis registry, How to set up an epidemiological study, EIRA - gene & environment interactions, Environmental factors in inflammatory disease and in myositis.* How can we use registers to understand more about risk factors and disease mechanisms? A web based myositis register for clinical research was demonstrated. What should we think of when setting up an epidemiological study? Some environmental risk factors in myositis and other inflammatory diseases were described; mainly factors such as infections and smoking were mentioned.
- Day 5 = Future perspectives: *Tissue arrays & biobank, Proteomics, Exercise in myositis, Medical treatment and Future perspectives.* The lectures covered questions such as how to use tissue arrays for gene and protein expression, and how to identify prognostic biomarkers. Current and future therapies in inflammatory myopathies: Role of biologics and physical training in myositis were also discussed.

**Other contents of the course were:**

- The clinical lecture involved one patient demonstration in which a patient communicated her experience of the disease and how she had undergone treatment for the disease. This step also gave the patient an opportunity to give students feedback on what she considered to be

important in research on her disease. Here the students got the opportunity to meet a patient with the disease myositis, which is very useful for students who do not meet patients otherwise. Moreover, the students were given the opportunity to ask questions of different nature directly to the patient.

- The first evening, during dinner time, oral presentations of pre-prepared posters were given by the students and these were discussed within the group. This part was greatly appreciated as each participant got the chance to give a presentation of his/her work and also get feedback and scientific questions to consider.
- In the afternoons of day 2 to day 4, group assignments were given to the students. The students had been divided into five groups with six people in each group. The composition of the groups was people from different countries. The groups had discussions to solve their assignments, which were presented both orally and as written report. These assignments covered the main points of the lectures given during the mornings and also from day 1. During the group discussions, each group had one “expert”/lecturer within the assigned field with whom the students were able to discuss the questions and learn more from.
- The participants had also been assigned some clinical cases that they should score and enter into the EuroMyositis registry. This enabled for the participants to have a practical exercise and to become acquainted with the registry. One of the cases was later demonstrated by the organizers so that the participants were able to assess their own compatibility with an experienced clinician and also to understand the difficulties with the scoring, and also the technical issues. In case of questions, all participants were urged to contact the EuroMyositis committee.
- During the evenings of the boarding the students and teachers had informal interactions:
  - The third evening, a quiz had been organized: the questions given were of scientific and social content. The participants themselves created small groups of people who would answer the quiz. This enabled for more informal interactions between the participants and teachers and also had a social effect. The answers were announced during the dinner the next day, and the winners got a USB-memory stick (with the ESF logotype and EuMyoNet logotype on) as a price.

- The last evening all participants and teachers (who were there) joined for karaoke. This created a great social interaction and fun.

### **Assessment of the results and impact of the event on the future direction of the field**

The aims of the course were achieved very successfully:

- All participants and teachers increased their knowledge in the scientific fields that are important in order to understand disease mechanisms and to develop novel therapies and to identify prognostic biomarkers in myositis.
- This boarding course facilitated interactions between participants from the different countries both within and outside the EuMyoNet. This interaction was between students, and also students and teachers, which increased the contacts and possibilities for future scientific collaborations.

The general view was to collaborate within and outside the network, with countries/centres that wish to. Countries that wish to join the EuMyoNet are welcome to do so if they can fulfil the formal requirements.

### **References**

1. Mahdi H, Fisher BA, Kallberg H, et al. Specific interaction between genotype, smoking and autoimmunity to citrullinated alpha-enolase in the etiology of rheumatoid arthritis. *Nature genetics* 2009;41:1319-1324.
2. O'Hanlon TP, Carrick DM, Targoff IN, et al. Immunogenetic risk and protective factors for the idiopathic inflammatory myopathies: distinct HLA-A, -B, -Cw, -DRB1, and -DQA1 allelic profiles distinguish European American patients with different myositis autoantibodies. *Medicine* 2006;85:111-127.
3. Chinoy H, Adimulam S, Vincze M, et al. The interaction of HLA-DRB1\*03 and smoking for the development of anti-Jo-1 antibodies in adult idiopathic inflammatory myopathies: a european-wide study. *Annals of the rheumatic diseases* 2010;69.

## Programme Summer School in Inflammatory Myopathies, Myositis (Sigtunahöjden, Stockholm, Sweden, September 5-9, 2011)

Sept 2011	8.30-9.45	9.45-10.15	10.15-11.00	11.00-11.45	11.45-12.45	12.45-14.15	14.20-15.00	15.00-15.20	15.20-16.00	16.10-17.45	18.30
<b>Monday 5</b>  <i>Clinical phenotype</i>	<b>Arrival &amp; check in, plus registration</b>				Lunch	- Welcome <i>IL</i> - Presentation	Outcome measures <i>JV</i>	Coffee	Muscle Pathology <i>JDB</i>	Muscle Physiology <i>HW</i>	Dinner & Posters
						- Clinic <i>RC</i> - Case demonstration <i>IEL</i>				Muscle atrophy <i>GN</i>	
<b>Tuesday 6</b>  <i>Immunology</i>	Innate immunity <i>HE-H</i>	Coffee	10.00-10.30 CD28 null T cells <i>AF</i>	11.10-11.45 Autoantibodies - validation & methodology <i>PC</i>	Lunch	12.45-13.30 Autoantigens & modifications <i>GJMP</i>	13.30-16.00 Group assignment & coffee		16.00-17.30 Group presentations	Dinner & Other activities	
	Adaptive immunity <i>VM</i>		10.30-11.10 Autoantibodies & clinical profiles <i>HG</i>								
<b>Wednesday 7</b>  <i>Genetics &amp; animal models</i>	Genetics in Rheumatoid Arthritis <i>RP</i>	Coffee	Genetics in myositis <i>HC</i>	Ethics in research <i>MH</i>	Lunch	12.45-13.30 Animal models in myositis <i>KN</i>	13.30-16.00 Group assignment & coffee		16.00-17.30 Group presentations	Dinner & Other activities	
	Genetics in rheumatic diseases <i>LP</i>										
<b>Thursday 8</b>  <i>Epidemiology</i>	Registries <i>JA</i>	Coffee	How to set up an epidemiological study <i>HK</i>	EIRA - gene & environment interactions <i>CB</i>	Lunch	12.45-13.30 Environmental factors in myositis <i>LA/SBH</i>	13.30-16.00 Group assignment & coffee		16.00-17.30 Group presentations	Dinner & Other activities	
	Euromyositis registry <i>NSK/JV</i>										
<b>Friday 9</b>  <i>Future perspectives</i>	Tissue arrays & biobank <i>TH</i>	Proteomics <i>P-JJ</i>	Coffee	Exercise in myositis <i>HA</i>	Future perspectives <i>IL</i>	Lunch	<b>Departure</b>				

## **Faculty and Topics - Summer School in Inflammatory Myopathies, Myositis**

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**AF: Andreas Fasth**, PhD, Karolinska Institutet (KI) - CD28 null T cells in myositis

**CB: Camilla Bengtsson**, PhD, KI – Epidemiological investigation in Rheumatoid Arthritis (EIRA) - gene and environment interactions

**GJMP: Ger J.M. Pruijn**, Ph.D, Professor, Nijmegen - Modifications of autoantigens

**GN: Gustavo Nader**, Assistant Professor, KI - Regulation of muscle mass in inflammatory disorders

**HW: Håkan Westerblad**, Professor, KI - Muscle physiology – weakness and fatigue

**HG: Harsha Gunawardena**, MD, PhD, Bath - Autoantibodies and clinical profiles

**HC: Hector Chinoy**, MD, PhD, lecturer, Manchester – Genetics in myositis

**HE-H: Helena Erlandsson-Harris**, Associate Professor, KI - Innate immunity in myositis

**HA: Helene Alexanderson**, Assistant Professor, physical therapist, PhD, KI - Exercise and clinical outcome measures in myositis

**HK: Henrik Källberg**, PhD, KI – How to set up an epidemiological study

**IEL: Ingrid E. Lundberg**, Professor, KI – Clinical aspects of myositis – case demonstration

**JDB: Jan De Bleecker**, Professor, Gent University, Belgium - Muscle pathology – cytokines/chemokines

**JV: Jiří Vencovský**, Professor, Prague - Outcome measures and Euromyositis registry

**JA: Johan Askling**, Associate Professor, KI - Epidemiology- what can we learn from registers?

**KN: Kanneboyina Nagaraju**, Associate Professor, Children´s National hospital, Washington DC, US - Animal models in myositis

**LA: Lars Alfredsson**, Professor, KI - Environmental risk factors in inflammatory diseases

**LP: Leonid Padyukov**, MD, PhD, KI - Gene-gene and Gene-Environment Interactions in rheumatic diseases

**MH: Mats Hansson**, Professor, Uppsala University - Ethics in research

**NSK: Niels Steen Krogh**, IT, Expert, Copenhagen - Euromyositis register function

**P-JJ: Per-Johan Jakobsson**, Associate Professor, KI - Proteomics in the perspective of myositis

**PC: Peter Charles**, Lead Scientist, University of Oxford, London - Autoantibodies in myositis and validation of novel methodologies

**RC: Robert Cooper**, M.D. Consultant & Honorary Reader in Rheumatology Manchester - Clinical aspects of myositis

**RP: Robert Plenge**, M.D., PhD, Harvard Medical Scholl, US - Genetics in RA

**SBH: Sevim Barbasso Helmers**, PhD, KI - Environmental risk factors in myositis

**TH: Thomas Häupl**; PhD, Berlin - Transcriptomics & biobank

**VM: Vivianne Malmström**, Associate Professor, KI - Adaptive immunity in myositis