

**What are the pattern recognition receptors really doing ?
Turku, Finland, 2-5 September 2004**

Executive summary

Subject of the meeting

Pattern recognition receptors (PRR) are used by antigen presenting cells to recognize foreign molecules. The same molecules seem to have key functions in scavenging modified endogenous molecules, in apoptosis, and even more strikingly in physiologic cell-cell adhesion. The structural and functional basis for the dual function of pattern recognition molecules in binding of endogenous (host-derived) and exogenous (non-host origin) ligands is not understood at the moment.

As PRR are important i) in most bacterial and fungal infections for eradication of the disease, ii) in the process of atherosclerosis for depositing of modified LDL and other particles in the arterial wall and iii) in regulation of leukocyte and cancer cell migration through the vessels, targeting of PRR holds immense potential in controlling many important disease classes. Detailed understanding of the mechanisms, which dictate specificity of ligand recognition will be crucial before these potent molecules can be therapeutically exploited to control infection and inflammation. Clearly, PRR research requires an *interdisciplinary* approach and this workshop was the first attempt to bring the European scientists with different expertise in the PRR field together.

Meeting place and participants

The workshop was held September 2nd-5th 2004 in MediCity, Turku University, Finland and it was organized by Professor Sirpa Jalkanen and Dr. Marko Salmi with the help of two local secretaries (Elina Wiik, financial issues and Anne Sovikoski-Georgieva for scientific and practical issues (lodging, travel, meals etc.). The participants were from research laboratories of Finland, England, Holland, Sweden,

Germany and Italy studying different pattern recognition molecules. They represented a wide variety of different disciplines such as immunology, bacteriology, cell biology, glycobiology, medicine. Both sexes were almost equally presented, 14 females and 11 men. Among the participants there were both young and more experienced scientists at all levels of a scientific career (the ages varied from 23 to 67 years).

Program

The principal aim of the program was to bring together scientists who share an interest in at least one of the pattern recognition receptors, but who would not easily meet in more conventional meetings.

The meeting consisted of 13 talks of 30 minutes and 15 min discussions after the talks. In addition, enough time for general discussion was reserved. The social program was organized so that it 'forced' the participants to be as a group and thus, optimized the possibilities for fruitful discussions. Since certain groups had brought young scientists (who were not listed speakers) to this workshop, the organization of the workshop allowed also them to actively participate in the discussions and get new collaborators.

Outcome of the meeting

During the lively discussions it came evident that the participants of many of the groups would benefit from collaborative arrangements. In fact, several collaborations have already been launched. Immediate actions have included reagent exchanges and visits to the collaborating laboratories. It was also decided that the participants will actively search for possible EU instruments for funding more intensive collaboration between the groups.

Scientific content of the event

The program started by a keynote lecture of Siamon Gordon who is the Grand Old Man of the field. He gave a broad overview of the current status of the pattern recognition receptor-field and summarized his own studies.

In the next session Stephen Dower talked about Toll-like receptors, which are important in host defence. He also discussed about the possibilities to use Toll-like receptors as drug targets. Also Emmanuelle Caron talked about host defence and the role of complement receptor 3 and small GTPases in that.

In the following session Yvette van Kooyk talked about an interesting receptor of dendritic cells called DC-SIGN. This receptor is needed for recognition of certain microbes, especially certain carbohydrate structures of bacteria. Both Paul Crocker and Ten Feizi continued about fundamental importance of certain carbohydrate structures in microbial recognition.

Heikki Irjala, Luisa Martinez-Pomares and Claire Isacke all discussed about different aspects of macrophage mannose receptor and members of the mannose receptor family. They included lymphocyte adherence to lymphatic vasculature, cancer spread and microbial elimination.

Sergeij Goerdt and Marko Salmi talked about Clever-1/stabilin-1 molecule. These talks demonstrated that research groups studying completely different aspects in biomedicine can find the same molecule. The future experiments should elucidate the molecular mechanisms behind the findings of these groups.

Timo Pikkarainen summarized the current knowledge of a novel scavenger receptor, MARCO. It has a unique localization in alveolar macrophages and in the spleen. It is capable of binding microbes and it is of fundamental importance in the lungs for protection against *Streptococcus pneumoniae* infection. Antonio Mantovani talked about pentraxins, especially about pentraxin 3 (PTX3) and their role in vitro and also in vivo in clinical settings. In acute myocardial infarction high PTX3 concentrations predict poor outcome.

Assessment of the results, contribution to the future direction of the field, outcome

Scientific aspects

It was jointly agreed that although certain aspects of PRR are known, the knowledge is rather scattered and many aspects are completely unknown. The field needs extensive work and the best results will be obtained by collaborative efforts. A list of the areas in need of efforts is as follows:

- Concept of PRR should be clarified. It includes characterization of PRR structures and their ligands
- Functional properties of PRR (development of *in vivo* imaging tools would be helpful)
- Experimental models in inflammation, infarction, repair (better models are needed, new antibodies, knockout animals)
- Clinical studies
- Signaling via PRR (cytoplasmic functions not well known)
- Role of glycosylation of PRR (may be responsible for cell specific functions)
- Evolution of PRR (is there something to be learned?)
- Final destination of PRR bound microbes

Teaching/training

It was also agreed that exchange of students between the laboratories would facilitate the training aspect. Some discussions are already ongoing between certain laboratories about practical possibilities in this aspect.

Financial aspects

It was agreed that financing at the European level will be actively sought for the collaborative studies by the participant laboratories.

Final Program

Thursday, 2nd of September

16.00-16.30 *Opening words & coffee*

Keynote lecture

16.30-17.30 Siamon Gordon, UK: Pattern recognition receptors: Doubling up for the innate immune response?

Toll-like receptors and CR3

17.30-18.15 Stephen Dower, UK: Toll-like receptors as potential therapeutic targets for multiple diseases

18.15-19.00 Emmanuelle Caron, UK: CR3 in phagocytosis

20.00- *Dinner*

Friday, 3rd of September

Prototype adhesion molecules used for microbial recognition: a way for microbes to survive or host to eliminate them?

09.00-09.45 Yvette van Kooyk, The Netherlands: DC-Sign and microbial infections

09.45-10.15 *Coffee*

10.15-11.00 Paul Crocker, UK: Sialoadhesins

Macrophage mannose receptor family: recognition domains and new functions

11.00-11.45 Ten Feizi, UK: A central role for carbohydrates

11.45-13.15 *Lunch*

13.15-14.00 Heikki Irjala, Finland: Mannose receptor in lymphocyte trafficking

14.00-14.45 Luisa Martinez-Pomares, UK: What we can learn from mannose receptor knockout mice

14.45-15.15 *Coffee*

15.15-16.00 Claire Isacke, UK: Unique features of Endo180

Why so many functions for one molecule (Clever-1/stabilin-1/FEEL-1)?

16.00-16.45 Sergij Goerdts, Germany: Role of stabilins

16.45-17.30 Marko Salmi, Finland: Clever controls both lymphocyte entrance and exit

19.00- *Dinner*

Saturday, 4th of September

Are multitude of receptors needed for health?

09.00- 09.45 Timo Pikkarainen, Sweden: MARCO and other scavenging receptors

09.45-10.30 Alberto Mantovani, Italy: Pentraxins and health

10.30-11.00 *Coffee*

11.00-12.30 *Discussion*

12.30- *Lunch and trip to Turku Archipelago: Informal discussions about future*

23.00 *Back to Turku*

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Statistical information on participants

Age bracket: **Between 23 and 67 years**

Sex: **14 women**
 11 men

Countries of origin: **The Netherlands** **1**
 Italy **1**
 Germany **3**
 Sweden **3**
 UK **7**
 Finland **10**