

The highlights of translational research on display

The EAU RF organises a meeting in Amsterdam incorporating researchers and EC officials



Prima-coordinator Prof. Jack Schalken



EU project advisor Marion Bussemakers

By Franz-Günter Runkel

The collaborative translation of our understanding of prostate cancer development and progression to the bedside of the patient is the theme of a unique meeting about prostate cancer translational research in Europe. The EAU Research Foundation has taken the initiative for this meeting in Amsterdam on 22-23 June 2009.

"We expect between 200 and 250 participants at the Beurs van Berlage congress venue," says Prima-coordinator Jack Schalken, Radboud University Nijmegen Medical Centre, in an interview with European Urology Today (EUT). Schalken is very happy that the EAU has taken up the challenge to compose and organize a meeting of these consortia and calls it a "bottom-up initiative".

Top-speakers were recruited from EC framework programmes. Researchers, EC officials, US fund raisers (PCF) and representatives of the patient advocacy groups are invited to join the meeting. US-based scientists representing the "Specialized Programs of Research Excellence (SPORE) of the US National Institutes of Health (NIH) and the National Cancer Institute (NCI) will strive to improve "across-the-pond" collaboration. "Translational research," defines the US National Cancer Institute, "transforms scientific discoveries arising from laboratory, clinical, or population studies into clinical applications to reduce cancer incidence, morbidity, and mortality."

"If you organize a good meeting," explains Schalken, "you hope there will be many young people around. These young people will devote their future to urologic research. That is one of the main targets of the EAU Research Foundation. We want as many people as possible to work on our research topics. We would like to attract students and young clinicians to join our meeting and generate their enthusiasm towards urologic research."

According to Marion Bussemakers, EU project advisor at the Radboud University Nijmegen Medical Centre, the poster session will hopefully stimulate the young people. "We will have overviews of the working group leaders. But there will also be individual posters from all the PhD students and the young faculty working in these programmes."

Research efforts have increased steadily over the past two decades, and the funding of cancer research is competitive. Within the European Community based framework programme eight prostate cancer consortia were funded in the last five years totalling € 40 million. All of them have a number of research teams which can vary between six and 16 partners. Sometimes a team is even involved in two consortia. There are many interfaces between the teams.

Thus, the "Prostate Cancer Translational Research in Europe" meeting is about to present the highlights. For instance the Prima network has worked for five years and the funding is down now. Other consortia have just started. In general the funding situation of the eight consortia is stable. There is no stagnation at all, because new networks are arising from the 40 current partners. They are forming new consortia and get funded again. The interactions between these networks are very dynamic and also competitive. Two new consortia, called Marie-Curie Initial Training Networks, are the new interesting findings.

In total it is a European structure and there is one working group from Israel. Apart from technology many of them are hooked to the respective clinical department of urology. They have tissue repositories and specific expertise. If researchers want to run

clinical studies with patient material they will have ideal conditions for this.

The European Union wants to disseminate the achievements of these projects. Bussemakers explains why this meeting is so important for the EU: "It is sort of a dissemination event and now we can combine several projects which have already been finished or are about to be finished. It is to show Europe what they have done with their money but also to engage in a discussion about the future of urologic research or prostate cancer research."

Bussemakers already discussed this programme with scientific officers in Brussels: "They are very enthusiastic that we are putting on such a big event. We also invite one of the head of sections for the cancer division - Maria Vidal, scientific Officer, DG Research, European Commission, - to get feedback from what the EC expects and how they see the future. This is why we also invited the American funding agency - the SPORE and NIH programme - because the EC also wants to get more collaboration with the US."

The EU project advisor believes that also "the US realise how good the research is we are doing in the EU". This is why we also want to showcase our results and start a discussion about collaboration. "The SPORE's often single-institutional and long-term funded," explains Jack Schalken, "and they have not this dynamic change in interaction between the various partners which is typical for our networks. The SPORE's are very much interested in our clinical studies."

Schalken experiences a subtle difference between Europe and US networks. The rather unique thing of European research is that "we are more willing to work together in consortia. In Europe there is a better balance between competition and collaboration than in the US. I think within these networks we have found a good balance between collaboration and competition."

What is this meeting about? Molecular genetics of prostate cancer is one of the programme highlights. In total four consortia are working on genetic changes of prostate cancer. Two consortia, Polygene and PROMark, will present results on their studies regarding genetic conditions that pre-disposed to prostate cancer. Another group works on genetic changes in the cancer cells and that is primarily related to the Prima and the P mark consortium. And finally there is a new consortium (PROSPER) studying so called micro-RNA's. Thus we now have a better understanding of genetic changes that pre-dispose to the development of prostate cancer or genetic and epigenetic changes acquired by the prostate cancer cells. The goal is how urologists can use this first of all in the early diagnosis, the prediction of the clinical course of the disease and eventually there is a therapeutic target. This is about understanding the molecular basis of the disease.

Clinical molecular diagnostics, biomarkers above all, are another highlight of the programme. "This," highlights Jack Schalken, "is really to translate molecular genetics to the clinical practice. I think the big change in the diagnosis and therapy of prostate cancer caused by today's research will be individualised therapy. The first example for this change is the PCA 3 marker. This shows whether you have to immediately treat a patient or can wait for some time. Another example are the so called gene fusions. I think markers on the one side, new therapies on the other. That will be the future."

Many people talk about targeted therapies, especially focused on renal cell cancer. But what are the options for prostate cancer? "The oldest form of targeted therapy is related to prostate cancer: endocrine therapy targeting the androgen receptor. In the last years we have seen that the androgen receptor is not the wrong target as assumed before, but that we failed to adequately inactivate it in the prostate cancer cells. We got the wrong approaches to getting the targets activated. We already knew that in 1983 but did not use this knowledge consequently. In 2003 it was shown again that in fact the prostate gland and the cancer cells produce their own hormones, particularly DHT. Castrating a man does not result in the fact that there is no testosterone in the tumour cells," Schalken points out.

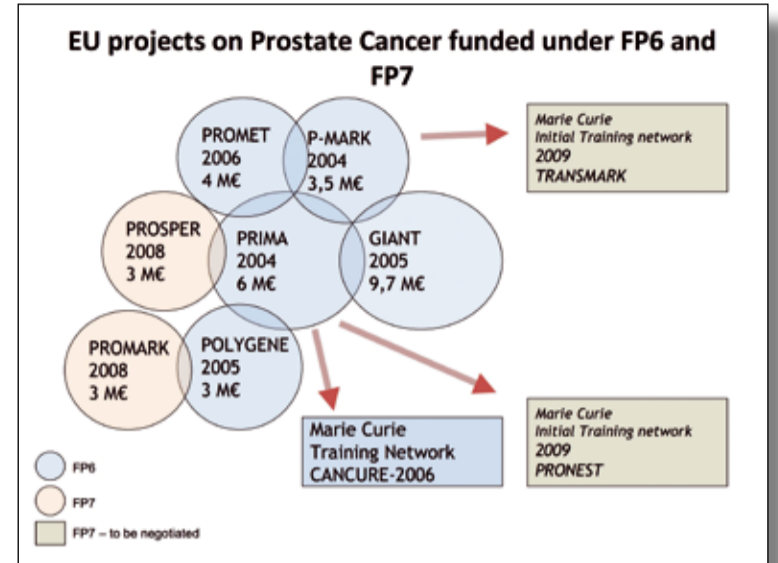
Actually they produce testosterone from precursors such as DHEA or may be even cholesterol. The new targeted therapies try to inactivate the DHT production by the cancer cells. In fact the androgen receptor is the oldest and still the hottest target in prostate cancer.

The Prima coordinator also points to a pretty critical assessment of targeted therapies provided by John Isaacs, called "From magic bullet to smart bomb!" Isaacs states that it is unlikely that one will be able to treat a cancer by aiming one target only. Doing so he will tone down the enthusiasm for targeted therapies a little bit, at the same presenting an alternative.

In conclusion, Marion Bussemakers is convinced that the June meeting might give the European Community some good leads for future funding and health research policies: "There is one session where we also want to hear the feedback so that they can see what we do. Of course we can discuss where the future of research should go. So in these brainstorm sessions about the future of research, they may get some ideas, although on average these EC programmes are long-term procedures."

Of course pharmaceutical companies are invited, but they have no influence on the programme, as Jack Schalken states. In every consortium there must be so called SME's. They are small and medium enterprises which means companies whose headcount or turnover falls below certain limits. The abbreviation SME occurs commonly in the European Union and in international organisations. Their role is to participate in the projects and take care of new products.

"They commercialise the results of our research projects which is public-private interaction at its best. Scientists have to cooperate with companies since knowledge without marketing does not work. Then they make it available to the patients and doing so generates a lot of jobs. This is also an added value for



EU projects on prostate cancer funded under FP 6 and FP 7

the economy. Of course this is a development which is absolutely different from what was going on fifteen years ago. Making money from your scientific work was not the job of the university at that time," Schalken recalls.

But how will diagnostics and therapy of prostate cancer change in future? Diagnostics has already changed with the PCA 3 marker. The markers which will be developed by these consortia will see the patients sooner than the therapies. "But the Prima consortium," according to Jack Schalken, "has yielded three new lead compounds for the treatment of prostate cancer. But there is no guarantee that these compounds will be successful in the end." There are still a lot of clinical studies to be done. Gene therapy is even in a more difficult position since there are so many legal regulations.

<http://pctre2009.uroweb.org>

Research Foundation

Prostate cancer translational research in Europe

22-23 June 2009
Amsterdam, The Netherlands

European Association of Urology

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For more information on registration please check <http://registrations.uroweb.org> or contact the EAU Congress Organiser at pctre2009@congressconsultants.com

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Prostate cancer is still a major health concern in the Western male population. Research efforts have increased steadily over the past two decades, and the funding of cancer research is competitive. It is, therefore, particularly remarkable that within the European Community based framework programme many prostate cancer consortia were funded in the last 5 years totaling approximately € 40 million. In all these collaborative efforts the translation of our understanding of prostate cancer development and progression to the bedside of the patient, plays a pivotal role. So, it is time to present the highlights of these efforts in a unique event entitled "Prostate Cancer Translational Research in Europe". The unifying theme will be how today's research will change the diagnosis and therapy of prostate cancer in the immediate future.

The European Association of Urology, provides an excellent forum to disseminate knowledge in specialized meetings. Therefore, the EAU Research Foundation has taken the initiative for this meeting. Top-speakers, were recruited from EC framework programs and researchers, EC officials and those representing the patient advocacy groups will be invited to attend. Furthermore, US based scientists will join to see how we can improve "across the pond" collaboration. This meeting gives you a view on the individualized diagnosis and treatment of prostate cancer in the near future.

Peter Mulders Jack Schalken Per-Anders Abrahamsson
Chairman *PRIMA* *EAU Secretary-General*
EAURF *Consortium*

Monday, 22 June 2009

09.00 **Welcome and opening**
P-A. Abrahamsson, Malmö (SE)
P.F.A. Mulders, Nijmegen (NL)
J.A. Schalken, Nijmegen (NL)

 **European Association of Urology**

09.15 – 10.30 **Molecular genetics of prostate cancer**
Chair: G. Jenster, Rotterdam (NL)

09.15 – 09.40 **Identification of common genetic variants that affect the risk of prostate cancer**
T. Rafnar, Reykjavik (IS)

09.40 – 10.05 **Identification and validation of new prostate cancer targets using high throughput technologies**
M. Wolf, Helsinki (FI)

10.05 – 10.30 **microRNAs in diagnosis and therapy**
T. Visakorpi, Tampereen Yliopisto (FI)

10.30 **Break**

11.00 – 12.05 **From molecular target to clinical molecular diagnostics**
Chair: A. Bjartell, Malmö (SE)

11.00 – 11.15 **What is the best practice in bio-banking?**
F.C. Hamdy, Oxford (GB)

11.15 – 11.40 **Clinical validation and implementation of new biomarkers**
C.H. Bangma, Rotterdam (NL)

11.40 – 12.05 **PCA3 and gene fusion based molecular diagnostics**
J.A. Schalken, Nijmegen (NL)

12.05 **Round table - Biomarkers in prostate cancer, where do we go?**

Chair: L.A. Kiemeny, Nijmegen (NL)
Panelists: C.H. Bangma, Rotterdam (NL)
A. Bjartell, Malmö (SE)
F.C. Hamdy, Oxford (GB)
T. Rafnar, Reykjavik (IS)
J.A. Schalken, Nijmegen (NL)
T. Visakorpi, Tampereen Yliopisto (FI)

13.00 – 14.00 **Lunch and poster viewing**

14.00 – 16.10 **Research- and training networks**
Chair: P.F.A. Mulders, Nijmegen (NL)

14.00 – 14.20 **The EC perspective**
M.J. Vidal-Ragout, Brussels (BE)

14.20 – 14.40 **The NCI SPORE programs**
Representative NCI SPORE program (TBD)

14.40 – 15.00 **The Prostate Cancer foundation's pragmatic approach to research funding**
H. Soule, Santa Monica (US)

15.00 – 15.20 **What's does the patient with prostate cancer expect from us?**
L.J. Denis, Antwerp (BE)

15.20 – 15.40 **Training the next generation prostate cancer researches (MC training networks)**
C. Robson, Newcastle upon Tyne (GB)

15.40 – 16.10 **Discussion: Can we integrate the networks?**
Chair: P.F.A. Mulders, Nijmegen (NL)

16.10 **Poster viewing and discussion**

17.00 **Continued with drinks**

Tuesday, 23 June 2009

08.30 – 11.00 **Targeted therapies**
Chair: J.A. Schalken, Nijmegen

08.30 – 09.00 **The androgen receptor**
J. Trapman, Rotterdam (NL)

09.00 – 09.30 **Tumor-bone interactions in the pathogenesis of bone metastasis**
G. Van Der Pluijm, Leiden (NL)

09.30 – 10.00 **Optimising targeted gene therapy for prostate cancer**
N.J. Maitland, York (GB)

10.30 – 11.00 **A critical view on targeted therapies; from magic bullet to smart bomb!**
J. Isaacs, Baltimore (US)

11.00 – 11.30 **Break**

11.30 – 12.15 **Keynote lecture**

Faculty

P-A. Abrahamsson, Malmö (SE)
C.H. Bangma, Rotterdam (NL)
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J. Isaacs, Baltimore (US)
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