EU collaborative project

ProspeR pursues deeper insights on non-coding RNAs in prostate cancer

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In addition to the androgen signalling pathway, no major mechanisms of prostate cancer growth have been identified. Patients diagnosed with advanced disease are treated by androgen withdrawal therapy, either by surgical or chemical castration, or administration of antiandrogens.

However, although almost all patients initially respond to androgen withdrawal therapy, eventually practically all of them relapse with incurable castration resistant prostate cancer. The lack of understanding of the molecular mechanisms of prostate cancer tumorigenesis has hampered the development of new therapeutics and diagnostic tools

A recent breakthrough discovery in molecular biology has been the discovery of the importance of ribonucleic acid (RNA) as regulatory molecules of cellular processes. For this role, the Science Magazine awarded "the new roles of RNA" with the status of the '2002's Breakthrough of the year.' During the past few years, thousands of RNA molecules that do not seem to contain any extensive open reading frame have been identified. These, so called non-coding RNAs (ncRNAs), seem to be involved in many fundamental functions of the cell.

For example, they have been implicated in regulation of gene transcription and translation, chromatin structure dynamics, DNA imprinting and methylation, and gametogenesis. ncRNAs are usually categorised into three groups: micro, small, and medium-large RNAs, based on their length. Maybe the best known ncRNAs are the smallest, so called microRNAs (miRNA). They regulate expression of protein-coding genes at the translational level, either by triggering degradation or preventing translation of the target mRNAs.

More than half of the known miRNAs have been reported to be located in cancer-associated genomic regions and to show copy number alterations in cancer. Furthermore, deregulation of several miRNAs has been detected in various different cancers.

Functional studies on individual miRNAs have shown that they can act as oncogenes or tumor suppressor genes.

Based on the emerging knowledge on the function of ncRNAs and our own data on the expression of ncRNAs in prostate cancer, it is conceivable that they may play a role also in the development and progression of prostate cancer. The study of ncRNAs could lead to major breakthroughs in treatment of prostate cancer by providing both novel diagnostic and predictive biomarkers, as well as drug targets.

ProspeR consortium
ProspeR (Prostate cancer: profiling and evaluation of ncRNA) project is an EU funded collaborative project of the 7th Framework Programme. The four year project of seven partners (Table 1) commenced February 1st 2008. The people involved include prominent basic prostate cancer researchers in Europe (Tapio Visakorpi, Guido Jenster, Yvonne Ceder, Hans Lilja, and Olli Kallioniemi), urologists (Jim Catto, Freddie Hamdy, Anders Bjartell, and Teuvo Tammela), and industrial partners (Thomas Litman, Pekka Kallio), as well as vast expertise (Figure 1).

The general aim of ProspeR is to elucidate the role of ncRNAs in the development of prostate cancer, and evaluate the utility of ncRNAs as diagnostic/prognostic tools and therapy targets in clinical practice. The ProspeR project will pursue two major clinical problems: 1) early identification of cases requiring aggressive curative treatment, and 2) develop efficient therapies against hormone-refractory prostate cancer.

In the project, novel ncRNAs will be sought, expression of the ncRNAs in clinical tumours will be analysed, and genetic and epigenetic alterations in ncRNA will be screened. Once altered ncRNAs have been identified, their value as diagnostic or prognostic markers will be tested. Also, proof of concept as being a treatment target will be tested.

Biorepositories
ProspeR will heavily rely on the excellent biorepositories in Europe. Another asset is the close connection between prostate cancer researchers in the continent, partly as a consequence of strong previous support of EU to prostate cancer research. Most of the researchers in ProspeR have previously been involved in EU programs, such as PRIMA, CANCURE, and P-MARK.

The discovery phase of ProspeR is based on the biorepositories that have been collected and stored at Tampere, Rotterdam, Sheffield and Malmö over the years for various study purposes. The repositories contain, for example, samples of blood from prostate cancer patients and in some cases from their family members, urine from patients, and tissue samples of prostate cancers of various clinical stages. The total number of samples at the project's disposal exceeds 550,000 and roughly 45,000 of these are tissue samples. In addition to the large number of samples, the follow-up time of the patients in most of the sample sets is over five years, which enables statistical long term survival analysis.

Site	Country	Principal investigator
University of Tampere	Finland	Tapio Visakorpi (coordinator)
Erasmus Medical Center	The Netherlands	Guido Jenster
University of Sheffield	United Kingdom	Jim Catto
Lund University	Sweden	Yvonne Ceder
Exiqon A/S	Denmark	Thomas Litman
Orion Corporation	Finland	Pekka Kallio
University of Turku	Finland	Olli Kallioniemi

Table 1: Participants of ProspeR

After the initial discovery and validation phases, tools based on the newly identified ncRNA will be developed for diagnostics and prognostics. Prostate cancer cell lines will be used as *in vitro*, and prostate cancer xenografts as *in vivo* models in the validation and implementation phases.

ProspeR will deepen our understanding of the role of ncRNA in prostate cancer predisposition, development and progression. By doing so, novel biomarkers will be identified and validated for clinical use. It should also indicate novel drug targets for the lethal form of the disease, hormone-refractory prostate cancer.
The project will produce results of different levels: 1) scientific publications, 2) PhD theses and other forms of research training, 3) innovations for diagnostics to be exploited further by industry, 4) diagnostic kits to be directly commercialised, and 5) innovations for drug development to be exploited further by industry.

Further information about the ProspeR project can be obtained from Dr. Outi Saramäki, Project Manager of ProspeR,
via e-mail
(outi.saramaki@uta.fi) and from the ProspeR web-site at
www.uta.fi/imt/ProspeR.

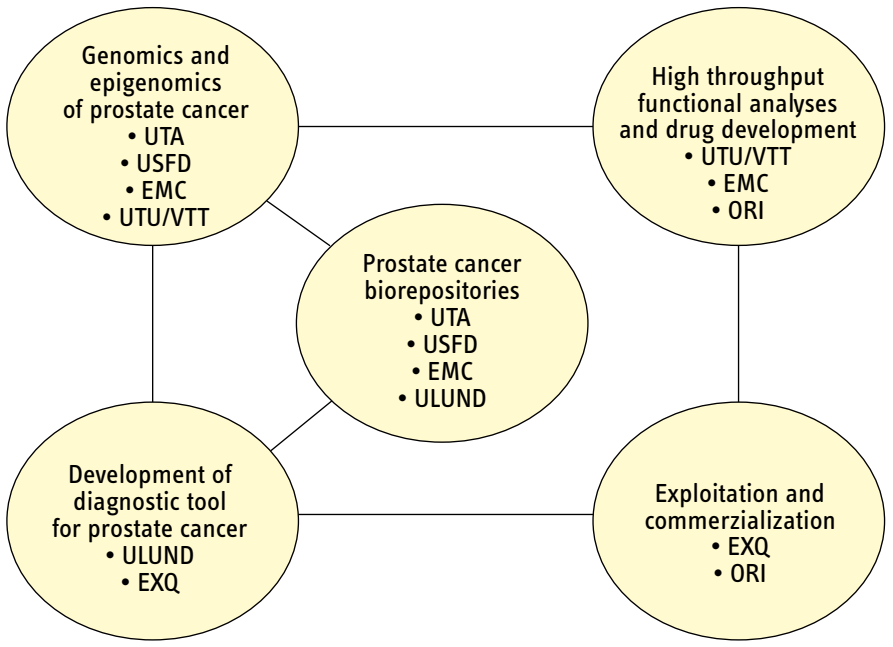

Figure 1: Expertise of ProspeR

Congress calendar 2009

5-8: New Orleans, LA, United States
2009 Society for Basic Urologic Research Fall Annual Meeting
Website: www.sbur.org/meetings/
E-mail: info@sbur.org

18-21: Paris, France
Annual Meeting Association Française d'Urologie (AFU)
Phone: +33 1 44 641 515
Fax: +33 1 44 641 516
E-mail: am.merienne@colloquium.fr
Website: www.urofrance.org

19-20: Budapest, Hungary
Semmelweis Symposium 2009
"New trends, innovations and technology in urology"
Venue: Semmelweis University
Contact: Prof. I. Romics
E-mail: romimre@urol.sote.hu

27-29: Barcelona, Spain
2nd European Multidisciplinary Meeting on Urological Cancers (EMUC)
Contact: Congress Consultants
E-mail: emuc-meeting2009@congressconsultants.com
Website: www.emucbarcelona2009.org

For more elaborate information on all EAU meetings please contact Congress Consultants or consult the EAU website:
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For more elaborate information on all ESU courses please contact the European School of Urology or consult the EAU website:
Phone: +31 (0)26 389 0680
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E-mail: esu@uroweb.org
Website: www.uroweb.org

Full, continually updated urological meeting calendar at www.uroweb.org

www.reviews

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www.uropathology.org

This web site is entirely dedicated to uropathology and is the official site of the British Association of Urological Pathologists. The site is simple and easy to navigate. From the home page it is possible to have information about previous activities and courses, but more interestingly users can also click on future scheduled courses, which redirects or provides the option to register directly on line. Don't forget to visit the EQA page, where an interesting web-based course on prostate biopsy is presented!

www.uroportal.net

Although mainly written in Spanish, this web site merits more than a cursory visit. The home page is very rich and allows for easy navigation to the website's various pages. All aspects of urology are reported. It is also possible to have free access to a full video clip of urological procedures, as well as videos and slides of urological courses on different topics held or presented in important events and courses all over the world. In other words: this website provides handy updates without you leaving the comfort of your favourite chair.