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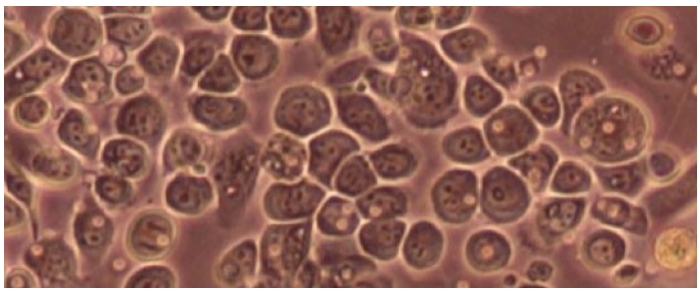
Uncovering the Genetics of Prostate Cancer

Germany will contribute another project to the International Cancer Genome Consortium (ICGC). Coordinated by the German Cancer Research Center and the University Medical Center Hamburg-Eppendorf, physicians and molecular biologists will now start to investigate the genetic causes of early prostate cancer. The German Ministry of Research and Education will provide funds of 7.5 million euros for the project.

Prostate cancer is known to occur typically in older men. Yet some patients are younger than 50 years at the time of diagnosis. Scientists assume that these cases might be the key to understanding the biology of this disease. Early prostate cancer might be a subtype which is characterized by a relatively small number of genetic modifications. Cancer researchers believe it is likely that these include a number of what are called 'driver mutations' which extremely promote the development and growth of prostate cancer. Moreover, researchers assume that prostate cancer with hereditary background, which is not yet entirely understood, is more likely to occur in men under age 50.

In a research network funded by the German Ministry of Research and Education with € 7.5 million, physicians and scientists are now planning to uncover the genetics of early prostate cancer. This is the aim of a collaborative effort involving scientists from the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), the National Center for Tumor Diseases (NCT) in Heidelberg and colleagues from the University Medical Center Hamburg-Eppendorf (UKE) and Martini-Klinik in Hamburg-Eppendorf. The European Molecular Biology Laboratory (EMBL) in Heidelberg and the Max Planck Institute of Molecular Genetics in Berlin will also participate in the project.

The project is part of the International Cancer Genome Consortium (ICGC). This consortium globally captures characteristic genetic modifications of the most important types of cancer. By now, more than 20 countries have joined the endeavor.



After the project was officially approved in December, work will start in January to decipher the tumor cell genome of 250 prostate cancer patients aged 50 or younger and to compare it with the gene sequences from healthy cells of the same men. This will help to discover those gene mutations that cause and promote prostate cancer. With this giant project, the researchers aim to produce a complete map of all genetic modifications involved in prostate cancer.

"We have high hopes for the project to find new markers for diagnosis and new treatment approaches for prostate cancer," said Associate Professor (PD) Dr. Holger Sültmann of DKFZ, coordinator of the network. "Focusing our project on young patients is also very likely to produce findings about the causes of hereditary prostate cancer," says Professor Guido Sauter, Director of UKE's Institute of Pathology and co-coordinator of the research project. "Our long-standing collaborations with the project partners, which have been established primarily with the support of the Research Ministry, have created excellent conditions for this project," Sültmann confirms.

With more than 60,000 cases newly diagnosed each year just in Germany, prostate cancer is the most common tumor affecting men; each year, 10,000 men die from prostate cancer. As life expectancy is rising, these figures will dramatically increase over the years to come. Therefore, we urgently need new and better diagnostic methods for prostate cancer. Early detection of aggressive tumors and their discrimination from benign diseases of the prostate is crucial for determining the best possible treatment for each individual patient. Study participants were recruited from more than 2,000 prostate cancer patients undergoing surgery at UKE's Martini-Klinik every year. Martini-Klinik is the only hospital in Germany which specializes exclusively on prostate cancer. "More than 150 patients each year belong to the group of patients aged 50 or younger," says Dr. Thorsten Schlomm, Scientific Director of Martini-Klinik.

The molecular analysis of prostate cancer is not the only project participation of DKFZ in the International Cancer Genome Consortium. Coordinated by DKFZ, researchers from Heidelberg, Dusseldorf and Berlin have been working together in the "PedBrain" network since January 2010 to analyze the genome of childhood brain tumors. Furthermore, scientists from DKFZ are partners in the German ICGC network for the analysis of malignant lymphomas.

Tasks distributed: Gathering, Sequencing, Analyzing

The various tasks of the ICGC project on early prostate cancer are headed by internationally acclaimed experts. The common goal is a comprehensive molecular analysis of prostate tumors. Using various methods, the researchers will capture the sequence of DNA building blocks in the cell nucleus. The sequence of DNA segments containing a blueprint for proteins will be analyzed separately. Another subproject will investigate DNA areas which are silenced by chemical labels known as epigenetic mutations. Yet another research group will study the small RNA molecules that regulate the activity of individual genes.

An extraordinary challenge is the analysis and storage of the unimaginable masses of data which are produced in the course of the International Cancer Genome Project. The genome of a cell is composed of about three billion building blocks, which are captured up to 30 times in various analyses in order to assure the quality of results. All data of the German ICGC projects will be joined together by Professor Roland Eils, who is head of the Theoretical Bioinformatics Division of DKFZ. To this end, Eils has built one of the world's largest data storage units for life sciences at the BioQuant Center of Heidelberg University. It will have a

storage capacity of several petabytes - a petabyte is equal to one million gigabytes, or a one followed by 15 zeroes!

Subprojects and Project Heads

- Patient selection, tissue preparation, histopathological and clinical classification of tumors, preparation of nucleic acids and clinical validation of genetic modifications: Guido Sauter (project co-coordinator), Institute of Pathology of the University Medical Center Hamburg- Eppendorf; Thorsten Schlomm, Hartwig Huland, Martini-Klinik Eppendorf
- Paired-end sequencing: Jan Korbel, European Molecular Biology Laboratory (EMBL)
- Sequencing of genomic DNA: Hans Lehrach, Marie-Laure Yaspo, Max Planck Institute of Molecular Genetics, Berlin, Stefan Wolf, German Cancer Research Center
- Methylome sequencing: Christoph Plass, German Cancer Research Center
- Transcriptome and miRNA sequencing: Holger Sültmann (project coordinator), Christof von Kalle, German Cancer Research Center and National Center for Tumor Diseases (NCT) Heidelberg
- Data management and bioinformatics: Roland Eils, Benedikt Brors, German Cancer Research Center and University of Heidelberg

Joint Press Release of the German Cancer Research Center (DKFZ) and the University Medical Center Hamburg-Eppendorf (UKE)