

## HANS BOS, SCIENTIFIC DIRECTOR OF THE CANCER GENOMICS CENTRE:

# THE CGC IS WELL EQUIPPED TO PLAY A KEY ROLE IN CANCER RESEARCH

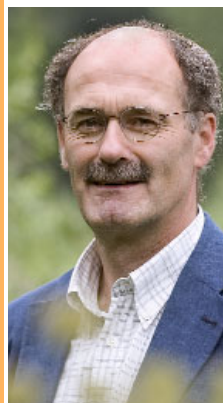


Photo Hans Bos: Henk Rougoor, Amstredam

Photo DNA lab: Hans Bosschieter, RSG De Nieuwe Veste

The Cancer Genomics Centre (CGC) started at the end of 2002 as one of the centres of excellence within the Netherlands Genomics Initiative. The idea behind clustering the best cancer research in the Netherlands in this centre is to combine the best expertise and knowledge in order to improve cure rates for cancer patients.

Every year, 69,000 people in the Netherlands are affected by cancer, and approximately 37,000 die from the disease. Multiply these numbers by 20 and you have a picture of those affected across Europe.

The aging of the population will lead to a further rise in the incidence of cancer and will soon make the disease the primary cause of death for individuals at young, middle and old age. So increasing the research efforts in this area is more than justified. Other objectives of the centre are knowledge valorisation and informing the Dutch society at large about cancer genomics research and its (im)possibilities for cancer diagnosis and treatment.

**H**ans Bos, professor of Physiological Chemistry at the University Medical Centre Utrecht (UMC Utrecht), who became the new scientific director of the Cancer Genomics Centre in March 2004, says that the CGC is well equipped to play a key role in cancer research. "The four main areas of research within the CGC are molecular profiling of tumors, mechanisms of genetic stability, functional screens and cancer proteomics. Research in these areas ranges from small-scale experiments to large-scale clinical trials using genomic approaches. This will help us to get a complete picture of the genetic hinges that turn a normal cell into a tumor cell, allowing us to define suitable targets for diagnosis and therapeutic intervention."

#### Disease of the genes.

A limited number of genetic mutations can turn a healthy cell into a tumor cell. Over the past 25 years, researchers have acquired a basic understanding of the tumor cell. A number of cancer-causing genes (oncogenes) have been identified, and some pathways in which these genes act have been uncovered. However, to effectively attack each of the

different cancers, a detailed picture of the underlying mechanisms that can turn a normal cell into a cancer cell is needed. This requires large-scale data acquisition and analysis, extensive studies into the correlation of molecular parameters and patient histories, and studies in model systems that permit full exploitation of the power of experimental molecular genetics and genomic analysis.

#### Genomics and clinical practice

The rapid developments in the field of genomics are expected to lead to a further increase in the potential for early diagnosis, the fine-tuning of prognostic features of specific tumors and the detection of cancer predisposition. Each new development and each new technique raises the question of how to assess its consequences for putative users. Little is known about how these genomics-related developments will affect the ways in which doctors, patients or the lay-public perceive, define and cope with cancer risks, diagnosis and therapy. In order to define how these new diagnostic tools might shape their likely future actions, studies are needed of how aforementioned groups have used genetic information in the past and at present in conceptualising cancer risks and defining medical coping strategies. A collaborative research project of the Cancer Genomics Centre and the Centre for Society and Genomics (CSG, another centre of excellence of the Netherlands Genomics Initiative) will address these questions.

#### Strong research groups

The Cancer Genomics Centre brings together research groups from the Netherlands Cancer Institute, the Hubrecht Laboratory, the Erasmus Medical Center and the University Medical Center Utrecht. Participants contribute complementary expertise combined with the largest collection of clinical material, patient databases and clinical expertise in the Netherlands. The CGC was established in October 2002 with a 14.6 million euro, five-year grant from the Netherlands Genomics Initiative (NGI). Hans Bos: "We divide the money on the basis of equality. For instance the three groups in Utrecht, lead by Hans Clevers, Ronald Plasterk and myself, receive each one third of the money reserved for Utrecht." When questioned if it is not difficult to 'manage' the ten top research groups headed by internationally renowned researchers, Hans Bos shakes his head and states that it is rather the contrary: "The great advantage of working with strong research groups is that every group is an entity of its own, with its own coordination and its own responsibility. My role as a director of the CGC is mainly being coordinator: I absolutely don't have to waste any energy on 'managing' these groups."

#### Knowledge valorisation

In addition to excellent research, the centres of excellence put much emphasis on two other issues: knowledge valorisation and informing the public. These days the magic word in research and subsidy country is 'knowledge valorisation'. How suffocating is this concept to a researcher? Hans Bos says he understands the wish from

the subsidizing ministries to see value for money. Industrial and commercial developments are essential not only to establish how viable the research outcome is, but also to generate new funds for further research. Yet he warns against inflated hopes for the near future. "A valorisation system like this does not work right away. It needs time to develop and find its way." The issue was important enough to install a special 'valorisation officer', **John de Koning**.

#### Informing the public



Hans Bos underlines the fact that he is merely the scientific director - i.e. coordinator - of the CGC. Daily management and visibility towards the public are explicit tasks of managing director **Annelies Speksnijder** who has given the centre a clear energetic push since her arrival in July 2004. "She is the one to remember, she is the one to address your questions to", Bos insists. Indeed, Annelies Speksnijder has been busy with several projects that enhance the visibility of the centre. One is a symposium on October 15th 2005 on 'Genen, fout DNA en kanker' that the CGC organized together with the Borstkanker Vereniging Nederland (Dutch association of breast cancer patients). Speksnijder: "The idea of a symposium like this is that we want to discuss the relevance of genomics research with those whom it concerns most: cancer patients. They have questions such as: 'Why do DNA tests take so long?' or 'What about the use of laboratory animals, our right on privacy, the use of new or experimental therapies?'" On the occasion of the symposium the CGC publishes a book containing the contributions of all symposium speakers that will be sent to the 6500 members of the Borstkanker Vereniging Nederland, October is a busy month for the CGC: on October 1st the public website [www.watisgenomics.nl](http://www.watisgenomics.nl) launches its new theme 'Cancer & Genomics' in collaboration with the CGC. The aim is to inform the public about how a healthy cell turns into a cancer cell and how genomics research is of importance in the development of

### Genomics offers new promising opportunities for cancer research

novel therapies and diagnostic tools.

On October 27/28th the two-day CGC/CBG meeting focuses on 'Approaches and Molecular Mechanisms in Cancer'. Internationally renowned speakers from all over the world will be there. And the CGC is very proud to have Nobel Prize Laureate Harold Varmus (Sloan Kettering Memorial Cancer Center, New York, USA) as the first day's keynote lecturer. (For more information and registration go to [www.cancer-genomics.nl](http://www.cancer-genomics.nl))

#### CBG was the cradle of the CGC

Hans Bos: "The CGC owes a great deal to the Centre for Biomedical Genetics (CBG). The CBG was almost literally the cradle to the Cancer Genomics Centre: it was in many ways 'a piece of cake' to have our research groups work together,



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because we already did in several areas within the Centre for Biomedical Genetics. The CBG is a national research combination just like the CGC. The core of the Centre for Biomedical Genetics is formed by six research schools with their roots in four Universities. From these schools, 15 groups have been selected based upon the quality of their research. Together, these groups combine a wide range of expertise required to carry out the research programme, including Genetics, Molecular and Cell Biology, Biochemistry and Structural Biology. Most groups work in a medical setting which facilitates transfer of knowledge to clinical groups. The same goes for the Cancer Genomics Centre."

## DNA laboratories for schools

The Netherlands Genomics Initiative encourages its centres of excellence to not only inform the public, but also aim at education. The CGC will start in January 2006 with a so-called DNA-lab on cancer genomics. Speksnijder's assistant Marc van Mil has developed the material for the DNA-lab that will be taught on secondary schools (4/5/6 have en vwo) in the Netherlands. The lab will first be tested in the region of Utrecht, but contact has been established with about 500 schools, so they hope that a lot of schools will show interest. During a two-hour biology class, motivated students of Utrecht University will give this interactive DNA lab. The series of a total of 5 DNA-labs of the different centres of excellence of the Netherlands Genomics Initiative is called 'De reizende DNA-labs' (mobile DNA labs). The laboratory developed by the CGC is called 'Lees de taal van de tumor' ('reading the tumor') and tries to show how research on the DNA of a tumor can help the physician to come to a better diagnosis and treatment of the patient. Marc van Mil says that he is not afraid of high school students being shied away by the subject: "On the contrary, I expect most of them to be quite curious. Some of them will also know cancer from a situation in their family. During the lessons we will actually show a sample of cancer tissue, and explain how through genomics a lot more information is available than just the location of the tumor in the body. Role-playing is an important part of the DNA-lab. We ask the students to act as genetic researchers and find DNA defects. To this effect, they actually carry out DNA isolation as well as duplication by PCR (Polymerase Chain Reaction). Based on the results of their laboratory exercise, they are supposed to advise the physician on the best treatment for the patient. In the end they will also discover answers to their questions like: can I prevent cancer? Which treatments are possible? Is cancer hereditary? Is it contagious? Cancer is not only a mys-

terious, terrible disease, but also a biological phenomenon with a clear message: be careful with your DNA."

## Added values

Do centres like the CBG or CGC, but also the ABC truly present added values in terms of research outcome? Peter van der Vliet, director of the Centre for Biomedical Genetics that was given the go-ahead to continue operating until the end of 2008 by NWO and the minister of OC&W, confirms this: "We did indeed achieve several goals, amongst which the (new) collaborations between different research groups and the outcome in terms of research and publications are the most important." Also Hans Bos says that clustering knowledge and expertise present clear added values. "Think of the infrastructure in terms of state-of-the-art equipment and expertise centres. Think of the increased solidarity and collaboration, as well as the improved visibility towards both colleagues in the world as well as the public. Also in Utrecht, I honestly think that starting the ABC as a cluster of all Life Sciences, and setting up state-of-the-art infrastructure, was a very good move. It shows that the UU-board has vision and guts to start something that didn't or even doesn't exist in other universities."

## Promises for the future

Finally we ask the journalist's inevitable question if a major breakthrough in cancer research is to be expected soon. Hans Bos smiles: "Breakthroughs are of course impossible to predict, but it is not difficult to predict that in the next decade genomics will have a profound impact on how we look at cancer. Genomics will play a role in diagnosis, in predicting the prognosis and in designing optimal therapies. In addition, we will get a much better insight in the molecular mechanism of cancer. With respect to my own field of research, signal transduction, which - at the cellular level - refers to the movement of signals from outside the cell to inside, I predict that this will be a main playing field for finding new targets for novel therapies. Indeed in cancer cells signal transduction is defect due to mutations in the genome." The essence of life seems to be merely communication after all!

## Cancer Genomics Centre: objective and mission

The Cancer Genomics Centre brings together prominent cancer research groups from the Netherlands Cancer Institute, the Hubrecht Laboratory, the Erasmus Medical Center and the University Medical Center Utrecht.

The primary objective of the CGC research program is to obtain a complete picture of the genetic changes that turn a cell into a tumor cell and a full understanding of how each of these changes contributes to the behavior of tumor cells.

The mission of the Cancer Genomics Centre is to improve diagnosis, therapy and cure rates for cancer patients. Genomics offers new promising opportunities for cancer research, with realistic expectations for therapy improvement in the coming decade. For instance, the genomics signature of the cancer and that of the patient may serve in the near future as a basis on which to choose the most effective therapy for the individual patient ('personalized medicine') to improve cancer patients chances of recovery and their quality of life.

## Research Themes of the Cancer Genomics Centre

### MOLECULAR PROFILING

Combining molecular profiling of expressed genes in tumor tissue with advanced bioinformatics tools is beginning to show its power in revealing disease characteristics that are otherwise indistinguishable. This can be used to refine current tumor classification methods and allows for a more accurate prediction for patients of the disease outcome. Using molecular profiling, treatment schemes can be tailored to the patient's needs. This research theme will focus on four main tumor types: breast cancer, melanoma, lymphoma and prostate cancer. Program director: Dr. L.J. (Laura) van 't Veer  
Contributors:

- NKI: Prof.dr. R. (René) Bernards, Prof.dr. S. (Sjoerd) Rodenhuis, Prof.dr. F.J. (Floor) van Leeuwen, Prof.dr. A. (Ton) Berns, Dr. L.J. (Laura) van 't Veer
- Erasmus MC: Prof.dr. J. (Jan) Klijn, Prof.dr. F.G. (Frank) Grosveld

### GENOME (IN)STABILITY

One of the hallmarks of cancer is the occurrence of genetic instability. It drives the initiation and progression of tumorigenesis (the emergence of a tumor) and frustrates effective therapy. Tumor cells display a wide array of derailments in genome control and repair systems, which allows tumors to rapidly acquire new properties. We aim to establish a comprehensive, systematic screening for genes that are implicated in genome stability. The mode of action of these genes will be examined at a molecular, cellular and organismal level. Knowledge of genome stability is highly relevant for the treatment of cancer and we expect this project to yield new critical targets for diagnosis and treatment and possibly novel etiological factors as well.

Program director: Prof.dr. J. (Jan) Hoeijmakers

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- Hubrecht; Prof.dr. R. (Ronald) Plasterk

### FUNCTIONAL SCREENS

Research in this theme aims to identify novel genes that are involved in cancer-relevant pathways. Such genes are prime targets for drug discovery programmes. We will use two types of functional screens: gain-of-function and loss-of-function, both to be performed in cultured cells and model systems. Identification of genes will be followed by validating them for therapeutic intervention, using RNAi inhibition techniques. The next step, identifying suitable drugs of therapeutic interventions, requires a more industrial approach. Therefore, we see this project as particularly suited to generate new spin-offs or collaborations with existing (bio)pharmaceutical companies

Program director: Prof.dr. R. (René) Bernards

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- Erasmus MC: Prof.dr. F.G. (Frank) Grosveld, Prof.dr. J. (Jan) Hoeijmakers
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- NKI: Prof. dr. R. (René) Bernards, Prof. dr. A. (Ton) Berns

### CANCER PROTEOMICS

The main focus of this theme is the identification and classification of differences in protein expression and modifications that underlie the cancer process. Using mass spectrometry and sophisticated pre-purification protocols, protein modifications and protein-protein interactions will be studied. This approach is particularly promising for early diagnosis and monitoring the response to therapy. In addition, better insight into those modifications that are of critical importance to the properties of the tumor will create possibilities for highly specific intervention strategies

Program director: Prof.dr. J.L. (Hans) Bos

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More information on the Cancer Genomics Centre: [www.cancer-genomics.nl](http://www.cancer-genomics.nl)

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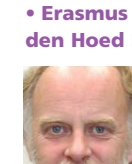
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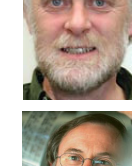


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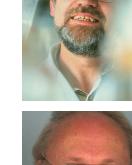


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