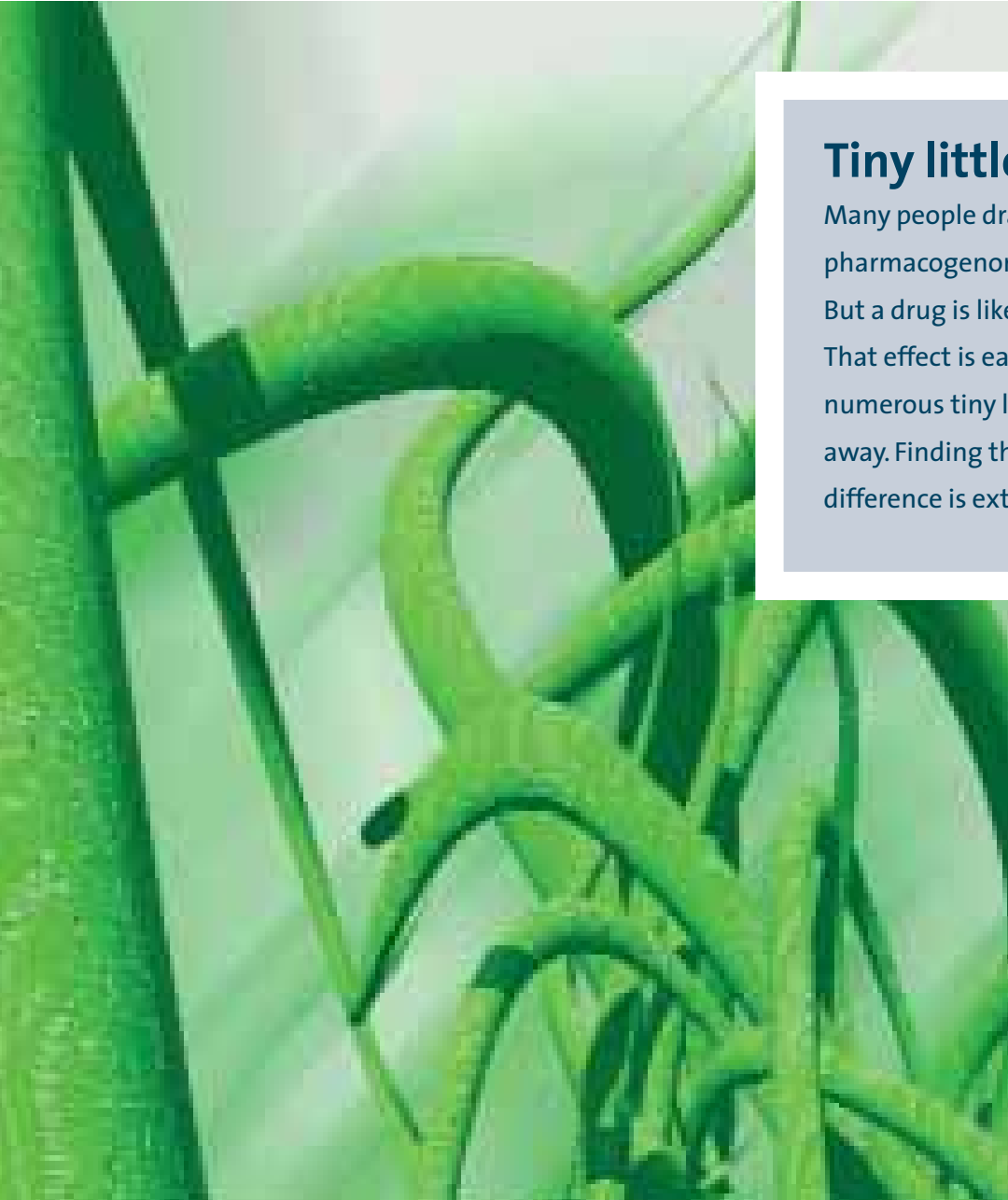


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Tiny little hammers

Many people draw a parallel between pharmacogenomics and nutrigenomics. But a drug is like a sledgehammer. That effect is easy to measure. In nutrition, numerous tiny little hammers are ticking away. Finding the one that makes a difference is extremely hard. [PAGE 2]

Scientists and artists merge in Arts & Genomics Centre

The Arts & Genomics Centre aims to bring together artists, genomics researchers and art historians to investigate the interactions between arts and genomics and to analyse the role of art in the cultural embedding of genomics into society. [PAGE 6]

Treasure hunting with ecogenomics

The Ecogenomics Consortium aims at unlocking soil's potential for (bio-)remediation, agriculture and nature conservation. Among the hidden treasures of the soil we may discover (micro-)organisms capable of producing chemicals that can be used for making medicines and other useful substances. [PAGE 4]

A marathon investment

Prof. Dr Peter Folstar [Director NGI]

NGI has, since its inception in 2002, established a strong genomics infrastructure in the Netherlands. The organisation's deliberate and focused approach from the very beginning of combining excellent research with business, industrial and societal involvement has proved successful. The genomics network, which includes 11 world-class centres of excellence, is up and running and the first results are in. Also, NGI has helped the Netherlands establish itself as a key player in the global genomics arena by demonstrating its firm resolve to be a leader in this increasingly important field.

Genomics has set in motion an irreversible dynamic that will bring about enormous changes and significant improvements in the areas of health and healthcare, food, the environment, and industrial production chains and processes. This raising of the Netherlands genomics infrastructure to a higher level has created new opportunities not only for Dutch science and industry, but for the country's economy and people.

At Genomics Momentum, this year held on 5th of October, you can find proof of these changes and improvements; more than 25 renowned speakers will lecture on the emerging benefits of genomics in their specific field of work. A wide variety of topics will be presented and discussed, like clinical diagnostics, personalised diets, biodiversity, healthy food ingredients, complex phenotypes and many more. At the Plaza, the lively heart of the Genomics Momentum, more than 35 exhibitors show their latest achievements, applications and research results.

Over the past years the Genomics Momentum has truly grown into *the* genomics network event in the Netherlands; it brings together everybody who deals with genomics in his work one way or the other. It forms an essential part of NGI's task to bring together research, business and society in the earliest phase possible. We are therefore looking forward to this 5th Genomics Momentum and hope to meet you there.

Nutrigenomics Consortium concentrates on how nutrition works



Michael Müller
[Nutrigenomics Consortium]



Rune Frants
[Leiden University Medical Center]



Ben van Ommen
[TNO Quality of Life]

Tiny little hammers

Keeping people healthy. That is in short the ambitious goal of the Nutrigenomics Consortium, one of the NCI Innovative Clusters and a joint effort of Wageningen Centre for Food Sciences and Centre for Medical Systems Biology. “The healthy state is our starting point,” says Michael Müller, professor of Nutrition, Metabolism and Genomics at Wageningen University and director of the Nutrigenomics Consortium. “From there we want to map out in detail how the body moves from that healthy state into disease and what role nutrition plays in this process.”

Overload

The consortium concentrates in particular on metabolic syndrome: a disorder characterised by obesity, high blood pressure and increased levels of fat in the blood. Research into metabolic syndrome is highly relevant considering the surge in numbers of people affected by obesity. Furthermore, metabolic syndrome is a major risk factor for developing type 2 diabetes and/or cardiovascular disease. Müller: “We are interested in the very early phase, before symptoms like obesity start to develop. Therefore we concentrate on ‘metabolic stress’, the precursor of metabolic syndrome. In metabolic stress, the body is chronically exposed to a certain nutritional overload, for example too much fat.”

Because nutrition is complex and the effects are very small, extremely sensitive measuring methods are required. “Using microarrays and metabolomics, we are measuring - in a mouse model - what exactly happens in the gut, liver, muscle and fat tissue during the nutritional overload. How do the organs compensate? And when does the system start to lose control?”

Danger zone

Müller explains that although this type of research provides fundamental insights into nutritional mechanisms there is also a clinical perspective. “We want to find biomarkers that indicate the transition from being healthy to being ‘not so healthy’. By measuring at an early stage whether someone is moving into the danger zone, dietary interventions can be applied to bring that person back into the healthy state before full blown metabolic syndrome develops.” There is an industrial perspective as well. Nutrigenomics research offers valuable information on satiety mechanisms and insulin sensitivity. These are important matters for the food industry according to Müller. “A major problem is that our satiety system is quite old-fashioned and not suited to cope with today’s convenience food, as produced by the industry. Food needs to be composed in such a way that the feeling of satiety is in line with the caloric intake. That is a challenge and an opportunity for industry: developing tasty food products that don’t trigger overeating.”

Sledgehammer

The Nutrigenomics Consortium also approaches the problem from the medical genetics side. Rune Frants is professor of Human Genetics at Leiden University Medical Center (partner in CMSB) and works on genetic predisposition to complex

diseases and how genetic factors influence the sensitivity to certain nutrients. “As a geneticist I see it as a responsibility to concentrate on genetic disorders or profiles that are most affected by a certain food component. So that we can warn people who are already at risk of developing disease due to the dangers of their diet.” Finding relationships between genetic defects and nutrient sensitivity is very difficult however. Frants: “Many people draw a parallel between pharmacogenomics and nutrigenomics. But a drug is like a sledgehammer. That effect is easy to measure. In nutrition, numerous tiny little hammers are ticking away. Finding the one that makes a difference is extremely hard.”

Screening

The entrance of genomics into medical research and drug development sparked the concept of ‘personalised medicine’, medical treatment that is specifically geared to the patient’s individual needs. How about nutrigenomics? Can we expect a ‘personalised diet’ in the future? That is probably one step too far according to both scientists. “A person’s genetic make-up is not the decisive factor. Lifestyle, food and environmental factors all play a role. We can at most indicate risks,” says Michael Müller. Rune Frants agrees: “The genetic component is only a small player. Environmental factors are very important and they in turn activate or deactivate other genes as well. Genetic screening of the general population aimed at providing personal food advice is therefore not feasible, the predictive value is simply too low.”

Healthy diet

Then what can the general population expect from nutrigenomics? A healthier overall diet. And that could already be a major step forward. Frants: “If we’re able to make ‘slow food’ better than ‘fast food’, we can really make a difference. Let’s say we’re able to slow the progress of obesity by five years; that would have enormous impact. We’re talking about one-third of the population!” Evidence-based nutrition is the key. Müller: “If we want to convince people to change their diet, we need to be able to really show them why. That requires understanding of how nutrition works at the basic level.” The Nutrigenomics Consortium has the expertise to bring nutrition research a big step forward. Rune Frants: “This consortium is a combination of nutritional research at population level and of medical genetics research. It’s the best of both worlds.”



Take food research to the next level



According to Ben van Ommen, many researchers feel that the traditional nutrition science approach needs a new impulse. "It's perfectly clear that there is a relationship between nutrition and health, but what that relationship exactly is remains elusive. Detailed research is needed." Van Ommen is Senior Research Fellow at TNO Quality of Life and project coordinator of the European Nutrigenomics Organisation NuGO. "Nutrition is very complex; we're talking about hundreds of bioactive compounds. Thanks to the '-omics' technologies, we are now able to measure and describe the effects of nutrition." Is the international nutrition science field open to nutrigenomics? "Yes, things are starting to come together. At present, nutrigenomics still embodies a revolution within nutritional research, but it should become an integral element over time; not an independent research field. We want to take food research to a higher level."

Metabolomics

Even though nutrigenomics is on the rise, the Nutrigenomics Consortium is still rather unique. Van Ommen: "I only know of one similar initiative: Nutrigenomics New Zealand. They have a budget of around € 8 million and primarily concentrate on gut health." When it comes to an international coordinated effort, NuGO is the only one so far. "We aim to bring all the top nutrigenomics research groups within Europe together. Our activities involve technology development and exchange, establishing standards and ultimately, we aim at a collective research agenda." NuGO was the first Network of Excellence to be funded by the EU Sixth Framework Programme and has a budget of € 17 million. Nutrigenomics is still a fast developing area, and Van Ommen already sees another important technology platform coming: metabolomics. "Nutrition is metabolism", he explains. NuGO is already on top of it. "We are currently working to set up an international nutritional metabolomics consortium."

Treasure hunting with ecogenomics

The Ecogenomics Consortium explores the living soil and aims at unlocking its potential for (bio-)remediation, agriculture and nature conservation. Among the hidden treasures of the soil we may discover (micro-)organisms capable of producing chemicals that can be used for making medicines and other useful substances.



➤➤➤➤ **Bram Brouwer** is professor of Environmental Toxicology at the Vrije Universiteit van Amsterdam, CEO of Bio Detection Systems BV and coordinator of the Ecogenomics Consortium. ◀◀◀◀

"With ecogenomics we are able to assess the potential of the living soil. Although we have walked the earth for thousands of years, there is still a lot we don't know about the micro-organisms and microbial communities it contains. Estimations are that at least ninety per cent of soil bacteria are 'unculturable', i.e. they refuse to grow in a Petri dish. Among these might be some species that are very interesting for instance because they produce new types of antibiotics."

"The strategy for unravelling the hidden treasures is to analyse the 'metagenome', that is the collective genomes of all living organisms in a soil. The US approach is to sequence all available DNA; an enormous task, much larger even than sequencing the Human Genome. Our approach is to extract and clone large chunks of DNA and establish their functionality. For instance by linking DNA-fragments to a certain type of enzyme activity. Or by analysing changes in gene expression in a DNA-array when applying nutrients or other chemicals to the soil. We hope this functional approach will lead the way to applications of soil ecogenomics in agriculture or soil remediation."

"One of the first steps of the Ecogenomics Consortium is to define a default: a soil ecosystem or a range of soil ecosystems that can be considered healthy and free of the stress of an excess amount of nutrients or polluting chemicals. Although a 'standard soil' does not exist, we hope to identify a so-called 'normal operating range' for different types of soil ecosystems. Any soil deviating from that range can be considered as being under stress, with possible consequences both for the soil ecosystem itself and for the way in which you want to use it, be it for nature conservation, for agriculture or any other use."



“As with any new technology, ecogenomics, its tools and results have to be embedded in society. That is why the Consortium pays a lot of attention to social acceptance of ecogenomics. The earlier you involve the stakeholders, the better the technologies you are developing can be adjusted to the needs of society.”



➤➤➤ **Jos Raaijmakers** is associate professor at the Phytopathology Department of Wageningen University and theme coordinator of the Consortiums research programme on disease suppressiveness and plant productivity. ◀◀◀

“The microbial community in the soil plays an important role in plant growth and health. On the one hand, many plant pathogens are located in the soil. They force farmers to apply broad-spectrum soil fumigants and/or rotate their crops. On the other hand the soil is also an untapped reservoir of micro-organisms that protects plants from pathogens and/or sustains their growth by making nutrients readily available. A classic example of the latter is the nitrogen fixation by both free-living and symbiotic bacteria.”

“Genomics gives us the tools to further identify the microbial community in the soil on a molecular level. By analysing the DNA in soil, the so-called metagenome, we try to define what makes a healthy microbial community for a certain crop. This knowledge can be used, for example, by applying micro-organisms to plants or seeds to suppress disease and stimulate their growth. In agriculture this has been done before, for instance by coating seeds with nitrogen fixing bacteria. In addition to soil bacterial communities, the ecogenomics project also focuses on the mycorrhizae, fungi that live in intimate association with plant roots. On a molecular level it should give us some clues about the mutual beneficial relation and how it can be enhanced and possibly even translated to other plants.”

“Genomics can also be used to establish if and how many beneficial and/or deleterious micro-organisms are available in the soil (‘the good, the bad and the ugly’). Eventually we hope to develop a micro-array for detecting microbial plant pathogens in soils. Depending on the type and abundance of specific pathogens, the farmer can use the information to take preventive measures, for instance by applying a fungicide. The ‘pathogen-chip’ will be expanded into a chip that also detects micro-organisms with a positive effect on plant health. Combined you get a ‘soil health’-chip, that helps the growers to decide what crop should be grown on which field and what type of measures should be taken to increase productivity.’

“The soil also contains micro-organisms that are able to make useful substances like enzymes, biocides or even antibiotics. A newly found species of soil bacteria, called *Collimonas fungivorans* has the capacity to ‘eat’ fungi. In itself it may be used as a biofungicide in the eternal struggle against fungal diseases of plants. But you might also use its enzymes for industrial applications or development of pharmaceuticals. Generally speaking I think the soil is a treasure cove for the discovery of a whole new range of micro-organisms and compounds. New developments in the genomics research area now allow us to further uncover this richness.’



➤➤➤ **Sytze Keuning**, CEO of Bioclear BV, Groningen, experts in environmental (bio-)technology. ◀◀◀

“We are very interested in ecogenomics, because knowledge of the DNA in soils and the related organisms helps us in the remediation of contaminated sites. Our company has a lot of experience in bio-remediation, which involves using micro-organisms to clean up the mess. Given time, oxygen and nutrients, most sites polluted by hydrocarbons can and will become clean again. Genomics will enhance our insight in the microbial profile of – polluted – soils, thus helping us to choose the most effective remediation approach. In some cases you will start an active remediation programme. In other cases the microbial profile and the contamination are such that you can decide to leave it alone and just monitor how nature takes its course.”

“Apart from the direct application in bio-remediation, ecogenomics is also instrumental in increasing our knowledge of the soil. The soil is a living, dynamic system characterised by an enormous biodiversity. Up until now our knowledge of soil was limited to its physical and chemical properties, but with ecogenomics we have a new instrument to evaluate its biological properties. These insights are helpful in deciding how much stress the soil system is enduring and how the stress can be relieved. They are also helpful in developing healthy ecosystems, whether for nature conservation or to create a more sustainable type of agriculture.”

“By opening up the possibilities of the soil and the organisms and processes therein, ecogenomics aims to create opportunities for innovation. I hope that during the next five or six years the foundations will be laid for a whole new dimension in soil research. We are happy to be part of that endeavour. Firstly because it gives you new insights in the living soil and secondly it could give us an advantage when we actually try to realise the options raised by ecogenomics research and translate them into new products and services.”

Awarded for knocking out rat genes



Dr Edwin Cuppen
[Hubrecht Laboratory, Utrecht]

Dr Edwin Cuppen of Hubrecht Laboratory in Utrecht received the European Young Investigators Award (EURYI) for his research on natural and induced genetic variation in the laboratory rat. Cuppen is project leader of the IOP 'Functional genome analysis in rat models'. He developed a method to knock out rat genes, which is quite unique. Worldwide only eight rat knockouts have been made, of which six in Utrecht. He and 24 other Awardees were selected on their potential to become one of next generations leading European researchers.

What does this prize mean to you?

"The effect is dual. On the one hand I have received € 1,2 million for my research group. That is a substantial amount, which is more than welcome. On the other hand it is a prestigious award that will add to the good reputation that is important for your network, and move others to get familiar with your work. That is very important since research funds are sparse."

What is the relevance of your research for society?

"Shortly put, it is fundamental research. It sounds simple but it is the truth. Of course we need fundamental knowledge as a basis to achieve applications. Looking at large developments in society and the pharmaceutical industry one can identify an important problem. A large part of the costs of public health care is for brain or geriatric diseases, such as depression and Alzheimer. A significant share of these costs is for medication. About 50 per cent of the profit of the pharmaceutical industry (as a whole) comes out of medicine for depression, so research in this field is economically worthwhile".

What has depression to do with rat models?

"If you look at which model organism is most suitable for examining this specific health care problem, then one has to conclude that the mouse model, which is the most used and defined, is not the best model. The rat, like us, is able to learn and unlearn fast. Also they react quite similarly in the field of addiction.

The reason that a lot of biomedical brain research is still done on mouse models is that the techniques to manipulate the mouse genome are well established. We took a different approach. If the rat is the best model organism for investigating brain diseases we have to develop the tools for that. And we succeeded. We are now able to knock out genes, for instance, the serotonin transporter, a gene involved in depression. Now we have a suitable model organism and the necessary tools to answer very specifically research questions about depression, addiction and so on."

Activities and initiatives directed to the public

Public communication has from the start been high on the agenda in NGI's plans. First of all because NGI, which is financed from public funds, wants to show 'society' what these public funds are used for. But more important is the fact that in the long run everyone will be confronted with genomics in their daily lives. NGI therefore sees it explicitly as its task to distribute accessible and usable information about genomics as widely as possible.

Website www.watisgenomics.nl

The website www.watisgenomics.nl (only available in Dutch) provides an informative and inspiring environment where visitors can form their own opinion about genomics. The website is intended for everyone who is interested in genomics, with special focus on students, teachers and journalists. www.watisgenomics.nl



GenomiX magazine

GenomiX magazine (in Dutch) primarily aims to familiarise its readers with the basic concepts of genomics. The magazine discusses genes and genomics in the context of topics that are interesting to young people, such as appearance, sex, pop stars and other celebrities, and crime. Approximately 700,000 copies of GenomiX were distributed by sealing them in with leading subscription youth magazines in the Netherlands. www.genomix.nl



Imagine...

Most life scientists will agree that the life sciences present unparalleled opportunities for alleviating problems in developing countries. In the near future, hunger and disease could be combated by boosting food production and rising nutritive values, with new vaccines and diagnostics, and in countless other ways. But what about the current state of affairs? Are concrete solutions for acute problems already available? 2004 marked the start of the unique Imagine... project that introduces scientists, pupils and public officials to the opportunities that fermentation and genomics technology can offer the Third World.

Imagine... is an initiative of the Kluyster Centre for Genomics of Industrial Fermentation, a Centre of Excellence initiated by NGI. www.kluystercentre.nl



The Arts & Genomics Centre, based at Science Park Amsterdam, is a new centre at the Swammerdam Institute for Life Sciences. Backed by a 4-year grant by the Social Component of Genomics Research programme of NWO/NGI it recently celebrated its official launch.

Scientists and artists merge in Arts & Genomics Centre

The Arts & Genomics Centre is part of a broad multidisciplinary research programme called "New Representational Space" which is carried out jointly at the Universities of Amsterdam, Leiden and Maastricht. Its aim is to bring together artists, genomics researchers and art historians to investigate the interactions between arts and genomics and to analyse the role of art in the cultural embedding of genomics into society. The centre provides support for different projects (like Kloone4000 – see below) and disseminates the results.

The underlying premise of the research programme is that, because of its specific character, art is able to critically examine genomics experiments and their results, visualise them and make genomics accessible for a broad public, without stereotyping. Art's role is especially relevant because the science depends on visualising a reality that is invisible to the naked eye (DNA, nanoparticles).

Artists who focus in their work on genomics (bio-genetic art) can contribute to the public debate and to the production of scientific knowledge in a new and special way. Their visual images are not only powerful tools in

forming the opinions and emotions of the public (more accessible than the numerical results of scientific research), but are able to point to new ways of thinking about the science itself. In order to achieve the dissemination of genomics research results from this artistic perspective, the centre initiates symposia, projects, debates, exhibitions and collaborations between artists and scientists.

Current activities of the centre are focused on creating a strong network of bio-genetic artists, both in the Netherlands and internationally and in creating opportunities for displaying and discussing their artwork. Also, the centre is establishing its own projects, such as an "Artists in Labs" programme in which an artist will be placed among scientists in a functioning lab.

Another of these projects is Kloone4000 by artist Anje Roosjen, which started on 16 September 2005 and will run for a period of six weeks. During this period, artists and scientists collaborate in a research project, a series of lectures and discussions on cloning, twins and genetic manipulation, and an ongoing changing exhibition. There is even a workshop on DNA isolation under the guidance of a bio-artist. The project is accessible to the public daily. The Arts & Genomics Centre has helped to facilitate the project by using their network in the scientific and artistic world, providing funds and giving administrative support. The Netherlands Genomics Initiative is supporting the Kloone4000 project as an example of how genomics and society can interact.



Anje Roosjen, "Can you believe this, Henry?" (Roseanna, Agnes, Suzy, Lucy, Isabella, Catherine, Josephine, Joanna, Olivia, Elisabeth, Camilla and Christina)

Anje Roosjen, Line-up sisters



Sylvia B., Les bêtes-noires



Netty van Osch, Symbiose



More info:

The Arts & Genomics Centre:
www.artsgenomics.org

The Kloone4000 project:
www.kloone.anjeroosjen.com

Genomics in Business 2005

Enhance the value!

From October 2 - 4, 2005, experts interested in exploiting the business potential of genomics in the Agro-Food industry come together at the international conference **Genomics in Business 2005**.

This unique international conference focuses on applying genomics in today's Agro-Food industry. Topics will concentrate on genomics applications in six areas: New Technologies, Food Quality, Food Safety, Plant Breeding, Animal Breeding, Applied Bioinformatics. Genomics in Business 2005 offers an interactive programme, including:

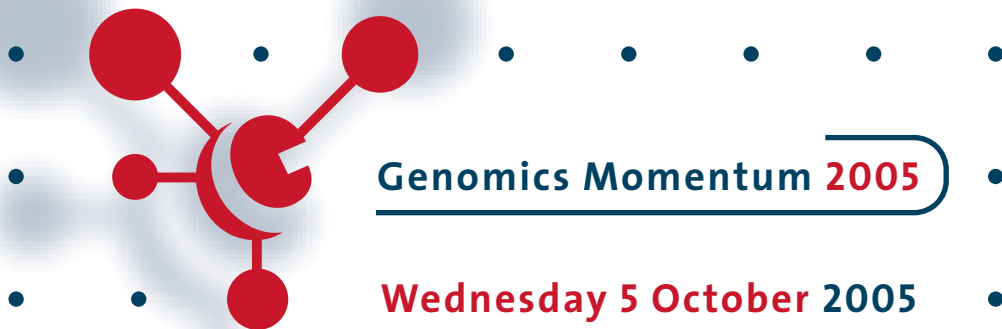
- Over 30 plenary and parallel session presentations and lectures by international leaders in business and science.
- Company presentations focusing on the commercial aspects in Genomics .
- Ample opportunity for making new contacts at the tabletop exhibition .

At Genomics in Business 2005 you will meet:

- programme directors, entrepreneurial scientists, industry researchers, research managers, financial managers and investors, managers from start-up companies as well as established industries and research programmes from 12 different countries worldwide.

Don't miss this chance to enhance the value and act quickly. The conference date is approaching soon. Check the conference website and register online now! → → → Register now at www.genomicsinbusiness.nl

C O M I N G U P S O O N



This fifth Genomics Momentum is going to be dynamic, lively and incredibly informative. It brings you up to date with the latest developments in genomics and life sciences. We have assembled for you:

- More than 25 renowned speakers
- More than 40 exhibitors
- More than 50 genomics topics
- More than 600 participants

Genomics Momentum 2005 offers you partnering sessions, business presentations, a special GeNeYouS session and much more.

Genomics Momentum is simply *the* opportunity to refresh your genomics knowledge and network. Don't miss it!

→ → → Register now at www.genomicsmomentum2005.org

NGI Highlights

- 2 - 4 October 2005
Genomics in Business 2005, international conference – sponsored by NGI - focused on applying genomics in today's Agro-Food industry.
www.genomicsinbusiness.nl
- 5 October 2005
Genomics Momentum 2005
www.genomicsmomentum2005.org
- 8 - 9 October 2005,
BioPOP Project - to encourage greater public understanding, Piazza Maggiore, Bologna, Italy
www.biopop-eu.org
- 27 - 28 October 2005
'Genomic Approaches and Molecular Mechanisms in Cancer'
International Meeting Cancer Genomics Centre
www.cancergenomics.nl
- 15 December 2005,
Societal Component of Genomics Research Themeday,
www.genomics.nl

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About the Netherlands Genomics Initiative
Backed by government authority and substantial resources, the Netherlands Genomics Initiative is shaping a national genomics strategy. We focus on doing only that in which we excel, that which is socially responsible and that which is truly innovative. We invite parties in science, industry and society to become involved.

For events, deadlines and additional information on the Netherlands Genomics Initiative and its activities, please visit

www.genomics.nl