GenomicsNL

Genomics NL is a special issue of the Netherlands Genomics Initiative (NGI), April 2007

HEALTH
At the basis of health and sickness lies a complex network of biological interactions. How does this network function, what exactly goes wrong when a disease develops, and how can we influence this process?

FOOD
What is the effect of food on our health? What determines the properties of a food crop? How can we make food tastier and healthier? Researchers are working hard on finding the answers to these questions.

SUSTAINABILITY
Producing more while at the same time causing less environmental burden is not easy, but it is most definitely necessary. The efficient use of microorganisms and sustainable agricultural crops can make a significant contribution.

PUBLIC COMMUNICATION
Investments in genomics are only worthwhile if society is willing to embrace the results. That calls for open communication in which people have enough room to form their own opinions.

Genomics is indispensable in converting the major challenges of the 21st century into opportunities for social well-being and economic growth. Health, food, safety and the environment are areas that touch us all. Areas in which genomics can make the difference.

Genomics makes the difference

Recognising the importance of this new technology, the Dutch government decided at the end of 2001 to make a large-scale investment - € 300 million - in genomics. This decision was based on three motivations:

- Genomics is essential to life sciences, which is one of the most innovative areas of contemporary science and industry, and an important pillar of the Dutch knowledge economy.
- A national, large-scale approach will generate an attractive climate for (young) scientists and innovative activity, two essential characteristics of a knowledge economy.
- Large investments in genomics and life sciences are being made in the EU, North America and Asia. The Netherlands will have to adopt a national approach if it wishes to remain an international leader in this field.

In order to regulate the use of available resources, a new structure was set up on the basis of a national strategy, which is formulated, implemented and monitored by a body specially set up for this purpose, the Netherlands Genomics Initiative (NGI), which assumed its role at the beginning of 2002.

NGI has been given the task, within a period of five years (2002-2007), to establish a national infrastructure for genomics that clearly places the Netherlands at the international forefront. This infrastructure must initiate excellent research that produces a steady stream of potential applications and new industrial activity, which is firmly embedded in society. Key points of the National Genomics Strategy, as drawn up by NGI, are:

- focus on areas in which Dutch science and industry play a major role internationally;
- bundling of the best research groups in consortia with sufficient critical mass;
- direct participation of industry in the consortiums;
- attention for the societal implications of genomics at all levels - from scientific research to public-oriented activities;
- high priority to the development of platform technologies
- stimulate, train and attract young talent;
- all activities must offer an international perspective.

This first phase of NGI will be completed in 2007. Various reviews performed by panels of international experts show that NGI has succeeded in bringing cohesion to the formerly fragmented field of genomics in the Netherlands, as well as establishing a vital genomics community that creates added value for all partners and for society. Many young talented scientists and engineers have been put to work. Cooperation between the various NGI Genomics Centres has given rise to new relationships and areas of research.

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‘MammaPrint® tells breast cancer patients how large their risk of metastasis is.’

Genomics?

Genomics is an indispensable toolkit filled with high-quality technologies that enable completely new biological experiments and perspectives. This definition underlines that genomics is a 'means', not a field of research in itself. Use of genomics leads to better and faster research within the life sciences while opening the door to completely new experiments, often extremely large-scale.
A more interesting question, however, concerns the purpose of genomics. By applying genomics, we gain insight into the relationship between genetic information, biological processes in living organisms and environmental factors. Essentially, everything hinges on translating this genetic information to the functioning of the complete organism. That may sound very fundamental, but the exceptional thing about genomics is that the basic insights that it gives us into the genetic and molecular principles of life are directly related to the development of products and applications that have an inestimable value for our health, safety, living environment and economy.

Thanks to genomics...

- we are better able to predict the risk of metastasis for breast cancer patients
- brewer’s yeast can convert wood waste into bioalcohol, an important alternative fuel
- crops are being developed with improved drought resistance
- a therapeutic vaccine against cervical cancer is within reach
- there is a simple test determining the presence of toxic gluten in foodstuffs
- we know better what determines the taste of cheese and how we can influence it
- we have more insight into the manner in which a virus infects its host
- we have discovered a bacterium that fights harmful moulds and can be used as an organic plant protection product
- a good model exists for studying migraine
- more alternatives to animal testing are available
- we know a lot more about the genetic basis of serious diseases, including diabetes, Alzheimer's and cancer, giving us a more targeted approach to finding new therapies
- companies are now working on a potato that can be cultivated with the use of significantly less pesticides
- profound improvements have been booked in bioremediation, which is the biological purification of contaminated soil
- a revolutionary therapy for Duchenne muscular dystrophy is under clinical development
- we understand better what determines the taste of the tomato
- food fermentation processes are more controllable
- an enzyme has been developed that can break down gluten efficiently in the stomach of celiac patients, thus preventing damage to the intestines
- water and soil quality can be determined quickly
- we have more efficient breeding techniques for agricultural crops.

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Genomics makes the difference

Industry has started with the further development of research results into commercial applications. Several hospitals are already using findings in practice. The Netherlands is clearly profiling itself within the EU as a leading player in genomics and assumes a pioneering role in various areas. New international initiatives have been initiated. Attention to communication and education has resulted in increased knowledge of, and appreciation for, genomics by the Dutch public. Combined, these results form a solid foundation for continued growth in the coming years and for getting the maximum benefit out of the opportunities offered by genomics. The time is therefore right to reinforce our commitment to genomics research. In its Strategic Plan 2008-2012, NGI foresees continuation of the coordinated, national approach, whereby the emphasis will be on harvesting; the further development and utilisation of knowledge within the context of prominent social themes. Core elements are the creation of coherence, flexibility and international context. The NGI strategy 2008 - 2012 consists of four action lines:

- Valorisation
- Strengthening the knowledge base
- Social research and communication with the public
- International positioning

NGI's role is characterised by leadership, steering of current activities, identifying and developing new, high-potential fields, as well as promoting Netherlands life sciences on the international stage.

While much has been achieved in the past five years, genomics is by no means 'ready'. The truth is that we are only starting to experience what effect genomics will have on our daily life. We can, may and, in fact, must expect further contributions from genomics to our well-being and prosperity. In the Netherlands, but also worldwide. Proper health care, sufficient good food and a clean and safe living environment are important to all of us, irrespective of where we live.

Fact is that the stone has only just been thrown into the pond, and the ripples have barely started. While we are as yet unable to see the impact and benefits of genomics, we need not doubt in the broad scope of its application. There is already sufficient evidence of that. We present a few highlights in this special edition of 'Genomics NL'.

Sticking plasters on to genes

A 'molecular plaster' can repair the genetic cause of Duchenne muscular dystrophy to such a degree that a much milder form of the disease arises.

Duchenne's Syndrome is a hereditary form of muscular dystrophy, with a deadly effect. Affecting one in 3,500 boys (not girls), it is one of the most common hereditary muscle diseases. The first signs of muscle weakness occur during the first and third year of life. As the patient grows older, more and more muscles are affected. Ultimately, the heart muscle itself weakens, usually causing patients to die by early adulthood.
Duchenne muscular dystrophy is caused by errors in the gene responsible for creating the protein dystrophin, which is required inside muscle cells for structural support. This protein is completely absent among Duchenne patients, however. Researchers from the Centre for Medical Systems Biology have now developed a 'molecular plaster' against this disease. It concerns substances that can 'cover' the errors in the dystrophin gene, enabling the patient's body to again make dystrophin. While not completely perfect, this mechanism warrants expectations that the patient will acquire a much milder form of the disease and can look forward to a more normal life expectancy. Tests in cultivated muscle cells and mice have proven the effectiveness of the molecular plaster.
The spin-off company ProSensa started a clinical study in September 2006 with this new therapy. Initial results are highly promising.

MammaPrint® can spare patients from chemotherapy

The MammaPrint® by Agendia gives breast cancer patients insight into the risk of later metastasis. If the risk is small, subsequent chemotherapy is no longer required.

Patients who have overcome cancer always live with the fear that the disease will return. And justifiably so. In case of breast cancer, for example, there is a realistic risk of later metastasis to the bones. It is for precautionary reasons therefore that many breast cancer patients following the operation, and possibly even radiation therapy, have to undergo chemotherapy.

The risk of metastasis is not the same for all patients, however. Some tumours are more aggressive than others. It all depends on the activity of certain genes in the tumour cells. Researchers from the Cancer Genomics Centre have measured the activity of a large number of genes in various breast tumours.
The researchers were able to determine a selection of 70 genes, on the basis of which it was possible to make a reliable prediction of aggressiveness and the risk of metastasis. Using this profiling method, patients can be classified into various risk categories. 35 to 40% of breast cancer patients appear to have a favourable profile, meaning that the risk of the tumour returning is minimal.

35 to 40% appear to have a favourable profile

This group would then be spared the need to undergo chemotherapy, with all its unpleasant side-effects Building on from this research, the spin-off company Agendia has brought the so-called MammaPrint onto the market. With the aid of this MammaPrint, doctors can make a prognosis for an individual patient, using it as the basis for a decision on the most appropriate follow-up treatment. The MammaPrint was recently approved by the FDA for the American market. Similar tests are also being developed for other types of tumours.

Genomics NL in figures

- 11 Genomics Centres
- 33 research institutes and universities
- 166 companies
- 1,100 new jobs for researchers and engineers
- 1,486 scientific publications
- 86 theses
- 143 new public-private projects
- 11 new (spin-off) companies
- 88 patent applications
- 26 new clinical applications
- 700,000 young people reached with special GenomiX magazine
- 25,000 pupils reached with mobile DNA Labs
- 600 young researchers part of GeNeYouS network
- 12,000 visitors per month for the public website www.watisgenomics.nl

GeNeYouS

Genomics Network for Young Scientists

As genomics can be used in many fields of science, it also serves as an excellent denominator under which many young researchers, working in various disciplines, can establish contact with one another. GeNeYouS, the Genomics Network for Young Scientists, is clear proof of the multidisciplinary character of life sciences research. Already, some 600 researchers, mainly doctoral candidates, have joined GeNeYouS, which was established in 2002 by a small group of active young researchers. The members cover the entire field of life sciences, ranging from plant research to biomedical sciences and from ecology to bioinformatics. GeNeYouS informs members about career and course opportunities, and organises various activities, including lectures, symposia and excursions.

Terry Vrijenhoek, Chairman of GeNeYouS and actively involved with the network right from the start, tells about the future plans of GeNeYouS. "From this year, we will be focusing more on expanding the network through our local contacts. By involving people in activities at a local level, the network will get stronger." Does this mean that more attention will be given to the various disciplines? "Yes, each member now falls under one of the five research areas: medical research, fundamental, biotechnology, bioinformatics, or societal aspects. Nanotechnology will no doubt be added to this in the future. Our members really enjoy making contact with researchers from other fields of science. The exchange of knowledge is highly appreciated. At our symposium in 2006, for example, it appeared that researchers from the medical field had learned a lot from a presentation about yeast." According to Terry, the local approach actually strengthens the multidisciplinary character of GeNeYouS.
"We think crossdisciplinary and bring together people within an institution. That works because many researchers within their daily work already maintain contact with people from other areas. And as personal contact has already been established, this new strategy is proving highly successful."

Growing old healthy thanks to good genes

How can people stay healthy for longer? The new Netherlands Consortium for Healthy Ageing is looking for genetic factors that contribute to good health at an advanced age.

While growing 'old' is usually associated with an increase in physical 'inconveniences', this does not apply to all people in the same degree. While some people of 70 barely manage to get out of the house, others are still doing sports and volunteer work at the age of 85. The reason for this difference is not yet known. Much medical research is predominantly focused on diseases that afflict people during their 'productive years'. Yet very little is known about ageing and age-related diseases. The Netherlands Consortium for Healthy Ageing (NCHA), which was established in 2006, performs research into the process of ageing to enable the elderly to have a healthy and active life for longer.

The ageing process starts when we are still young, long before the first grey hairs appear. From an early age, continuous mistakes are being made in our body, during the copying of DNA, for example, while cells and organs are damaged by biological and biochemical stress situations. Fortunately, most damage is immediately corrected by repair mechanisms available in the cells. A small part of that damage remains permanent, however. Due to gradual accumulation of such small incidents of damage, organs and ultimately no longer function properly, giving rise to age-related diseases.

> yet very little is known about ageing and age-related diseases

Using genomics, NCHA wants to uncover the genetic mechanism of this ageing process. Factors such as food, lifestyle and environment also play an important role. Researchers of the consortium want to use this knowledge to develop measures that will keep people healthy for longer. By analysing earlier organ damage, for example, researchers hope to be able to forecast later ageing problems. Ultimately, the research must lead to new methods for the prevention, diagnostics and treatment of age-related diseases.

Health

Insight into the fundamentals is required to combat disease and promote health. Not an easy task, considering the complexity of the network of molecules and processes that determined the status of our health. Genomics technologies make it possible to study this network down to the very smallest detail, thus contributing to a deeper and broader understanding of what it means to be 'healthy', what really goes wrong when a disease develops, and how the disease can best be tackled.

Vaccine helps the immune system in the battle against cancer

Researchers from the Centre for Medical Systems Biology have developed a vaccine that helps the body in its fight against tumour cells. Initial clinical trials by ISA Pharmaceuticals have shown that it works well.

Foreign cells that enter the body are immediately confronted by the defensive mechanisms of the immune system. The same thing applies to cancer cells, although they do not come from outside, but are instead the product of normal cells that have undergone genetic mutation. In principle, the immune system should recognise cancer cells as foreign and subsequently proceed to destroy them. But because cancer cells still share certain properties with normal cells, the immune system is misled and the immune response is weak. Researchers from the Centre for Medical Systems Biology have discovered a way of helping the immune system by means of a vaccine, in this case against cervical cancer. Such a therapeutic vaccine should not be confused with a preventive vaccine against cervical cancer, which received regular media attention during this past year. As cervical cancer is caused by a virus, the possibility exists to vaccinate people and prevent infection. A therapeutic vaccine, however, is intended for people who are already infected, and whom have developed a tumour.

> the immune system should recognise cancer cells and subsequently destroy them

Researchers have identified the foreign, signal substances emitted by tumour cells and then duplicated these. A cocktail of various pieces of these substances proved highly effective as a therapeutic vaccine. The spin-off company ISA Pharmaceuticals B.V. has already carried out a successful clinical trial with this vaccine. Deviations caused by the virus completely disappeared in four of the eleven patients involved in the tests. In three of these four patients, furthermore, all traces of the virus had been cleared from the body. This form of therapeutic vaccination can, in principle, be used against many forms of cancer. ISA Pharmaceuticals has, for example, also started clinical trials with a therapeutic vaccine against ovarian cancer.

Genetic test predicts effects of cancer therapy

Genetic variations in cancer cells can cause resistance against certain cancer medicines. Tests based on genetic profiles can show these variations and clarify whether a treatment could indeed have the desired effect.

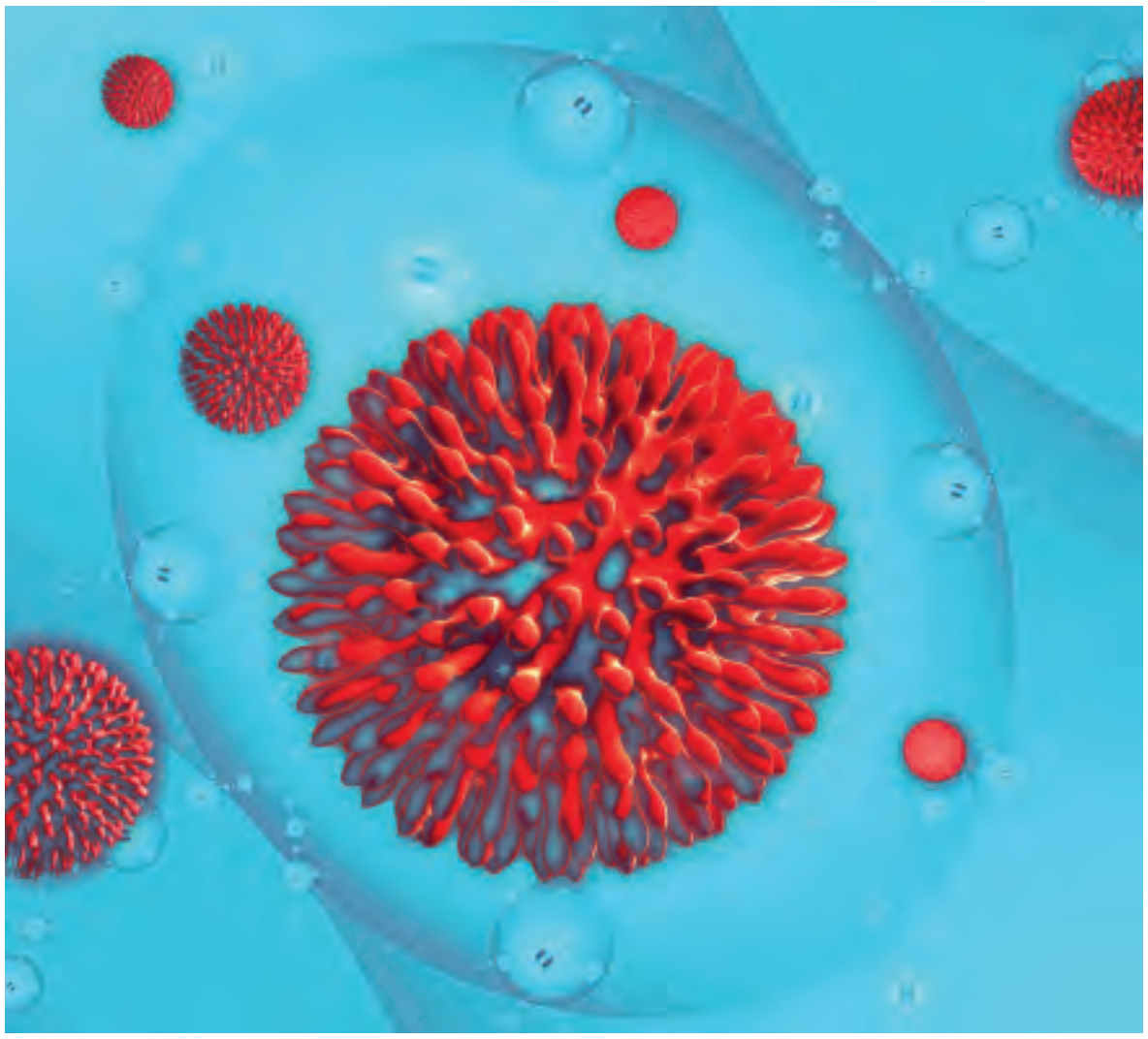
Cancer cells adapt quite easily to circumstances. If, for example, a cancer medicine blocks an important signal molecule, the cancer cells will try to find another way to pass on the signal. Once that is successful, treatment with the medicine in question is pointless as the cancer cells have become resistant. Resistance against cancer medicine is a huge practical problem, for example with the medicines trastuzumab (brand: Herceptin) and tamoxifen.

Trastuzumab is a targeted medicine against breast cancer. It is only applied in breast cancer patients that show an overexpression of a certain receptor, Her2/neu, in the tumour cells. Treatment with trastuzumab cuts the risk of re-occurring breast cancer by half. Resistance is very common, however. Researchers within the Cancer Genomics Centre have discovered that switching off one specific gene in cultivated breast cancer cells leads to resistance against trastuzumab. It is possible that the reason for the resistance against trastuzumab among patients could also lie in errors in this gene, although other genes may also play a role.

> determining the risk of resistance

Once it becomes clear which genes play a role, researchers can apply this genetic profile in the development of a diagnostic test. Doctors can then use this test to determine the risk of resistance and whether treatment with trastuzumab is worthwhile or not. Researchers from the Erasmus MC have already determined such a resistance profile for the cancer medicine tamoxifen. The spin-off company Agendia will, after validation, continue with development and bring it on the market as a diagnostic test.

Vaccines against viral respiratory infections: a matter of perseverance



VIRGO researchers are using innovative methods to develop vaccines and anti-viral drugs against viral respiratory infections. Their thorough approach requires long-term vision, but has already brought forward a great deal of knowledge and various candidate vaccines.

viral respiratory infections are among the most common causes of death for both humans and animals

A cold or case of flu is something that most people simply take in their stride: a nuisance, but otherwise not serious. Nevertheless, viral respiratory infections are among the most common causes of death among both humans and animals worldwide. Vaccines and anti-viral drugs are often not available or simply not effective enough.

The VIRGO Consortium has declared war on these infectious diseases from a completely different perspective. Instead of the traditional method of trial and error, the researchers are striving for a rational design of vaccines and anti-viral drugs. With the aid of various genomics techniques, scientists are uncovering exactly what happens when a virus enters a host (human or animal). At three different levels (cell, animal, human), researchers are identifying the genes that are being read, the proteins that are being activated and the parts of the virus involved in this process. After an initial period of preparation and investment, research is now proceeding at an impressive pace. The research investments are slowly but surely yielding results. Examples include the development of various new candidate vaccines against influenza (flu) and avian influenza. These vaccines have undergone the first test phases with success, while the preparations for clinical testing are in an advanced phase. It is now gradually becoming clear why certain (classic) vaccination strategies offer negative effects in the battle against SARS, the RS virus and the human metapneumo virus.

researchers are striving for a rational design of vaccines

NGI Genomics Centres

Overview of the NGI Genomics Centres and their public partners, industrial participations, innovative output and spin-off companies.

11 Genomics Centres

- Centre for BioSystems Genomics
  Unravelling plants for consumers and the environment
  www.cbsg.nl
- Centre for Medical Systems Biology
  Improved diagnosis, treatment and prevention of common diseases
  www.cmsb.nl
- Cancer Genomics Centre
  Improving the chances of curing cancer
  www.cancergenomics.nl
- Kluyver Centre for Genomics of Industrial Fermentation
  Optimising micro-organisms in industrial fermentation
  www.kluyvercentre.nl
- Centre for Society and Genomics
  Investigating and debating the social and cultural impact of genomics
  www.society-genomics.nl
- Netherlands Proteomics Centre
  Tools for characterisation and functional analysis of proteins
  www.netherlandsproteomicscentre.nl
- Netherlands Bioinformatics Centre
  Shaping the future for bioinformatics in the Netherlands
  www.nbic.nl
- Celiac Disease Consortium
  Safe food, better diagnosis and more effective treatment
  www.celiac-disease-consortium.nl
- Ecogenomics Consortium
  Using the full potential of the soil
  www.ecogenomics.nl
- Nutrigenomics Consortium
  Improving the prevention and treatment of metabolic stress
  www.genomics.nl
- VIRGO Consortium
  New intervention strategies for respiratory virus infections
  www.virgo.nl

3 Centres under establishment

- Netherlands Toxicogenomics Centre
  Genomics to revolutionise toxicity testing
  www.toxicogenomics.nl
- Netherlands Metabolomics Centre
  High quality technologies to improve personal health and quality of life
  www.metabolomicscentre.nl
- Netherlands Consortium for Healthy Ageing
  Living healthier for longer
  www.genomics.nl

Research institutes and universities involved

- Academic Medical Center Amsterdam
- Biomedical Primate Research Centre
- Delft University of Technology
- Erasmus Medical Center
- Foundation for Fundamental Research on Matter
- Hubrecht Laboratory, Netherlands Institute for Developmental Biology
- Leiden University
- Leiden University Medical Center
- Maastricht University
- National Institute for Public Health and the Environment
- National Research Institute for Mathematics and Computer Science
- Netherlands Cancer Institute
- Netherlands Institute of Ecology
- Netherlands Organisation for Applied Scientific Research
- NIZO food research
- Radboud University Nijmegen
- Sanquin Blood Supply Foundation
- SARA Computing and Networking Services
- Top Institute Food and Nutrition
- University of Amsterdam
- University of Twente
- University Medical Center Groningen
- University Medical Center St Radboud
- University Medical Center Utrecht
- University of Groningen
- University of Technology Eindhoven
- Utrecht University
- Free University Amsterdam
- Free University Medical Center Amsterdam
- Wageningen University and Research Centre

High-tech biology

Biology, the core of the life sciences, is not a disciplined immediately associated with advanced, cutting edge technology. But that has changed drastically thanks to the emergence of genomics.

Genomics is a collection of enabling technologies that facilitate a completely new approach to biological questions. An approach that allows for unknown complex and large-scale experiments. Not only do these technologies make such experiments possible, they are also essential tools for the extraction and interpretation of the results.

An overview of the most important 'omics' platform technologies:

- Genomics: besides the umbrella term, also a platform technology focusing on the DNA sequencing of genes (structural genomics), the activity of genes (transcriptomics) and the function of genes (functional genomics).
- Proteomics: proteins are the subject of attention here, which proteins are present in a biological system, what is their function and how do they interact with one another? The Netherlands Proteomics Centre (NPC) develops and maintains the procurement infrastructure for the Netherlands genomics field.
- Metabolomics: maps out the interaction between various types of biomolecules in various cells and fibres of the organism. The Netherlands Metabolomics Centre (NMC, under establishment) will become the national facility for metabolomics.

Besides these basic platforms, there are various 'omics' more related to their specific area of application. For example, the use of genomics, proteomics and metabolomics in toxicological research is referred to as toxicogenomics. Other such specific fields include pharmacogenomics (application: medicine research) and nutrigenomics (application: food research).

unprecedented complex and large-scale experiments

Bioinformatics

While not an 'omics' in the strict sense of the word, bioinformatics is nevertheless a crucial platform technology for all genomics research.

With the development of genomics, life sciences research has undergone a spectacular increase in scale. This has generated enormous quantities of measurement data that must be stored, managed, integrated and interpreted in an efficient manner. Bioinformatics plays an essential role in this process and establishes the necessary conditions for a modern research environment for life sciences. A state-of-the-art bioinformatics structure, as set up by the Netherlands Bioinformatics Centre (NBIC), is therefore an essential precondition for getting the most from the potential of genomics. Without bioinformatics it will simply not be possible to arrive at meaningful research results.

leads for the replacement of animal testing

Better methods, less animal testing

A significant part of the mapping of possible health hazards of chemical compounds, as required by (inter)-national legislation and regulations, relies on toxicological tests on animals. The use of animal testing for this purpose is under debate, also within the science community. There are limits to the predictive capacity of animal testing, and there are ethical considerations too. Toxicogenomics – genomics, proteomics and metabolomics applied in toxicological research – focuses on explaining the toxicity of substances at a genetic and molecular level. This yields fundamental insight into the effects of toxic compounds, which enables far more sharply focused, refined and reliable toxicological testing, while offering leads for the replacement of animal testing by other methods, for example, the use of cell models and body fluids.

Innovative output of the NGI Genomics Centres and programmes

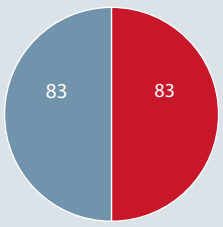
Genomics Centres and programmes	Patent applications	Licenses	Spin-offs	New clinical applications	New partnership projects
Centre for BioSystems Genomics	4	18	1	-	2
Centre for Medical Systems Biology	21	16	3	4	19
Cancer Genomics Centre	27	2	3	3	17
Kluyver Centre for Genomics of Industrial Fermentation	15	1	0	-	30
Netherlands Bioinformatics Centre – BioRange	-	-	3	-	17
Netherlands Proteomics Centre	15	1	1	4	34
Celiac Disease Consortium	1	-	-	-	5
Ecogenomics Consortium	3	-	-	-	4
VIRGO Consortium	4	-	-	-	20
IOP Genomics & Horizon Programma	13	-	-	-	9
Total	**103**	**38**	**11**	**11**	**157**

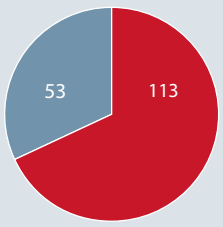
Spin-offs

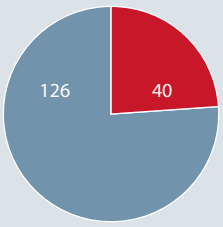
Since the outset of NGI Genomics Centres

Genomics Centres	Spin-offs
Centre for BioSystems Genomics	NSURE
Centre for Medical Systems Biology	Flexgen
	ISA-Pharmaceuticals
	PROSENSA
Cancer Genomics Centre	Agendia
	Dnage
	Agamyxis
Netherlands Bioinformatics Centre - BioRange	3DM
	PR-Sys Design
	Cross links
Netherlands Proteomics Centre	U-Balance
Total	**11**

Industrial participation in the National Genomics Strategy (166 companies in total)







Test kit guarantees safe food for celiac patient

More than 1 in 200 Westerners suffer from celiac disease, or gluten intolerance. An intestinal disease that arises when the immune system responds excessively to proteins in various types of grain.

These types of grain are processed in practically all foodstuffs, meaning that only a strict diet can spare patients from serious complaints. Building upon findings by the Leiden University Medical Center, researchers from the Celiac Disease Consortium have developed a test kit that can recognise toxic gluten fragments in foodstuffs. This makes it possible to screen the safety of food for gluten-intolerant consumers. A highly significant result in dealing with this common form of food intolerance.

The test improves on existing tests available commercially, which are less specific or detect only a portion of the toxic fragments. The test will undergo further development, with a commercial partner, in order to guarantee its usability in routine laboratories or even in the home situation. The food industry has responded enthusiastically to the test. It should ultimately lead to a range of new products being brought on the market .

over 1 in 200 Westerners suffer from it

Food supplement neutralises toxic gluten

It's an attractive future perspective for people who are intolerant to gluten: an oral supplement that neutralises gluten in foodstuffs.

This scenario may become reality thanks to a finding of the Celiac Disease Consortium in cooperation with TNO and DSM Food Specialties. The enzymes normally present in the gastrointestinal tract have difficulty dealing with proline-rich proteins, such as gluten. As a result, toxic gluten fragments remain behind after digestion, which cause damage in the small intestine of celiac patients.
Researchers discovered an enzyme from the yeast *Aspergillus niger*, which is highly efficient in breaking down gluten. What's more, the enzyme, ANPEP, works well under the natural (physiological) conditions of the gastro-intestinal tract. Ideally, the enzyme can be developed into an oral supplement that enables patients to safely eat gluten. Extensive clinical studies will be required before reaching this stage, however. These are currently under preparation.

gluten-intolerant people will then be able to eat glutenous foodstuffs

Food is extraordinarily complex; it contains an enormous amount of nutrients, flavours and fragrances, all of which have a distinct - and often very small - effect. Determining which nutrient and substance does exactly what is therefore extremely difficult. Genomics is used to study food at molecular and genetic level. The objective on the one hand is to better understand the relationship between food and health, and on the other hand to gain insight into the genetic bases of taste, fragrance and other properties of food crops and products.

Understanding the taste of cheese

Cheese is the most typical of Dutch products, yet little is known about how this dairy product gets its taste.

The lactic acid bacteria that are responsible for the taste in cheese are inaccessible for standard genomics techniques, meaning that scientists have found themselves locked out until now. But researchers from the Kluyver Centre for Genomics of Industrial Fermentation have found a solution. They have developed a method to measure the gene expression of lactic acid bacteria in poorly accessible environments, such as cheese. With this method, a detection system is used after cheesemaking to determine that gene expression of the lactic acid bacteria.
Knowledge about which genes are switched on and off in the bacteria can help to declare how cheese gets its taste. Active genes say something about the biochemical reactions that occur in the bacteria and about the taste-determining substances that result from this process. Backed by this knowledge, it is possible to modify bacteria strains, thereby influencing the taste of cheese.

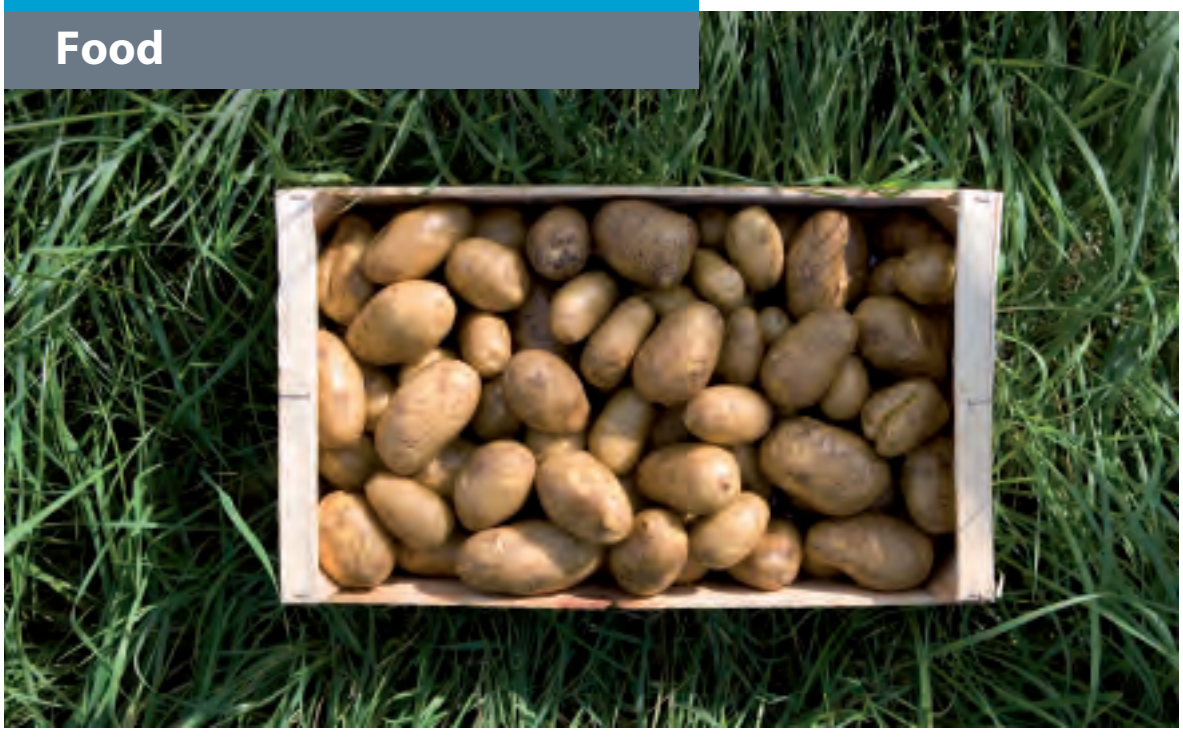
biochemical insight into the taste of cheese

Mini factories make essential vitamins

Bacteria functioning as mini factories: that is one of the promises of the bio-based economy. With the aid of bacteria, we can make more efficient use of raw materials and energy than is the case with normal chemical synthesis.

A significant step in the right direction is the development of two strains of lactic acid bacteria that make folic acid and vitamin B12. By removing a number of bottlenecks, researchers at the Kluyver Centre for Genomics of Industrial Fermentation have managed to develop bacteria strains that have a high output of folic acid (vitamin B9). Tracking down these bottlenecks was made possible thanks to transcriptomics and metabolomics. Dairy products made with the aid of these modified bacteria strains are naturally enriched with folic acid. As a food supplement, folic acid is primarily found in fermented dairy products and leafy vegetables. Also, it is important for public health. It provides protection again cardiovacsular diseases and intestinal cancer, while taking folic acid during pregnancy reduces the risk of giving birth to a child with spina bifida. Vitamin B12, like folic acid, is an essential vitamin, but it is only found in animal products like meat, fish or milk. The Kluyver Centre has mapped the genes that are responsible for the production of vitamin B12. By studying the conditions under which bacteria are most productive, it is possible to enrich food with vitamin B12.

natural enrichment of foods with important vitamins



Why some tomatoes are tastier

Taste can differ greatly from one tomato to the next; every consumer knows that. Nevertheless, explaining the science behind a specific taste is a serious challenge.

Researchers at the Centre for BioSystems Genomics have found the way to tackle it: metabolomics. Their approach involves mapping the complete biochemical composition, i.e. the metabolites, of nearly one hundred varieties of tomato. By linking the outcome to taste trials by human panels, it becomes possible to create a biochemical expression of taste.
Using this knowledge about 'good' and 'bad' metabolites, one can select tomato lines with valued taste properties. In 2006, three tomato improvement companies carried out crossbreeding with these lines and cultivated new populations. CBSG researchers will now analyse these populations in order to find biomarkers that are indicative of certain taste properties. These biomarkers are valuable to improvement companies as they enable a vast selection of new varieties.

Fuel from residual materials in your tank

While we know that our oil reserves are finite, we still want to keep driving our cars. Serious effort is therefore being put into finding new types of fuel. These must be sustainable, meaning renewable, and CO_2 neutral.

Ethanol is such a fuel. It has a number of advantages, such as it can easily be mixed with petrol without the need for any major modification of car engines. And it can be distributed through existing petrol stations. Cars have been running on ethanol for decades in Brazil, for example. Global production is already 40 million tonnes. The fuel is made primarily from sugar cane, but other agricultural crops are also suitable. Baker's yeast converts the sugars in crops into ethanol. One has to make a choice, however: produce either sugar or fuel. This could have the undesired side-effect of pushing up the price of agricultural products.

Using the residual flow

Beside crops that are suitable for human consumption, there is an enormous potential in organic waste and residual flows. It would be ideal if cars could be run on maize foliage, beet pulp, non-recyclable paper, wheat straw, verge mowings... One problem: the sugar contained in these flows consist primarily of xylose, also known as wood sugar. Baker's yeast is unable to convert these into ethanol. The Kluyver Centre for Genomics of Industrial Fermentation realised an international breakthrough by developing a new strain of Baker's yeast that is up to the task. Genomics techniques, genetic modification and evolution in the laboratory came together to enable a fast and efficient conversion. A patent has already been applied for. The Netherlands assumes a leading position within this highly competitive international field of study. The conditions for a maintaining this position, and in fact reinforcing it, are excellent.

> First practical tests are highly promising

Into practice

Under laboratory conditions, using uncontaminated raw materials, these yeast strains perform excellently. In industrial practice, however, the residual flows are all too often contaminated and the composition is not constant. Together with its industrial partners, the Kluyver Centre is making the process suitable for industrial production. Will the strains continue to function as they should? The results of the first practical tests are highly promising. Researchers are trying in the meantime to improve the robustness of microorganisms under industrial conditions. This brings us one step closer to the large-scale industrial production of ethanol from residual flows. Preparations are already underway for the first pilot plant.

Sustainability

Meeting the growing demand and the high quality requirements of consumers and companies without harming the environment. That is one of the greatest challenges facing industry and the agricultural sector. How can we produce more (products) with less (raw materials, emissions, waste, energy consumption)? With the aid of genomics, work is being carried out on optimising the use of microorganisms in a bid to develop sustainable and economically viable methods for the production of foodstuffs, pharmaceutical ingredients, fuels and fine and bulk chemicals, to name but a few. Genomics is also applied to realise a faster selection of sustainable agricultural crops that can meet the wishes of both consumers and the processing industry.

Biological degradation of soil contaminants: Finding the right bacterium

What do some six hundred thousand locations in the Dutch subsoil have in common? They are all contaminated and must undergo remediation during the coming thirty years.

Excavating all that contaminated soil would be far too expensive. Fortunately, an alternative soil remediation method is now available: bioremediation. This involves the cleaning up and stabilising of contaminated soil with the aid of microorganisms. There are two conditions for bioremediation. First, the soil must contain a bacterium that can help break down the contamination. Second, the growth conditions of this bacterium must be such that it can produce sufficient active enzymes. In practice, this often requires a 'consortium of bacteria', involving the interaction of a range of microorganisms. But where can you find those consortia? How will you recognise them? And under which conditions do they perform optimally?

> excavating all that contaminated soil would be far too expensive.

Detection, identification, utilisation

Those are the questions that the Ecogenomics Consortium (EC) wants to answer. The partners within this consortium are working on the detection, identification and utilisation of soil microorganisms with optimal properties for the enzymatic degradation of soil contaminants. Research is initially focusing on contamination with benzene, toluene, ethylbenzene and xylene. By monitoring the genetic activity in the soil with the aid of DNA chips, researchers can determine whether the bacteria can tackle the contamination by themselves, or whether extra nutrients are required. Improved bioremediation systems are the result. Also, consortia of soil microorganisms are isolated and put to work at contaminated locations. Various pilots are being carried out and an affordable solution for soil remediation is coming within reach.

Zero growth: All the benefits without the burden

Biotechnological production processes make use of microorganisms. Unfortunately, high product output goes hand in hand with the fast growth of the producing organisms. Meaning that the more product harvested, the greater the quantity of biomass that remains after the production process. Industry has to incur high costs to get rid of this biomass. In order to find out whether this can be done more efficiently, the Kluyver Centre has started a research project. The 'zero growth project' will map the link between growth and production, which up to now has been inseparable. The objective is to find leads for disconnecting these two processes. Is it possible to develop microorganisms that can make the target product without reproducing themselves? Finding an answer to this question requires a long-term approach. Development of such organisms will mean a significant breakthrough for industrial biotechnology.

Finding resistant populations!

The modern consumer wants healthy food crops cultivated in an environmentally friendly manner. That's why potato breeders and growers have a preference for sustainable varieties.

Commercially interesting potato varieties result in a high-quality, uniform and reliable yield. However, certain varieties that have all the desired properties are not suitable for large-scale cultivation. The reason: they are highly susceptible to disease.
Farmers could of course make large-scale use of pesticides in the cultivation of these varieties, but that would lead to sharply higher costs, a worsening of working conditions and possible environmental damage.

Billions of euros loss

Phytophthora is the world's major potato fungal disease, causing vast losses. The global fight against this disease costs around € 3 billion a year. Despite these measures, annual crop losses still amount to several billion euros. The Centre for BioSystems Genomics (CBSG) has identified several hundred new sources of resistance genes against the *Phytophthora*. By screening national collections and related wild varieties, etc., CBSG has discovered new avenues that may yield more resistant varieties of potato.

Unprecedented large-scale screening

Three years ago, CBSG launched a programme in cooperation with the potato industry. Under laboratory conditions, 5,000 potato varieties were screened for *Phytophthora* resistance. These varieties represent genotypes of potato species that are more or less related to the consumption potato. This unprecedented large-scale screening yielded over 500 varieties that were either partially or entirely resistant to the dreaded fungal disease. Further selection and targeted crossbreeding of these varieties resulted in interesting potato populations. Various crop improvement companies have already started preparing these varieties for the consumer market.

Public communication

Investments in genomics are only worthwhile if the results - in the form of products and services - answer the needs and expectation of citizens, being a patient or consumer. That's why it's critical that science and industry, on the one hand, and society on the other, are informed of one another's activities, expectations and perceptions. Genomics research can only lead to societal added value if it is backed up by open communication in all its facets. NGI and the NGI Genomics Centres, in close cooperation with various Science Centres and parties active in science communication, are developing a number of activities aimed at the general public. Important target groups are pupils, teachers and patient associations.

Genomics reaches 25,000 pupils

Over 10,000 pupils have already participated in the mobile DNA Labs. This successful project brings genomics into the classrooms of pupils in general and pre-university secondary education.

DNA Labs are mobile laboratories that visit schools on request and give pupils an opportunity to carry out tests with DNA and genomics. Students supervise the tests. Subjects covered by the labs include tumour profiling, plant research, industrial biotechnology and protein folding. There are five different DNA Labs, each handling a different aspect of modern DNA research. Each in their own particular way, the DNA Labs show that knowledge of genes and the molecules in a cell play a large role in areas that are important to all of us: food, health and the environment. Furthermore, the laboratories clearly show that scientific progress sometimes give rise to social questions. The DNA Labs effectively serve to raise the level of knowledge and awareness of high school pupils. Since been started in 2005, the DNA Labs have reached 25,000 pupils in over 275 schools, which is nearly half of all Dutch schools offering general and pre-university secondary education. Additionally, the labs are also used during manifestations in Science Centres such as NEMO and at events for patient associations.

> website for teachers who want to use the subject of genomics in their classes

Coordination of the DNA Labs is the responsibility of the VWO Campus of Wageningen University. The DNA Labs are directly linked to the public website www.watisgenomics.nl.

Genomics website attracts thousands of visitors a month

Website www.watisgenomics.nl fulfils a clear need. The number of visitors has risen from 3,500 per month in 2005 to 9,000 per month in 2006, and even to as high as 12,000 in the final months of 2006.

The site offers understandable and clearly structured information about genomics. Visitors are given an impression of current scientific developments and informed about ongoing social discussions about genomics. This website is intended for everyone who wants to know more about genomics or is keen to form an opinion on the subject. For example, pupils who need information for a project or who wish to orient themselves on the jobs market, but also teachers who wish to use genomics in their lessons. in 2006, the themes 'DNA labs' and 'the environment' were launched, while the subject of 'infectious diseases' will be getting extra attention in 2007. The Centre for Society and Genomics manages the site, both technically and in terms of content. Scientific input is provided by the various NGI Genomics Centres.

Imagine... pupils conceive projects for developing countries

Central in the Imagine... project is the concrete application of genomics in developing countries, wrapped up in an annual competition for high school pupils.

Researchers submit a proposal for the application of a specific and affordable technology, after which pupils write a business plan for the proposal of the choice. Backed by financing from the foundation Imagine..., the winning project is actually implemented and the pupils in question will trip to the country in which the project will be carried out.
In 2006, the competition was won by five pupils from Amersfoort. Their plan 'Seeds for life' describes the possibilities for revitalising a rundown plantation in Surinam by planting *Bixa orellana*, from the seeds of which the highly sought-after and much-used colorant Annatto is extracted. The winners will be visiting Surinam in 2007.

> the winning project is actually implemented in a developing country

Last year, the winners from 2005 visited Kenya, where 'their' project to extract oil from unripe avocados was set in motion.

Netherlands Genomics Initiative

The Netherlands Genomics Initiative (NGI) is an independent taskforce within the Netherlands Organisation for Scientific Research (NWO) which has the task of creating an infrastructure for excellence genomics research - research that contributes to economic development and growth, and is firmly embedded in society. Principals of NGI are the Dutch ministries of: Education, Culture and Science; Economic Affairs; Agriculture, Nature and Food Quality; Health, Welfare and Sport; Housing, Spatial Planning and the Environment. During the first term, 2002 - 2007, NGI has created a powerful and dynamic network with at the core eleven large Genomics Centres that are focused on socially significant themes, such as food, health and sustainability.

Netherlands Genomics Initiative

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