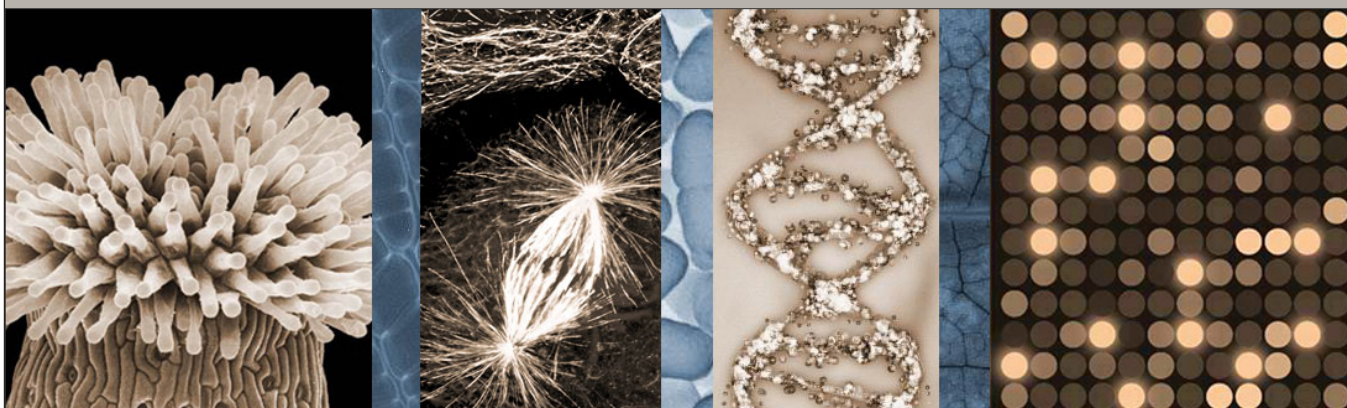


# Science-Matrix

## Genomics in the Netherlands

October 2002



## Overview of Research in Genomics in the Netherlands and Prospects for Scientific Cooperation with Canada

Prepared for  
Genome Canada

# Science-Metrix

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## Executive Summary

This report on genome research in the Netherlands uses public information sources available on the Internet, such as the Medline database, together with data from the Science Citation Index and the United States Patent and Trademark Office.

The first section presents an overview of genomic research programmes. Like Canada, the Netherlands invested in a national effort in the field of genomics. This programme, the *Netherlands Genomics Initiative*, came as a welcome effort since scientific output in genomics started to dwell in the late 1990s. Section I also presents data from the Internet on Dutch institutions that are active in the field.

Section II compares the Netherlands' position in genomics to that of Canada's and other leading countries'. A series of scientometric and technometric indicators shows that, given their converging strengths, Canada and the Netherlands can enter mutually beneficial collaborative activities in a number of scientific specialties, particularly within the field of clinical medicine, biomedical research and biology.

Drawing from the Medline database, Section 3 examines the distribution of papers in genomics by sector, institution, city, and researcher. The distribution of research in genomics in the Netherlands is concentrated in three locations:

- Amsterdam: its output of papers is unmatched; it hosts three of the seven leading hospitals, a quarter of the leading universities and of the leading researchers.
- Leiden: the city has the most productive hospital (*Leids Universitair Medisch Centrum*) and the largest number of leading researchers. It ranks second in scientific output and *Leiden Universiteit* is the second most productive university. Leiden is also prominent for the large number of firms active in the field that are based there.
- Utrecht: the performance of both *Universiteit Utrecht* and the *Universitair Medisch Centrum* makes the city of Utrecht another major research hub.

Other Dutch urban centres with significant output comprise Rotterdam, Nijmegen, Groningen, and Wageningen.

The views presented in this report are those of Science-Metrix and do not necessarily reflect the opinions of Genome Canada.

## I. An Overview of Genomics in the Netherlands

The Netherlands is a modern and industrialized nation with an economy that benefits greatly from foreign trade. The country is a founding member of NATO and the European Union and participated in the introduction of the euro in 1999. It is noted for stable industrial relations, moderate inflation, a sizeable current account surplus, and its central role as a European transportation hub. Industrial activity is predominantly centered on food processing, chemicals, petroleum refining, and electrical machinery.

At the world level, the Netherlands ranks third in agricultural exports. Its economy has expanded by 3% or more in each of the last four years (CIA. 2001. *The World Factbook 2001*). The population of the Netherlands is half that of Canada's but both countries' GDP per capita are in the same range (Table 1).

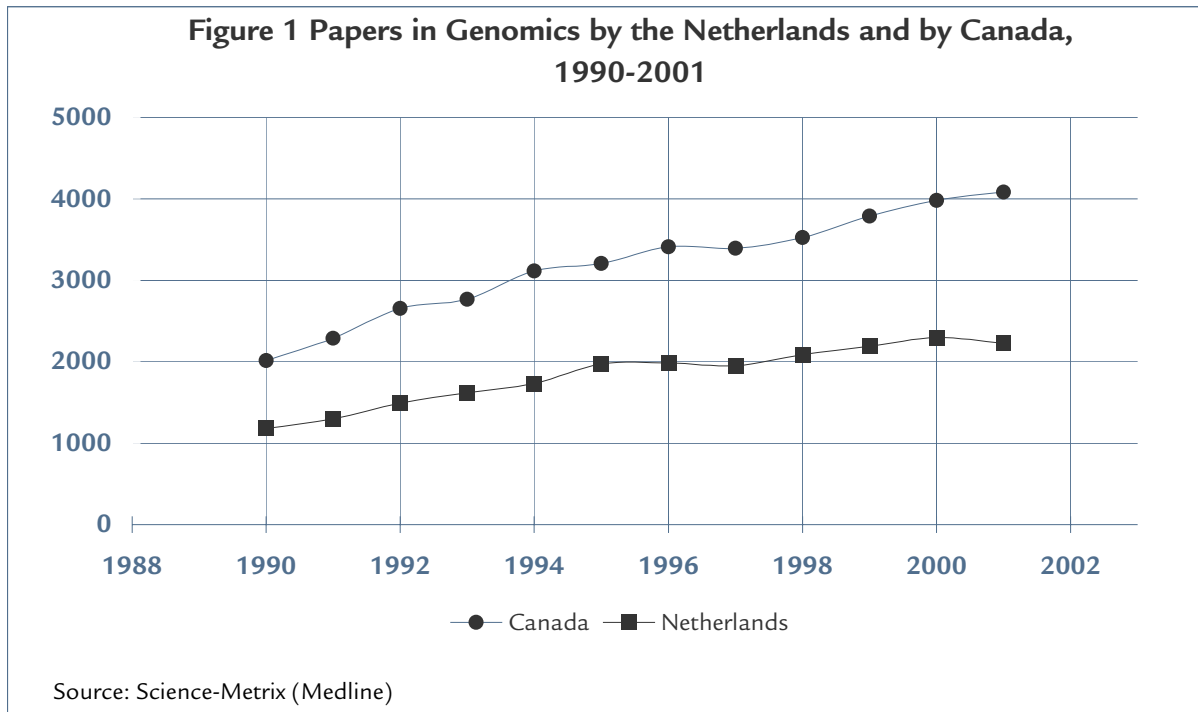
**Table 1 Basic Socio-Economic Statistics**

|                             | Netherlands             | Canada                  |
|-----------------------------|-------------------------|-------------------------|
| Area (sq km)                | 41,526                  | 9,976,140               |
| Population (July 2001 est.) | 15,981,472              | 31,592,805              |
| Labour force (2000)         | 7,200,000 (45% of pop.) | 16,100,000 (51%)        |
| GDP*                        | US \$388.4 billion      | US \$775 billion        |
| GDP per capita*             | US \$24,400             | US \$24,800             |
| Government type             | Constitutional monarchy | Parliamentary democracy |

\* Purchasing power parity – 2000 est.  
Source: CIA. 2001. *The World Factbook 2001*.

From 1990 to 2001, the Netherlands published around 22,000 papers in genomics that were indexed by Medline (measured by first author of paper and Dutch affiliation). This compares to around 38,250 papers published by Canadian authors during the same period.

Figure 1 reveals that the output of papers in genomics in the Netherlands grew slightly more slowly than in Canada during the 1990s – with a 6.1% average annual growth in the Netherlands compared to 6.7 % in Canada.



## National Research Programmes in Genomics

Genomics research in the Netherlands is organized around an explicit national strategy that stems from the "Cabinet standpoint on Genomics" presented in 2001. This has evolved into a national strategy that aims to make the Netherlands a leading player in the field of genomics by 2006. The national strategy is implemented by the *Nationaal Regie Orgaan Genomics* (Netherlands Genomics Initiative), a taskforce working under the umbrella of the *Nederlandse Organisatie voor Wetenschappelijk Onderzoek* (NWO – Netherlands Organization for Scientific Research). The national strategy aims to cover the complete chain of innovation from fundamental research to industrial application. It is structured around:

- a small number of Genomics Centres of Excellence<sup>1</sup>;

<sup>1</sup> The Genomics Centres of Excellence aim to foster cooperation between universities, research institutes and industrial groups. At the time of writing, the *Nationaal Regie Orgaan Genomics* has selected four national centres of excellence:

- The Cancer Genomics Consortium, led by Prof. Dr. A. Berns, cooperates with the Netherlands Cancer Institute, the Erasmus University of Rotterdam, the Utrecht Laboratory, and the University of Utrecht.
- The Centre for Biosystems Genomics, led by Prof. Dr. W. Stiekema, involves Wageningen University & Research Centre and the Universities of Utrecht, Nijmegen, and Amsterdam.
- The Kluyver Centre for Genomics of Industrial Fermentation, led by Prof. Dr. J.T. Pronk, comprises the Delft University of Technology, Wageningen University & Research Centre, University of Leiden, NIZO, TNO, the Wageningen Centre for Food Sciences, ATO, and the universities of Nijmegen and Utrecht.
- Multifactorial Diseases: Common Determinants, Unifying Technologies, led by Prof. Dr. G.J.B. van Ommen.

- an Innovation Oriented Program (IOP) on genomics<sup>2</sup>;
- the coordination of applications for genomics projects within an Interdepartmental Committee for Economic Structure programme (ICES/KIS-3)<sup>3</sup>.

The total financing of the national strategy of more than 415 million guilder (about 265 million Canadian dollars as of 31 Dec. 2001) stems from three sources: regular funding (246 million guilder)<sup>4</sup>, budgetary funding (170 million guilder)<sup>5</sup> and ICES/KIS 3 funding<sup>6</sup>.

## Genome Research in Dutch Universities

Whereas Section III measures the scientific output of universities, this section presents a summary of the data available on the Internet. Groningen is one of the most visible research communities in genomics in the Netherlands. A sizeable part of research is performed under the umbrella of the Groningen Genomics Centre (GGC). Located at the *Rijksuniversiteit Groningen* (RUG), GGC specializes in clinical and microbial genomics and emphasizes biomolecular research on the structural and functional relationships of proteins, on the cellular functions of proteins, and on biocatalysis. The Groningen Bioinformatics Centre (GBIC), which is located at the Institute of Mathematics and Computing Science (itself located in RUG's Faculty of Mathematics and Natural Sciences) and at the Department of Medical Genetics (part of the Faculty of Medical Sciences), is an important player within the GGC.

Another important coordinating centre, also located at RUG, is the Groningen Biomolecular Sciences and Biotechnology Institute (GBB). Functional genomics is becoming the preferred approach in the majority of ongoing research projects, and transcript and protein profiling by

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<sup>2</sup> IOP on Genomics aims to stimulate strategic pre-competitive research in universities and research institutes. The research projects should match the medium- to long-term innovation needs of industry or should have potential to create spin-offs. Other important objectives of the programme include: transfer of knowledge and implementation of research results; stimulation of long-term collaborations; and formation of networks. The research performed within this programme focused on: pathogenesis of chronic and/or ageing related diseases; food functionality, quality and safety; biomolecular processes such as signal transduction and metabolic pathways.

<sup>3</sup> The *Nationaal Regie Orgaan Genomics* has been mandated to coordinate the ICES/KIS programme in the following areas: proteomics; bioinformatics; innovative clusters; enabling technologies & infrastructure.

<sup>4</sup> Ministry of Education, Culture and Science, 150 million guilder to be spent by 2006; NWO programmes with a total of 52 million guilder already allocated (biomolecular Informatics - 20 million, functional genomics and proteomics - 27 million, social and ethical issues - 5 million guilder); IOP genomics with 44 million guilder of which 25 has already been allocated: (34 million for the initial four-year phase initiated in 2000, with an additional 10 million from the Ministry of Economic Affairs Knowledge Incentive fund).

<sup>5</sup> Different departments committed 50 million guilder for 2001 and 100 for 2002, and 20 million guilder from the Department of Economic Affairs shall provide for continuity for the 2003-2006 period.

<sup>6</sup> 20 million guilder were spent during the 1998-2000 period and another 20 million will be made available for the strengthening of the knowledge infrastructure in the Netherlands. The percentage of these sums specifically allocated to ICES/KIS 3 on genomics is not available.

high-throughput technologies such as DNA micro-arrays and proteomics tools are being implemented.

Also significant is the Genomics Centre Utrecht Wageningen (GCUW), which was established from a strategic alliance between Utrecht University and Wageningen University and Research Centre (Wageningen-UR) and works in cooperation with two research institutes of the *Koninklijke Nederlandse Akademie van Wetenschappen* (KNAW – Royal Netherlands Academy of Arts and Sciences)<sup>7</sup>. GCUW performs research in biomedical, agrofood, and ecological sciences. The centre sees the active translation of genomics results into applications as a way to create products for society and stimulate new "bioentrepreneurial" initiatives.

The Dutch universities with the highest visibility on the Internet in genomics are presented in Annex I. In spite of weak presence on the Internet, Leiden's institutions are leading in terms of scientific output, as can be seen in the data presented in Part III of the report.

## Genome Research in the Health Sector

A major actor on the genomics research scene is the Leiden University Medical Centre, which performs research in genomics through the Centre for Human and Clinical Genetics. One of the centre's most prominent research groups is the Leiden Genome Technology Centre (LGTC), a multi-service research centre, whose activities include DNA sequencing and fragment analysis, bioinformatics, and bio-robotics.

The *Academisch Medisch Centrum* (AMC - Academic Medical Centre) of the *Universiteit van Amsterdam* is another significant player and hosts the Amsterdam Genomic Centre (AGC) and the Bioinformatics Laboratory (BL).

The Bioinformatics Group and the Genomics Laboratory are both part of the Utrecht University Medical Centre (UMC Utrecht). Whereas the Bioinformatics Group focuses on microarrays and genetic screens, the Genomics Laboratory uses bioinformatics and functional genomics to shed light on the mechanisms of transcription regulation. The Internet addresses of these university-hospitals can be found in Annex I.

Also of interest is the work performed by the Centre for Biomedical Genetics (CBG), a nationwide entity composed of six research schools from four Universities (University of Amsterdam, Utrecht University, Erasmus University in Rotterdam, and Leiden University). CBG performs research in four areas: signal transduction, cell cycle control and the regulation of DNA replication;

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<sup>7</sup> The *Nederlands Instituut voor Ontwikkelingsbiologie* (NIOB - Netherlands Institute for Developmental Biology) and the *Nederlands Instituut voor Ecologie* (NIOO - Netherlands Institute of Ecology).

mechanisms of genome maintenance and response to damage; transcriptional control; and gene dysfunction in disease.

## Genome Research in Governmental and Non-Governmental Organizations

The Centre for Human NutriGenomics<sup>8</sup> aims to establish an international centre of expertise combining excellent pre-competitive research and high-quality training on the interaction between genomics, nutrition, and human health.

KNAW performs research in genomics more particularly via the *Centraalbureau voor Schimmelcultures* (CBS - Fungal Biodiversity Centre) and the *Nederlands Instituut voor Ontwikkelingsbiologie* (NIOB - Netherlands Institute for Developmental Biology/Hubrecht Laboratory).

Although a private contract research organization, the *Nederlandse Organisatie voor toegepast-natuurwetenschappelijk onderzoek* (TNO - Netherlands Organization for Applied Scientific Research) has strong ties with the Dutch government. TNO carries out research in genomics, proteomics and bioinformatics in several of its research centres, most notably in *TNO Voeding* (Nutrition and Food Research), TNO Pharma and TNO-STB, which performs research on the economic and policy aspects of life sciences, among others.

Other important research organizations comprise the *Nederlands Kanker Instituut* (NKI - Netherlands Cancer Institute) and the *Koninklijke Nederlandse Chemische Vereniging* (KNCV - Royal Netherlands Chemical Society), which has a workgroup dedicated to bioinformatics.

## Genome Research in the Private Sector

One of the Cabinet's central goals is to favour the translation of genomics research into products for the market either through collaboration with existing firms or through spin-offs. As mentioned previously, the Netherlands Genomics Initiative includes an IOP (Innovation Oriented Program) in genomics which aims not only to stimulate strategic pre-competitive research on genomics in universities and research institutes but also to support research projects that match the medium- to long-term innovation needs of industry or have the potential to stimulate the creation of new companies.

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<sup>8</sup> The Centre for Human NutriGenomics is an innovation centre comprising the following partners: Wageningen University & Research Centre; TNO Nutrition and Food Research; University of Maastricht; National Institute of Public Health and Environment; and Nizo Food Research. The Centre's work focuses on the following areas: functionality and safety of food ingredients in relation to human health; molecular mechanisms underlying the health effects of food; genotypes and the relation of nutrition with human health; exposure, bioavailability, function and risk markers. One of the Centre's objectives is to set up international alliances with expert groups on genomics, nutrition, and human health.

In addition to multinational enterprises with headquarters in the Netherlands (e.g. Shell, Unilever, Organon International, etc.), Dutch enterprises in the food industry (e.g. NIZO Food research, Holland Genetics), agriculture (e.g. Plant Research International) and pharmaceuticals sector (e.g. Life Science Partners) perform research in genomics. There are also a number of smaller firms, most of them spin-offs of universities and/or research institutes, that are financed in part by investment firms such as Plant Research International and Life Science Partners.

The address of firms located in the Netherlands that perform such research in genomics can be found in Annex II.

\* \* \*

Like Canada, the Netherlands have invested in a national effort in the field of genomics. The Netherlands Genomics Initiative arrived as a welcome effort since scientific output in genomics slowed down in the late 1990s. The Dutch effort aims to implement a national policy by fusing traditional research funding with *ad hoc* programmes through a coordinating body called *Nationaal Regie Orgaan Genomics* – loosely translated in English as the Netherlands Genomics Initiative. It is also noteworthy that there is a very strong emphasis placed on the industrial applications of genome research.

## II. Strengths of the Netherlands and Canada in Genomics

This section compares Canadian and Dutch scientific output together with the level of protection of their intellectual property. The analysis uses data from the Science Citation Index (SCI) and the United States Patent and Trademark Office (USPTO). The aim is to identify fields where Canada and the Netherlands can cooperate in a mutually beneficial manner.

### Global Position in Genomic Science and Technology

The following table shows that, globally, the Netherlands is ahead of Canada (respectively 4<sup>th</sup> and 6<sup>th</sup> in the multicriteria ranking). However, these rankings vary when it comes to specific indicators. For instance, Canada leads in the absolute number of papers, but the Netherlands publishes significantly more scientific papers per inhabitants – ranking third at the world level. The Netherlands places more emphasis on genomics research than on other scientific undertakings than Canada does (index of specialization). Nevertheless, Canadian researchers have a modestly higher propensity than Dutch researchers to publish papers in journals that are cited often (impact factor).

**Table 2 Rank of Leading Countries in Genomics  
by Publication of Scientific Papers, 1990-1998**

| Rank | Number of papers   | Papers per inhabitants | Index of specialization | Relative impact factor | Global rank        |
|------|--------------------|------------------------|-------------------------|------------------------|--------------------|
| 1    | USA                | Switzerland            | USA                     | USA                    | USA                |
| 2    | Japan              | Sweden                 | Switzerland             | Switzerland            | Switzerland        |
| 3    | UK                 | <b>Netherlands</b>     | France                  | <b>Canada</b>          | UK                 |
| 4    | Germany            | USA                    | Sweden                  | <b>Netherlands</b>     | <b>Netherlands</b> |
| 5    | France             | UK                     | Japan                   | UK                     | France             |
| 6    | <b>Canada</b>      | <b>Canada</b>          | <b>Netherlands</b>      | France                 | <b>Canada</b>      |
| 7    | Italy              | Australia              | UK                      | Germany                | Sweden             |
| 8    | <b>Netherlands</b> | France                 | Australia               | Sweden                 | Japan              |
| 9    | Australia          | Germany                | <b>Canada</b>           | Australia              | Germany            |
| 10   | Sweden             | Japan                  | Germany                 | Spain                  | Australia          |
| 11   | Switzerland        | Italy                  | Italy                   | Italy                  | Italy              |
| 12   | Spain              | Spain                  | Spain                   | Japan                  | Spain              |
| 13   | USSR/Russia        | USSR/Russia            | USSR/Russia             | USSR/Russia            | USSR/Russia        |

Source: Science Citation Index and United Nations Statistics Division

The pattern for patents obtained in the world's largest market, the USA, is somewhat similar to that observed for publications. Canada is still ahead of the Netherlands in the absolute number of patents, but the Dutch number of patents relative to its population puts it 2<sup>nd</sup> worldwide, that is,

ahead of Canada. The Netherlands' patenting activity is also highly specialized in genomic research, ranking 2<sup>nd</sup> worldwide, just before Canada (3<sup>rd</sup> rank). However, the Dutch's patent growth rate is much less important than Canada's, respectively ranking 8<sup>th</sup> and 3<sup>rd</sup>. Globally, Canada ranks second and the Netherlands fourth.

Hence, whereas the Netherlands leads in terms of scientific output, Canada is in a better position in terms of the protection of intellectual property in the United States.

**Table 3 Ranking of Leading Countries in Genomics  
by Patenting Activities in the USA, 1990-1999**

| Rank | Number of patents in USA | USA patents per inhabitants | Index of specialization | Growth      | Global rank |
|------|--------------------------|-----------------------------|-------------------------|-------------|-------------|
| 1    | USA                      | USA                         | Australia               | Switzerland | USA         |
| 2    | Japan                    | Netherlands                 | Netherlands             | Australia   | Canada      |
| 3    | Germany                  | Switzerland                 | Canada                  | Canada      | Australia   |
| 4    | France                   | Canada                      | USA                     | France      | Netherlands |
| 5    | Canada                   | Sweden                      | USSR/Russia             | USA         | France      |
| 6    | Netherlands              | Japan                       | UK                      | Germany     | Switzerland |
| 7    | UK                       | Australia                   | Spain                   | Sweden      | Germany     |
| 8    | Australia                | France                      | France                  | Netherlands | Sweden      |
| 9    | Switzerland              | Germany                     | Sweden                  | UK          | Japan       |
| 10   | Sweden                   | UK                          | Germany                 | Italy       | UK          |
| 11   | Italy                    | Italy                       | Switzerland             | Japan       | Spain       |
| 12   | Spain                    | Spain                       | Italy                   | Spain       | Italy       |
| 13   | USSR/Russia              | USSR/Russia                 | Japan                   | USSR/Russia | USSR/Russia |

Source: U.S.A. Trademark and Patent Office and United Nations Statistics Division

## Positioning Canada and the Netherlands for Cooperation

There are substantial differences in the ranking of Canada and the Netherlands in specific scientific fields (Table 4). First, Canada is very strong in biology - it ranks 1<sup>st</sup> worldwide - whereas the Netherlands occupies 6<sup>th</sup> place. This field could be of interest for collaboration, but one must be aware that, with 6% of the total number of papers, biology is not at the core of genomics research. In biomedical research, Canadian researchers rank 5<sup>th</sup> while the Dutch occupy the 7<sup>th</sup> place. Both countries are thus in the same range and they might benefit from each other's expertise. Collaboration in Chemistry is not that promising, with Canada ranking 7<sup>th</sup> and the Netherlands 11<sup>th</sup>. In the core fields of genomics, clinical medicine appears most promising considering that both countries are similarly successful: the Netherlands ranks 3<sup>rd</sup> and Canada 7<sup>th</sup>.

**Table 4 Global Rank of Leading Countries in Genomics  
by Scientific Field, 1990-1998**

| Rank              | Biology            | Biomedical Research  | Chemistry         | Clinical Medicine    |
|-------------------|--------------------|----------------------|-------------------|----------------------|
| 1                 | Canada             | USA                  | Switzerland       | USA                  |
| 2                 | Australia          | UK                   | USA               | UK                   |
| 3                 | UK                 | Switzerland          | Sweden            | Netherlands          |
| 4                 | USA                | France               | Germany           | Sweden               |
| 5                 | Japan              | Canada               | France            | Switzerland          |
| 6                 | Netherlands        | Germany              | Japan             | Japan                |
| 7                 | Germany            | Netherlands          | Canada            | Canada               |
| 8                 | France             | USSR/Russia          | UK                | Italy                |
| 9                 | Spain              | Australia            | USSR/Russia       | France               |
| 10                | Switzerland        | Sweden               | Spain             | Australia            |
| 11                | Sweden             | Japan                | Netherlands       | Germany              |
| 12                | Italy              | Spain                | Australia         | Spain                |
| 13                | USSR/Russia        | Italy                | Italy             | USSR/Russia          |
| <b>Papers (%)</b> | <b>21,343 (6%)</b> | <b>205,864 (58%)</b> | <b>7,240 (2%)</b> | <b>117,948 (33%)</b> |

Source: Science Citation Index and United Nations Statistics Division

Some scientific specialties promise mutually beneficial collaboration between Canada and the Netherlands, that is, specialties where both countries exercise some form of leadership. Table 5 identifies scientific specialties providing the greatest opportunities. In particular, collaboration in Biology could prioritize Botany and Dairy and Animal Science.

Within the field of Biomedical Research, the specialties in which both countries exert leadership comprise Anatomy and Morphology, Genetics and Heredity, Microbiology and Virology. In Clinical Medicine, where both countries are among the leaders, a number of specialties are promising for collaboration. Those fields are Arthritis and Rheumatology, Cardiovascular Systems, Fertility, General and Internal Medicine, Obstetrics and Gynecology, and Radiology and Nuclear Medicine.

Both countries could also enter potentially fruitful collaborative arrangements in three other specialties: Environmental Science, Applied Mathematics and Miscellaneous Psychology.

**Table 5 Global Rank of Leading Countries in Genomics  
by Field and Sub-Field, 1990-1998**

| Field                              | 1           | 2           | 3           | 4           | 5           | 6           | 7           |
|------------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| <b>Biology</b>                     | Canada      | Australia   | UK          | USA         | Japan       | Germany     | Netherlands |
| Botany                             | Australia   | UK          | Netherlands | Germany     | Canada      | USA         | France      |
| Dairy & Animal Science             | Canada      | Netherlands | USA         | Australia   | UK          | Germany     | France      |
| Ecology                            | USA         | Australia   | UK          | Canada      | Sweden      | Switzerland | Netherlands |
| Entomology                         | Australia   | Canada      | USA         | France      | UK          | Sweden      | Netherlands |
| <b>Biomedical Research</b>         | USA         | UK          | Switzerland | France      | Canada      | Germany     | Netherlands |
| Anatomy & Morphology               | Canada      | Netherlands | USA         | Australia   | UK          | Japan       | Germany     |
| Cellular Biol., Cyt. & Histology   | Switzerland | USA         | France      | Germany     | Canada      | Italy       | Netherlands |
| General Biomedical Research        | USA         | UK          | Switzerland | France      | Canada      | Germany     | Netherlands |
| Genetics & Heredity                | UK          | Netherlands | Canada      | USA         | Australia   | Switzerland | France      |
| Microbiology                       | Netherlands | USA         | Switzerland | France      | Canada      | UK          | Germany     |
| Virology                           | USA         | UK          | Germany     | Canada      | Netherlands | Australia   | Switzerland |
| <b>Chemistry</b>                   |             |             |             |             |             |             |             |
| Applied Chemistry                  | Germany     | UK          | USA         | Canada      | Japan       | Netherlands | Australia   |
| Polymers                           | France      | Japan       | USA         | Germany     | Netherlands | Sweden      | Canada      |
| <b>Clinical Medicine</b>           | USA         | UK          | Netherlands | Sweden      | Switzerland | Japan       | Canada      |
| Allergy                            | Australia   | Switzerland | UK          | Netherlands | Japan       | Canada      | USA         |
| Arthritis & Rheumatology           | UK          | Canada      | Netherlands | USA         | Japan       | Australia   | Germany     |
| Cardiovascular System              | USA         | Netherlands | Canada      | Japan       | Germany     | Sweden      | Switzerland |
| Fertility                          | USA         | Canada      | Netherlands | UK          | Australia   | Sweden      | Switzerland |
| General & Internal Medicine        | UK          | USA         | Sweden      | Canada      | Netherlands | Switzerland | France      |
| Miscellaneous Clinical Medicine    | UK          | France      | USA         | Japan       | Switzerland | Netherlands | Canada      |
| Nephrology                         | USA         | Canada      | Switzerland | Germany     | Japan       | UK          | Netherlands |
| Obstetrics & Gynecology            | UK          | USA         | Canada      | Germany     | Netherlands | Italy       | Sweden      |
| Otorhinolaryngology                | USA         | Sweden      | Netherlands | Japan       | UK          | Germany     | Canada      |
| Pathology                          | Netherlands | UK          | USA         | Switzerland | Japan       | Canada      | Germany     |
| Radiology & Nuclear Medicine       | USA         | Netherlands | UK          | Germany     | Canada      | Sweden      | Japan       |
| Veterinary Medicine                | Australia   | UK          | Switzerland | Canada      | USA         | Japan       | Netherlands |
| <b>Earth and Space</b>             | Canada      | USA         | Australia   | Netherlands | Germany     | France      | Japan       |
| Environmental Science              | Canada      | USA         | Australia   | Netherlands | Germany     | Japan       | France      |
| <b>Engineering and Technology</b>  | USA         | Germany     | Canada      | Japan       | UK          | Italy       | Netherlands |
| Chemical Engineering               | Japan       | USA         | Canada      | Australia   | Germany     | Netherlands | UK          |
| Computers                          | USA         | UK          | Canada      | Germany     | Italy       | Japan       | Netherlands |
| <b>Mathematics</b>                 | UK          | USA         | France      | Canada      | Germany     | Japan       | Netherlands |
| Applied Mathematics                | USA         | UK          | Netherlands | Canada      | Italy       | France      | Spain       |
| <b>Psychology</b>                  | Canada      | USA         | UK          | Switzerland | Australia   | Netherlands | Germany     |
| Behavioral Science & Compl. Psych. | Canada      | USA         | Switzerland | UK          | Germany     | France      | Netherlands |
| Miscellaneous Psychology           | UK          | USA         | Netherlands | Canada      | Australia   | Sweden      | Germany     |

Source: Science Citation Index and United Nations Statistics Division

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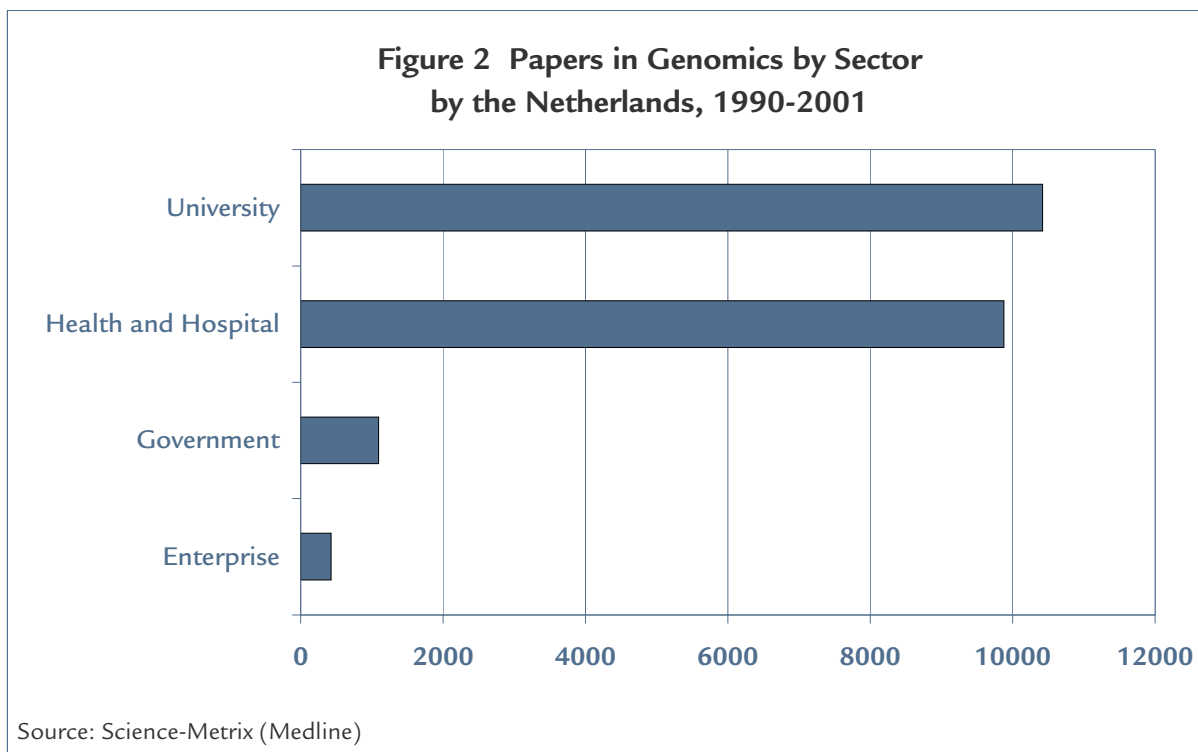
This analysis is an aggregate evaluation of Canadian and Dutch scientific performance. The fact that the scientific fields listed above present opportunities for *planned* collaborative research does not mean that mutually beneficial collaboration could not be performed at an individual level between leading researchers.

### III. Leadership Structure of the Netherlands Genomics Research

This section examines the distribution of papers in genomics by sector, institution, city, and researcher. The Medline database is used here, since more than 91% of papers in genomics are published in journals classified in the fields of Biomedical Research and Clinical Medicine. From 1990 to 2001, the Netherlands published around 22,000 papers in genomics that were indexed by Medline (measured by first author of paper and Dutch affiliation).

#### Distribution of Papers in Genomic Science by Sectors

In the Netherlands, 47% of papers in genomics are authored by researchers affiliated with universities (Figure 2). The health sector plays an important role in the development of research in genomics since 44% of the papers are authored by researchers affiliated with a health centre, a medical clinic, or a hospital (including university hospitals). Governmental organizations authored 5% of the papers, while private enterprises authored 2%. Other and unknown institutions have authored about 2% of the papers.



As figure 3 clearly shows, the production of papers amongst university-level institutions in the Netherlands is relatively evenly distributed. By comparison, in Sweden, the *Karolinska Institutet* is responsible for 41% of papers by the university sector. Utrecht and Leiden universities lead with

respectively 16% and 15% of university production followed by *Rijksuniversiteit Groningen* (12%), *Universiteit van Amsterdam* (11%), *Erasmus Universiteit Rotterdam* (11%), and *Wageningen Universiteit* (11%); all have published over a thousand papers. *Katholieke Universiteit Nijmegen* and *Vrije Universiteit Amsterdam* each account for 8% of the university output.

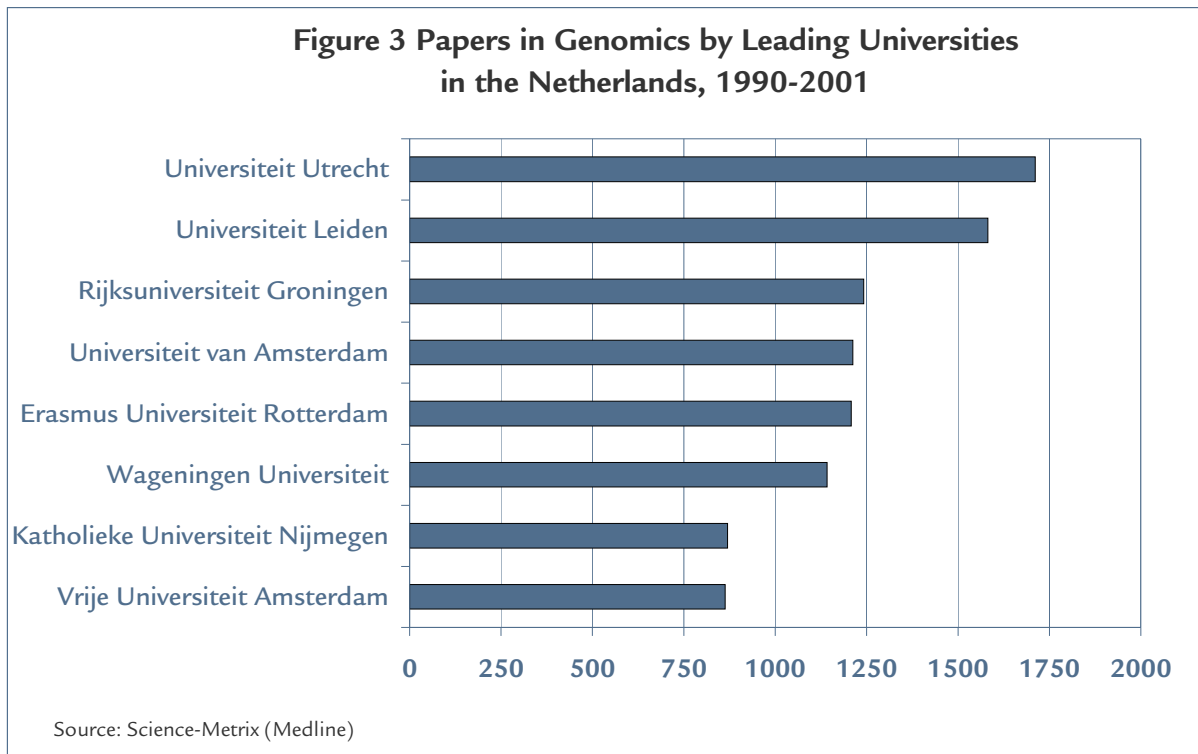
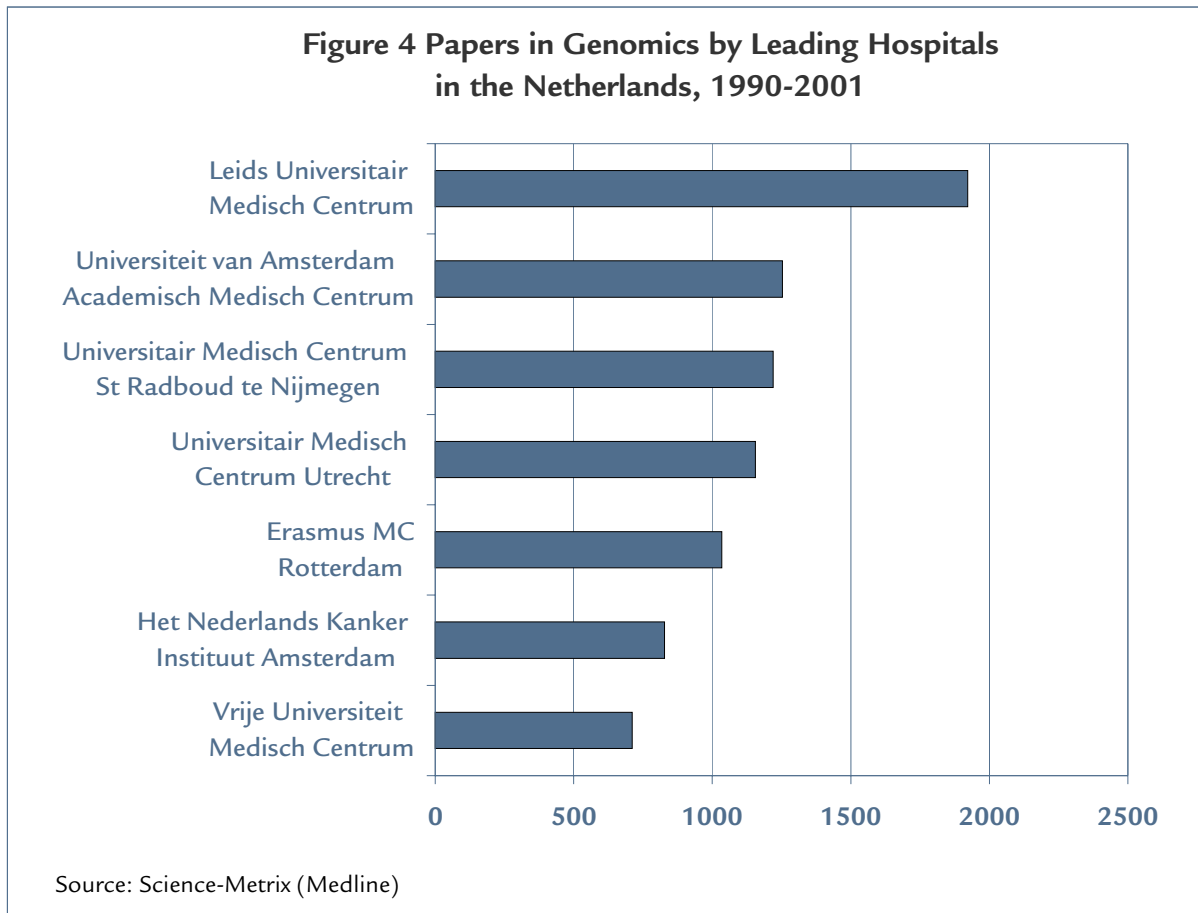


Figure 4 lists the most active institutions in the health and hospital sector. Not surprisingly, all of them, except the Netherlands Cancer Institute, are university hospitals. The leading institution in this sector is *Leids Universitair Medisch Centrum* (Leiden University Medical Centre), which with 1,922 papers represents close to 20% of the sector's output. The following four institutions, the *Universiteit van Amsterdam Academisch Medisch Centrum* (12.5%), the *Universitair Medisch Centrum St Radboud* of Nijmegen (12.2%), the *Universitair Medisch Centrum* of Utrecht (11.5%), and the *Erasmus Medisch Centrum* of Rotterdam (10.3%) have all produced over a thousand papers. *Nederlands Kanker Instituut* and *Vrije Universiteit*, both located in Amsterdam, each account for around 8% of the output. Hence, nearly every major university in the field of genomics in the Netherlands performs some clinical research through its associated university-hospital. This explains why the Netherlands is so strong in clinical research in genomics (see Part II).



Publications by private firms, in the Netherlands as in other countries, constitute a small part (2%) of the papers published in the field of genomics. NIZO, located in Ede, published 26% of private sector papers whereas Organon International, located in Oss, produced 20% of papers in this sector. NIZO's performance does not come as a surprise since the firm is one of the main participants in the Kluyver Centre for Genomics of Industrial Fermentation, one of the national centres of excellence established within the Netherlands Genomics Initiative. Also worth mentioning is the scientific output by Unilever (8%), Intervet International (5%) and DSM (5%). Leiden clearly is the most burgeoning city in terms of the absolute number of enterprises, hosting nine firms that published 14% of papers.

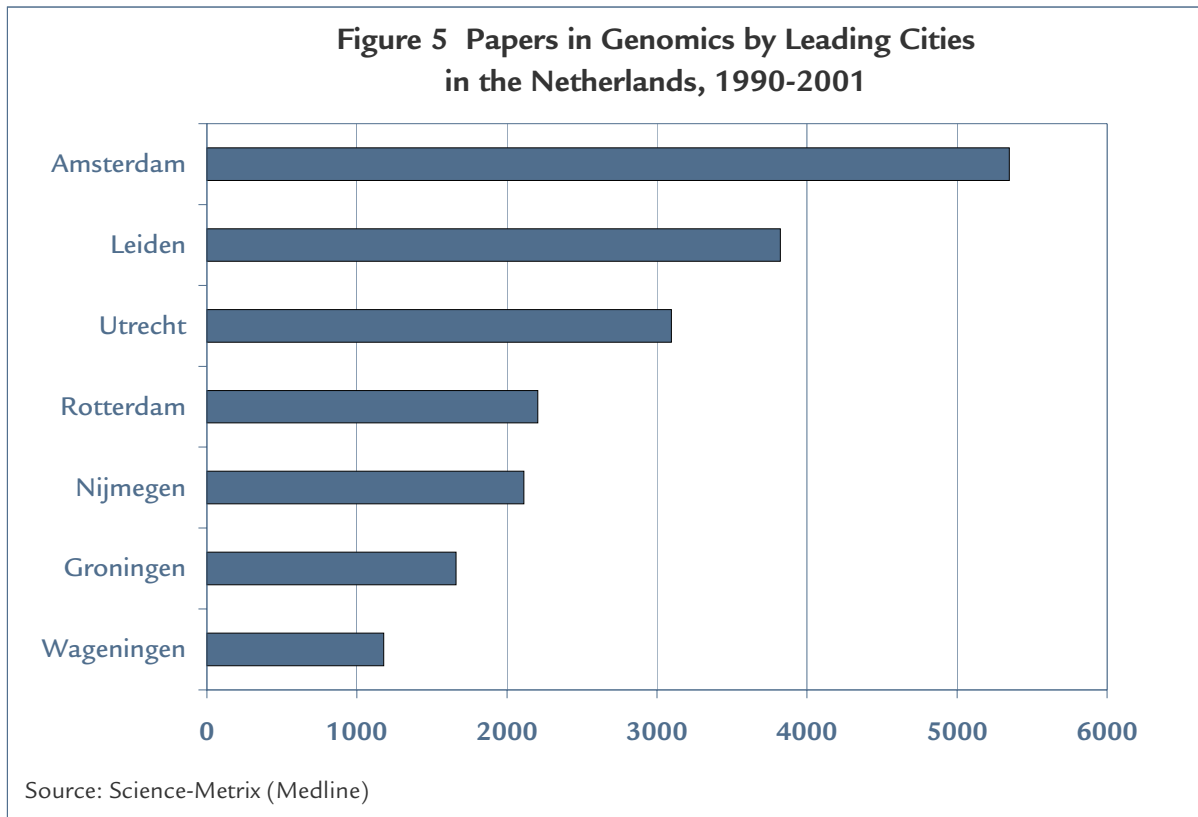
**Table 6 Ranking of Leading Enterprises in Genomics in the Netherlands.  
Number of Papers by City, 1990-1999**

| Rank         | Enterprise                   | Headquarters Location           | Ede        | Oss       | Leiden    | Vlaardingen | Boxtel    | Boxmeer   | Delft     | Amsterdam | Wageningen | Others    | Total      |
|--------------|------------------------------|---------------------------------|------------|-----------|-----------|-------------|-----------|-----------|-----------|-----------|------------|-----------|------------|
| 1            | NIZO                         | Netherlands (Ede)               | 114        |           |           |             |           |           |           |           |            |           | 114        |
| 2            | Organon International        | Netherlands (Oss)               |            | 83        |           |             | 28        |           |           |           |            |           | 111        |
| 3            | Unilever Research Lab.       | England (London)                |            |           |           | 34          |           |           |           |           |            |           | 34         |
| 4            | Intervet International       | Netherlands (Boxmeer)           |            |           |           |             |           | 22        |           |           |            |           | 22         |
| 5            | DSM                          | Netherlands (Heerlen)           |            |           |           |             |           |           | 18        |           |            | 3         | 21         |
| 6            | Syngenta MOGEN               | Switzerland (Basel)             |            |           |           | 19          |           |           |           |           |            |           | 19         |
| 7            | Ctre for Human Drug Research | Netherlands (Leiden)            |            |           |           | 14          |           |           |           |           |            |           | 14         |
| 8            | Ingeny International B.V.    | Netherlands (Goes)              |            |           |           | 11          |           |           |           |           |            |           | 11         |
| 9            | Shell                        | Netherl. (Hague) Engl. (London) |            |           |           |             |           |           |           | 10        |            | 1         | 11         |
| 10           | Crucell nv                   | Netherlands (Leiden)            |            |           |           | 6           |           |           |           |           |            |           | 6          |
| 11           | Introgene (Crucell)          | Netherlands (Rijswijk)          |            |           |           |             |           |           |           |           |            | 6         | 6          |
| 12           | Solvay                       | Belgium (Brussels)              |            |           |           |             |           |           |           |           |            | 6         | 6          |
| 13           | Dr. Van Haeringen Lab. B.V.  | Unknown                         |            |           |           |             |           |           |           |           | 5          |           | 5          |
| 14           | Genencor International B.V.  | USA (Palo Alto, CA)             |            |           |           | 1           |           |           | 4         |           |            |           | 5          |
| 15           | Keygene N.V.                 | Netherlands (Wageningen)        |            |           |           |             |           |           |           |           | 5          |           | 5          |
| 16           | Pharming Group N.V.          | Netherlands (Leiden)            |            |           |           | 5           |           |           |           |           |            |           | 5          |
|              | Others (n=17)                |                                 |            |           |           | 4           |           |           |           | 5         | 1          | 28        | 38         |
| <b>Total</b> |                              |                                 | <b>114</b> | <b>83</b> | <b>60</b> | <b>34</b>   | <b>28</b> | <b>22</b> | <b>22</b> | <b>15</b> | <b>11</b>  | <b>44</b> | <b>433</b> |

Source: Science-Matrix (Medline)

## Position of Dutch Cities in Genomic Science

Figure 5 shows that Amsterdam is the capital of genomics in the Netherlands producing 23.7% of the country's output by city. The city hosts several leading institutions active in the field of genomics: *Nederlands Kanker Instituut*, *Universiteit van Amsterdam Academisch Medisch Centrum*, *Vrije Universiteit*, *Vrije Universiteit Medisch Centrum*, Red Cross Amsterdam, BioCentrum Amsterdam, KNAW's Institute for Brain Research, and KNAW's Ophthalmic Research Institute. The city of Leiden ranks second with 16.9% of Netherlands scientific output, while Utrecht ranks third with 13.7%.



### Leading Dutch Researchers in Genomic Science

Figure 6 shows that 31.5% of the leading researchers are located at the *Leids Universitair Medisch Centrum*. Considering an additional researcher from TNO Prevention and Health, Leiden hosts 36% of Dutch leading researchers. The two most productive researchers are located in Amsterdam, and one of them, Prof. Dr. Jaap Goudsmit who is based at the *Academisch Medisch Centrum*, is listed in ISI's Highly-Cited Authors. *Vrije Universiteit Medisch Centrum* in Amsterdam and *Erasmus Universiteit* in Rotterdam host two leading researchers each. University of Utrecht could have been expected to rank better in terms of leading researchers: it ranks first in terms of output in genomics amongst Dutch universities but it hosts only one leading researchers, Prof. Dr. Johannes Frederik Gerardus Vliegthart. Importantly though, Vliegthart is listed on ISI's Highly-Cited Authors. By and large, there are no surprises here since most of these highly productive researchers come from the universities and urban centres with the largest scientific output.



\* \* \*

The distribution of research in genomics in the Netherlands is concentrated in the cities of Amsterdam, Leiden and Utrecht. *Leids Universitair Medisch Centrum* is the Dutch institution with the largest output (1,922 papers); *Universiteit Utrecht* comes second (1,711 papers); *Universiteit Leiden* ranks third (1,582 papers); and *Universiteit van Amsterdam Academisch Medisch Centrum* (1,253 papers) is fourth. Although these three cities lead in terms of output, Part I has shown that organizations in Groningen and Wageningen are aggressively promoting research in genomics and that these cities should not be overlooked, particularly in agrifood and nutraceuticals research.

## Annex I

## Dutch Universities Performing Research in Genomics

| University                        | Department  |
|-----------------------------------|---|
| Katholieke Universiteit Nijmegen  | Centre for Molecular and Biomolecular Informatics<br><a href="http://www.cmbi.kun.nl/">http://www.cmbi.kun.nl/</a>  |
|                                   | Department of Microbiology<br><a href="http://www-micrbiol.sci.kun.nl/research/carbon/genomicsmethanogens.html">http://www-micrbiol.sci.kun.nl/research/carbon/genomicsmethanogens.html</a> |
|                                   | Department of Molecular Animal Physiology<br><a href="http://www.kun.nl/molanphys/Homepage/home.htm">http://www.kun.nl/molanphys/Homepage/home.htm</a>                                      |
|                                   | Nijmegen Centre of Molecular Life Sciences<br><a href="http://www.ncmls.kun.nl/pdf/sections.pdf">http://www.ncmls.kun.nl/pdf/sections.pdf</a>   |
| Rijksuniversiteit Groningen       | Groningen Bioinformatics Centre (GBIC)<br><a href="http://www.cs.rug.nl/~ritsert/gbic.htm">http://www.cs.rug.nl/~ritsert/gbic.htm</a>   |
|                                   | Groningen Biomolecular Sciences and Biotechnology Institute (GBB)<br><a href="http://molgen.biol.rug.nl/molgen/index.php">http://molgen.biol.rug.nl/molgen/index.php</a>                    |
|                                   | Groningen Genomics Centre (GGC)<br><a href="http://www.genomics.rug.nl/">http://www.genomics.rug.nl/</a>  |
|                                   | Groningen Mibiton Proteomics Facility<br><a href="http://www.medicalproteomics.com/">http://www.medicalproteomics.com/</a>  |
|                                   | Institute of Mathematics and Computing Science<br><a href="http://www.cs.rug.nl/NieuweOpzet/">http://www.cs.rug.nl/NieuweOpzet/</a>   |
| Technische Universiteit Eindhoven | Molecular BioEngineering<br><a href="http://www.bmt.tue.nl/research/MBE.htm">http://www.bmt.tue.nl/research/MBE.htm</a>   |
| Universiteit Leiden               | Leiden Institute of Advanced Computer Science<br><a href="http://www.liacs.nl/CS/ALP/">http://www.liacs.nl/CS/ALP/</a>  |
|                                   | Medical Pharmacology<br><a href="http://wwwpharm.leidenuniv.nl/lacdrhomepage/medpharmhome/project.htm">http://wwwpharm.leidenuniv.nl/lacdrhomepage/medpharmhome/project.htm</a>             |
| Universiteit Utrecht              | Academic Biomedical Centre<br><a href="http://www.abc.uu.nl/aboutabc/3640main.html">http://www.abc.uu.nl/aboutabc/3640main.html</a>   |
|                                   | Bioinformatics Group<br><a href="http://www-binf.bio.uu.nl/">http://www-binf.bio.uu.nl/</a>   |
|                                   | Biomolecular Mass Spectrometry<br><a href="http://www.chem.uu.nl/bioms/research/research.html">http://www.chem.uu.nl/bioms/research/research.html</a>                                       |
|                                   | Faculteit Biology, Molecular Genetics Group<br><a href="http://www.bio.uu.nl/~molgen/index_uk.html">http://www.bio.uu.nl/~molgen/index_uk.html</a>  |
| Universiteit van Amsterdam        | Department of Biology<br><a href="http://www.bio.uva.nl/">http://www.bio.uva.nl/</a>  |
|                                   | Evolutionary biology<br><a href="http://www.bio.uva.nl/zma/core/00/01/b0.html">http://www.bio.uva.nl/zma/core/00/01/b0.html</a>   |
|                                   | Swammerdam Institute for Life Sciences<br><a href="http://www.science.uva.nl/research/sils/research/mas/">http://www.science.uva.nl/research/sils/research/mas/</a>                         |

| University                   | Department   |
|------------------------------|--|
| Vrije Universiteit Amsterdam | Biology<br><a href="http://www.bio.vu.nl/">http://www.bio.vu.nl/</a><br>Chair in Bioinformatics<br><a href="http://www.cs.vu.nl/~bal/bioinfprof.html">http://www.cs.vu.nl/~bal/bioinfprof.html</a><br>Department of Molecular and Cellular Neurobiology<br><a href="http://www.bio.vu.nl/vakgroepen/mnb/research/research1.html">http://www.bio.vu.nl/vakgroepen/mnb/research/research1.html</a>   |
| Wageningen Universiteit      | Laboratory of Molecular Biology<br><a href="http://www.dpw.wau.nl/molbi/">http://www.dpw.wau.nl/molbi/</a><br>Molecular Microbial Ecology<br><a href="http://www.ftns.wau.nl/micr/moleco/moleco.htm">http://www.ftns.wau.nl/micr/moleco/moleco.htm</a><br>Plant Research International<br><a href="http://www.plant.wageningen-ur.nl/">http://www.plant.wageningen-ur.nl/</a><br>Institute of Food Safety (RIKILT)<br><a href="http://www.rikilt.dlo.nl/default.htm">http://www.rikilt.dlo.nl/default.htm</a><br>Wageningen Centre for Food Sciences<br><a href="http://www.wcfs.nl/frameset.htm">http://www.wcfs.nl/frameset.htm</a><br>Wageningen Potato Centre<br><a href="http://www.agro.wau.nl/wpc/">http://www.agro.wau.nl/wpc/</a><br>Wageningen Institute of Animal Sciences<br><a href="http://www.wias.nl/mariecurie.html">http://www.wias.nl/mariecurie.html</a> |

Source: Science-Metrix (Internet)

### Dutch University Hospitals Performing Research in Genomics

| Hospital   | Department   |
|--|--|
| Academisch Medisch Centrum<br>Universiteit van Amsterdam | Amsterdam Genomics Centrum (AmGC)<br><a href="http://www.amc.uva.nl/r/05/001.html">http://www.amc.uva.nl/r/05/001.html</a><br>Bioinformatics Laboratory<br><a href="http://bioinfo.amc.sara.nl/HTM/htm_bioinfo.html">http://bioinfo.amc.sara.nl/HTM/htm_bioinfo.html</a>   |
| Leids Universitair Medisch<br>Centrum                    | Centre for Human and Clinical Genetics<br><a href="http://www.humgen.nl/">http://www.humgen.nl/</a><br>Leiden Genome Technology Centre (LGTC)<br><a href="http://www.lgtc.nl/">http://www.lgtc.nl/</a>   |
| Universitair Medisch Centrum<br>Utrecht                  | Centre for Biomedical Genetics (CBG)<br><a href="http://www.biomedicalgenetics.nl/">http://www.biomedicalgenetics.nl/</a><br>Bioinformatics group<br><a href="http://www.bioinformatics.med.uu.nl/">http://www.bioinformatics.med.uu.nl/</a><br>Genomics Laboratory<br><a href="http://www.genomics.med.uu.nl/">http://www.genomics.med.uu.nl/</a> |

Source: Science-Metrix (Internet)

## Annex II Companies Active in the Fields of Genomics, Proteomics and Bioinformatics in the Netherlands

Comprise enterprises that were active in Genomics between 1990 and 2002 or that acquired firms that were active in genomics during those years. Companies in brackets have either bought an interest, took control, or are partners of the firms listed.

### **Amgen B.V.**

P.O. Box 3345  
4800 DH Breda  
The Netherlands  
Tel: +31 76 573 2500  
Fax: +31 76 573 2501  
Internet: [www.amgen.com](http://www.amgen.com)

### **Amsterdam Molecular Therapeutics B.V.**

Meibergdreef 61  
PO Box 22506  
1100 DA Amsterdam  
The Netherlands  
Tel: + 31 20 566 7394  
Fax: + 31 20 566 9272  
Email: [info@amtbv.com](mailto:info@amtbv.com)  
Internet: [www.amtbv.com](http://www.amtbv.com)

### **Applied Biosystems**

Hoogerveenenweg 100  
Postbus 305  
2910 AH Nieuwerkerk a/d IJssel  
The Netherlands  
Tel: +31 180 39 2400  
Fax: +31 180 39 2409  
Internet: [www.appliedbiosystems.com](http://www.appliedbiosystems.com)

### **Aquasense**

Kruislaan 411a  
PO Box 95125  
NL-1090 HC Amsterdam  
The Netherlands  
Tel: +31 20 592 2244  
Fax: +31 20 592 2249  
Email: [info@aquasense.com](mailto:info@aquasense.com)  
Internet: [www.aquasense.nl](http://www.aquasense.nl)

### **Asfra B.V.**

Marchandweg 45  
3771 MN Barneveld  
The Netherlands  
Tel: +31 342 40 50 50  
Fax: +31 342 49 29 72  
The Netherlands  
Email: [info@asfra.com](mailto:info@asfra.com)  
Internet: [www.asfra.com](http://www.asfra.com)

### **B&L Systems (Incyte Genomics)**

Industrieweg 68  
3606 AS Maarssen  
The Netherlands  
Tel: +31 346 550 556  
Fax: +31 346 554 619  
Email: [post@blsystems.nl](mailto:post@blsystems.nl)  
Internet: [www.blsystems.nl](http://www.blsystems.nl)

### **BaseClear**

P.O.Box 1336  
NL-2302 BH  
Leiden  
The Netherlands  
Tel: + 31 71 523 3917  
Fax: + 31 71 523 5594  
Email: [dna@baseclear.nl](mailto:dna@baseclear.nl)  
Internet: [www.baseclear.nl](http://www.baseclear.nl)

### **Biogen International B.V.**

P.O Box 170  
2130 AD Hoofddorp  
The Netherlands  
Tel: +31 23 566 8181  
Fax: +31 23 566 8182  
Email: [Biogen\\_intbv@biogen.com](mailto:Biogen_intbv@biogen.com)  
Internet: [www.biogen.nl](http://www.biogen.nl)

### **Biotechnology Application Centre B.V. (Unilever)**

P.O. Box 2  
1400 CA Bussum  
The Netherlands  
Tel: +31 35 69 92 595  
Fax: +31 35 69 49 576  
Email: [ingeborg-van.gemeren@unilever.com](mailto:ingeborg-van.gemeren@unilever.com)  
Internet: [www.bac.nl](http://www.bac.nl)

### **Bio Rad**

P.O. Box 222  
3900 AE Veenendaal  
The Netherlands  
Tel: +31 318 540 666  
Fax: +31 318 542 216  
Email: [margreet\\_schreijer@bio-rad.com](mailto:margreet_schreijer@bio-rad.com)  
Internet: [www.bio-rad.com](http://www.bio-rad.com)

**Centocor B.V.**

postbus 251  
2300 AG Leiden  
The Netherlands  
Tel: +31 71 524 2444  
Fax: +31 71 521 6511  
Email: eroest@cntnl.jnj.com  
Internet: www.centocor.nl

**Centre for Human Drug Research**

Zernikedreef 10  
2333 CL Leiden  
The Netherlands  
Tel: +31 71 5246400  
Fax: +31 71 5246499  
Email: info@chdr.nl  
Internet: www.chdr.nl/main.jsp

**Crucell N.V. (A Life Science Partner)**

Archimedesweg 4  
2333 CN Leiden  
The Netherlands  
Tel: +31 71 5248701  
Fax: +31 71 5248702  
Email: info@crucell.com  
Internet: www.crucell.com

**Dopharma International**

Postbus 205,  
4940 AE Raamsdonksveer  
The Netherlands  
Tel: +31 162 58 20 00  
Fax: +31 162 58 20 25  
Email: pr@dopharma.com  
Internet: www.dopharma.com

**DSM Biologics**

P.O. Box 43  
6130 AA Sittard  
The Netherlands  
Tel: +31 46 477 32 30  
Fax: +31 46 477 31 79  
Email: info.biologics@dsm-group.com  
Internet: www.dsmbiologics.com

**European Biotech. Consultancy**

POB 50, 2240 AB Wassenaar  
the Netherlands  
Tel/Fax: +31 705176331  
Email: biotech.worldmail.nl  
Internet: home-2.worldonline.nl

**Eurosequence**

Meditech Centre  
L.J. Zielstraweg 1  
9713 GX Groningen  
The Netherlands  
Tel: +31 50 3172424  
Fax: +31 50 3172420  
Email: info@eurosequence.nl  
Internet: www.eurosequence.nl

**Galapagos Genomics B.V.**

Archimedesweg 4  
PO Box 2048  
2301 CA Leiden  
The Netherlands  
Tel: +31 71 524 88 00  
Fax: +31 71 524 88 01  
Email: laurens@galapagos.be  
Internet: www.galapagosgenomics.com

**Genecor International B.V.**

P.O. Box 218  
2300 AE Leiden  
The Netherlands  
Tel: +31 71 56 86 168  
Fax: +31 71 56 86 169  
Internet: www.genecor.com

**Genetwister Technologies B.V.**

Bornsesteeg 59 NL6708 PD  
P.O. Box 193  
NL6700 AD Wageningen  
The Netherlands  
Phone: +31 317 475115  
Fax: +31 317 478561  
Email: info@genetwister.nl  
Internet: www.genetwister.nl

**Genmab B.V.**

P.O. Box 85090  
3508 AB Utrecht  
Tel: +31 30 2504306  
Fax: +31 30 2504305  
Email: M.A.vanDijk@med.uu.nl  
Internet: www.genmab.com

**Genzyme B.V.**

Gooimeer 10  
1411 DD Naarden  
The Netherlands  
Tel: +31 35 699 1200  
Fax: + 31 35 695 3703  
Internet: www.genzyme.com

**Glaucus Proteomics B.V.**

Singel 2e  
P.O. Box 13  
3984 ZG Odijk  
The Netherlands  
Tel: +31 30 656 99 00  
Fax: +31 30 656 99 40  
Email: gp@glaucusprot.com  
Internet: www.glaucusprot.com/Glaucus.html

**Greenomics (Plant Research International)**

P.O. Box 16  
6700 AA Wageningen  
The Netherlands  
Tel: +31 317 47 73 77  
Fax: +31 317 41 80 94  
Email: greenomics@plant.wag-ur.nl  
Internet: www.greenomics.com

**Groenendijkgenomics**

PO Box 208  
6700 AE  
Wageningen  
The Netherlands  
Tel: +31 6 10856450  
Fax: +31 317484263  
Email: info@groenendijkgenomics.com  
Internet: www.groenendijkgenomics.com

**Holland Genetics**

P.O Box 5073  
6802 EB Arnhem  
The Netherlands  
Tel: +31 26 3898500  
Fax: +31 26 3898555  
Email: HG@cr-delta.nl  
Internet: www.hollandgenetics.com

**Hycult Biotechnology B.V.**

P.O. Box 30  
5400 AA Uden  
The Netherlands  
Tel: +31 413 251 335  
Fax: +31 413 266 605  
Email: hbt@hbt.nl  
Internet: www.hbt.nl

**Ingeny International B.V.**

Amundsenweg 71  
4462 GP Goes  
The Netherlands  
Tel: +31 113 222920  
Fax: +31 113 222923  
Email: info@ingeny.com  
Internet: www.ingeny.com

**Isogen Bioscience (B&L Systems)**

Industrieweg 68  
P.O. Box 1779  
3600 BT Maarssen  
The Netherlands  
Tel: +31 346 555 083  
Fax: +31 346 554 430  
Email: Post@isogen.nl  
Internet: www.isogen.nl

**IsoTis**

PO Box 98  
3720 AB Bilthoven  
The Netherlands  
Tel: +31 30 229 5 229  
Fax: +31 30 228 0 255  
Email: investor.relations@isotis.com  
Internet: www.isotis.com

**Keygene N.V.**

P.O. Box 216  
6700 AE Wageningen  
The Netherlands  
Tel: +31 317 466 866  
Fax: +31 317 424 939  
Email: info@keygene.com  
Internet: www.keygene.com

**Kreatech Biotechnology B.V. (Life Science Partners)**

Postbus 370s78  
1030 AB Amsterdam  
The Netherlands  
Tel: +31 20 691 91 81  
Fax: +31 20 696 35 31  
Email: info@kreatech.com  
Internet: www.kreatech.com

**LC Packings (Dionex)**

Abberdaan 114  
1046 AA Amsterdam  
The Netherlands  
Tel: +31 20 683 97 68  
Fax: +31 20 685 34 52  
Email: info@lcpackings.nl  
Internet: www.lcpackings.nl

**Leadd B.V.**

P.O. Box 9503  
2300 RA Leiden  
The Netherlands  
Tel: +31 71 5278736  
Fax: +31 71 5271736  
Email: leadd@leadd.nl  
Internet: www.leadd.com

**Life Sciences Partners**

Johannes Vermeerplein 9  
1071 DV Amsterdam  
The Netherlands  
Tel: +31 20 664 55 00  
Fax: +31 20 676 88 10  
Email: info@lsp.nl  
Internet: www.lsp.nl

**MacroZyme B.V.**

Tafelbergweg 51  
Zone A31105 BD Amsterdam Zuidoost  
The Netherlands  
Tel: +31 20 6521130  
Fax: +31 20 6521131  
Email: c.vanborkulo@macrozyme.com  
Internet: www.macrozyme.nl

**MicroSafe B.V.**

Niels Bohrweg 11-13  
2333 CA Leiden  
The Netherlands  
Tel: +31 71 523 1886  
Fax: +31 71 523 5980  
Email: info@microsafe.nl  
Internet: www.microsafe.nl

**Microscreen**

Microbial Diagnostics  
L.J. Zielstraweg 1  
9713 GX Groningen  
The Netherlands  
Tel: +31 50 3166787  
Fax: +31 50 3166797  
Email: g.bos@microscreen.com  
Internet: www.microscreen.com

**NIZO food research**

2 Kernhemseweg  
P.O. Box 20  
6710 BA Ede  
The Netherlands  
Tel: +31 318 659 511  
Fax: +31 318 659 522  
Email: info@nizo.nl  
Internet: www.nizo.nl

**Noldus Information Technology B.V.**

Costerweg 5  
P.O. Box 268  
6700 AG Wageningen  
The Netherlands  
Tel: +31 317 497677  
Fax: +31 317 424496  
Email: info@noldus.nl  
Internet: www.noldus.nl

**Notox Safety & Environmental Research B.V.**

P.O. Box 3476  
5203 DL 's-Hertogenbosch  
The Netherlands  
Tel: +31 73 640 67 00  
Fax: +31 73 640 67 99  
Email: notox@notox.nl  
Internet: www.notox.nl

**OctoPlus B.V.**

Zernikedreef 12  
2333 CL Leiden  
The Netherlands  
Tel: +31 71 5244044  
Fax: +31 71 5244043  
Email: octoplus@octoplus.nl  
Internet: www.octoplus.nl

**Organon Nederland B.V.**

Griekenweg 25  
Postbus 500  
5340 AM OSS  
The Netherlands  
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Fax: +31 412 666 980  
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