

Science-Matrix

Genomics in the Netherlands

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

Prepared for
Genome Canada



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).

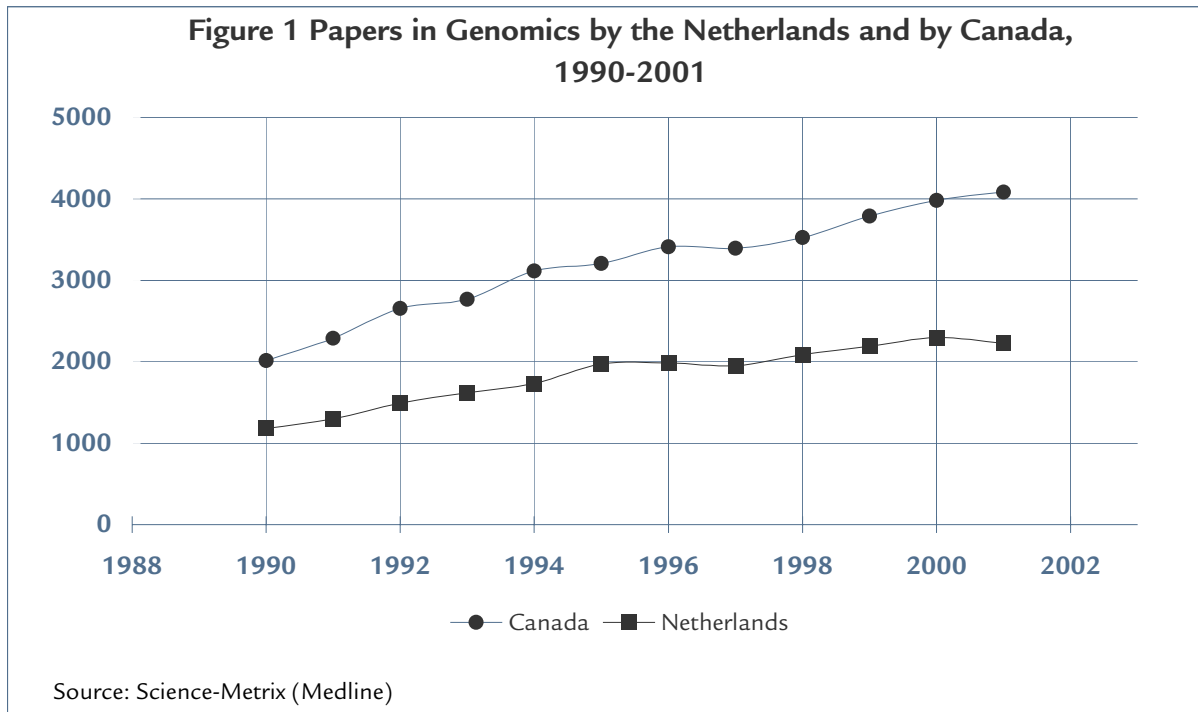
Table 1 Basic Socio-Economic Statistics

	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 Excellence¹;

¹ 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 genomics²;
- the coordination of applications for genomics projects within an Interdepartmental Committee for Economic Structure programme (ICES/KIS-3)³.

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)⁴, budgetary funding (170 million guilder)⁵ and ICES/KIS 3 funding⁶.

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

² 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.

³ 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.

⁴ 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).

⁵ 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.

⁶ 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)⁷. 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;

⁷ 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 NutriGenomics⁸ 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.

⁸ 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 4th and 6th 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	Netherlands	France	Canada	UK
4	Germany	USA	Sweden	Netherlands	Netherlands
5	France	UK	Japan	UK	France
6	Canada	Canada	Netherlands	France	Canada
7	Italy	Australia	UK	Germany	Sweden
8	Netherlands	France	Australia	Sweden	Japan
9	Australia	Germany	Canada	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 2nd worldwide, that is,

ahead of Canada. The Netherlands' patenting activity is also highly specialized in genomic research, ranking 2nd worldwide, just before Canada (3rd rank). However, the Dutch's patent growth rate is much less important than Canada's, respectively ranking 8th and 3rd. 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 1st worldwide - whereas the Netherlands occupies 6th 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 5th while the Dutch occupy the 7th 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 7th and the Netherlands 11th. In the core fields of genomics, clinical medicine appears most promising considering that both countries are similarly successful: the Netherlands ranks 3rd and Canada 7th.

**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
Papers (%)	21,343 (6%)	205,864 (58%)	7,240 (2%)	117,948 (33%)

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
Biology	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
Biomedical Research	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
Chemistry							
Applied Chemistry	Germany	UK	USA	Canada	Japan	Netherlands	Australia
Polymers	France	Japan	USA	Germany	Netherlands	Sweden	Canada
Clinical Medicine	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
Earth and Space	Canada	USA	Australia	Netherlands	Germany	France	Japan
Environmental Science	Canada	USA	Australia	Netherlands	Germany	Japan	France
Engineering and Technology	USA	Germany	Canada	Japan	UK	Italy	Netherlands
Chemical Engineering	Japan	USA	Canada	Australia	Germany	Netherlands	UK
Computers	USA	UK	Canada	Germany	Italy	Japan	Netherlands
Mathematics	UK	USA	France	Canada	Germany	Japan	Netherlands
Applied Mathematics	USA	UK	Netherlands	Canada	Italy	France	Spain
Psychology	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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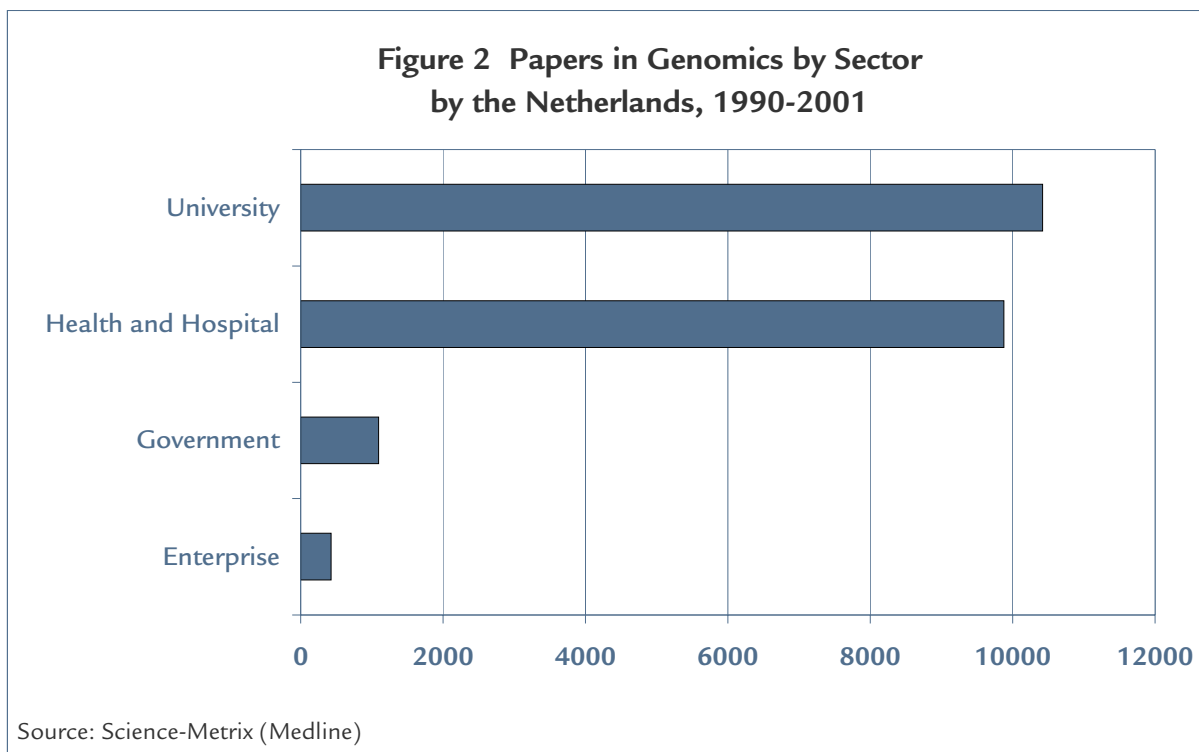
This analysis is an aggregate evaluation of Canadian and Dutch scientific performance. The fact that the scientific fields listed above present opportunities for *planned* collaborative research does not mean that mutually beneficial collaboration could not be performed at an individual level between 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.

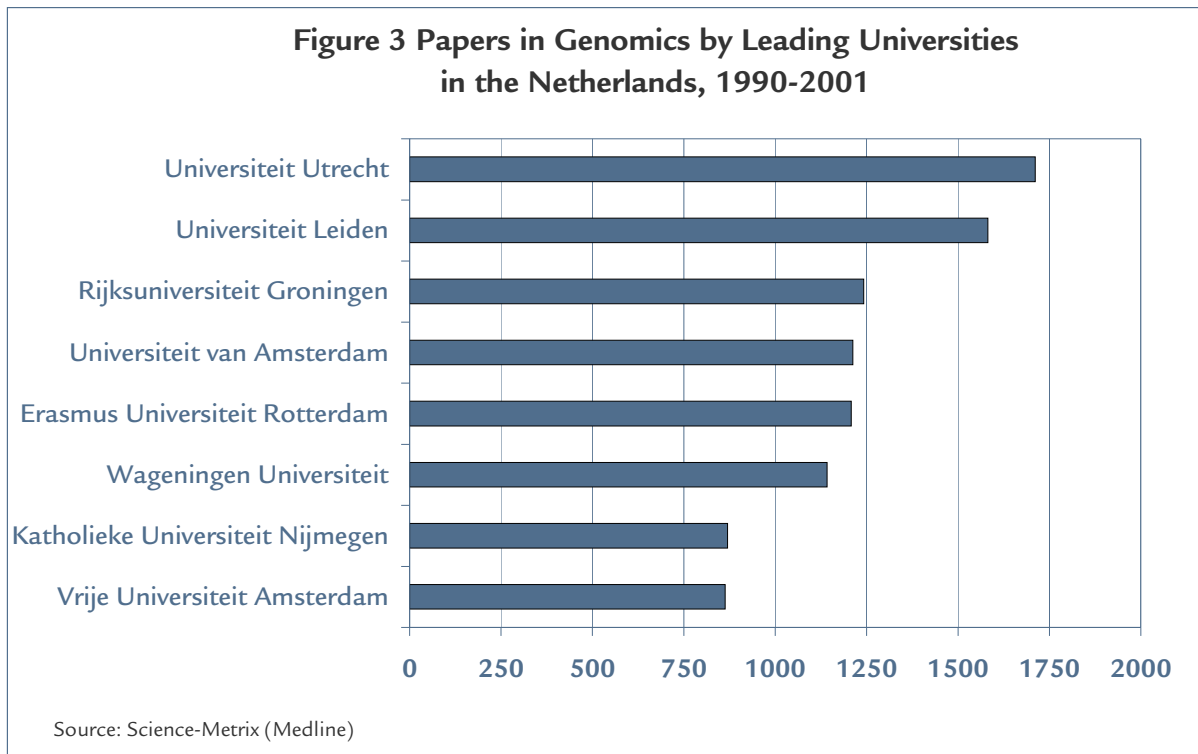
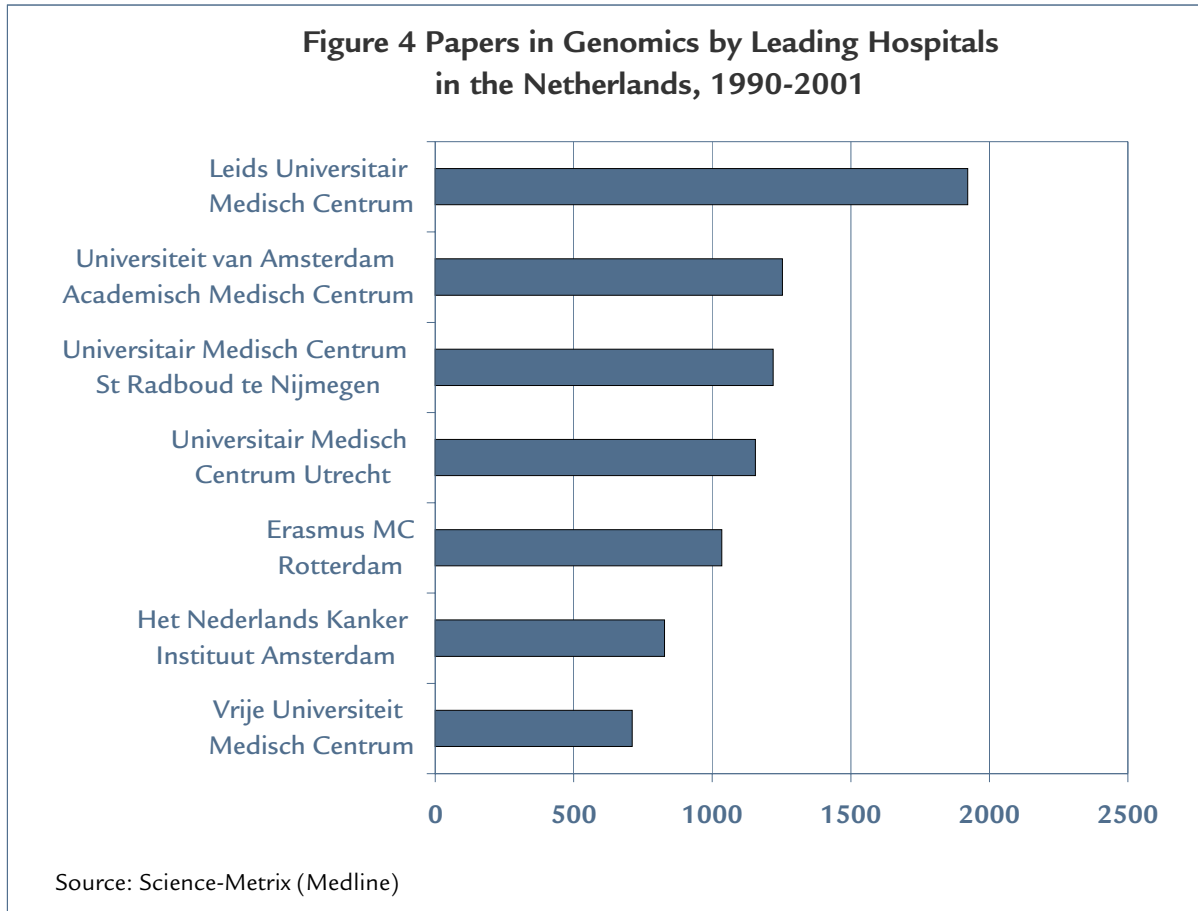


Figure 4 lists the most active institutions in the health and hospital sector. Not surprisingly, all of them, except the Netherlands Cancer Institute, are university hospitals. The leading institution in this sector is *Leids Universitair Medisch Centrum* (Leiden University Medical Centre), which with 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.

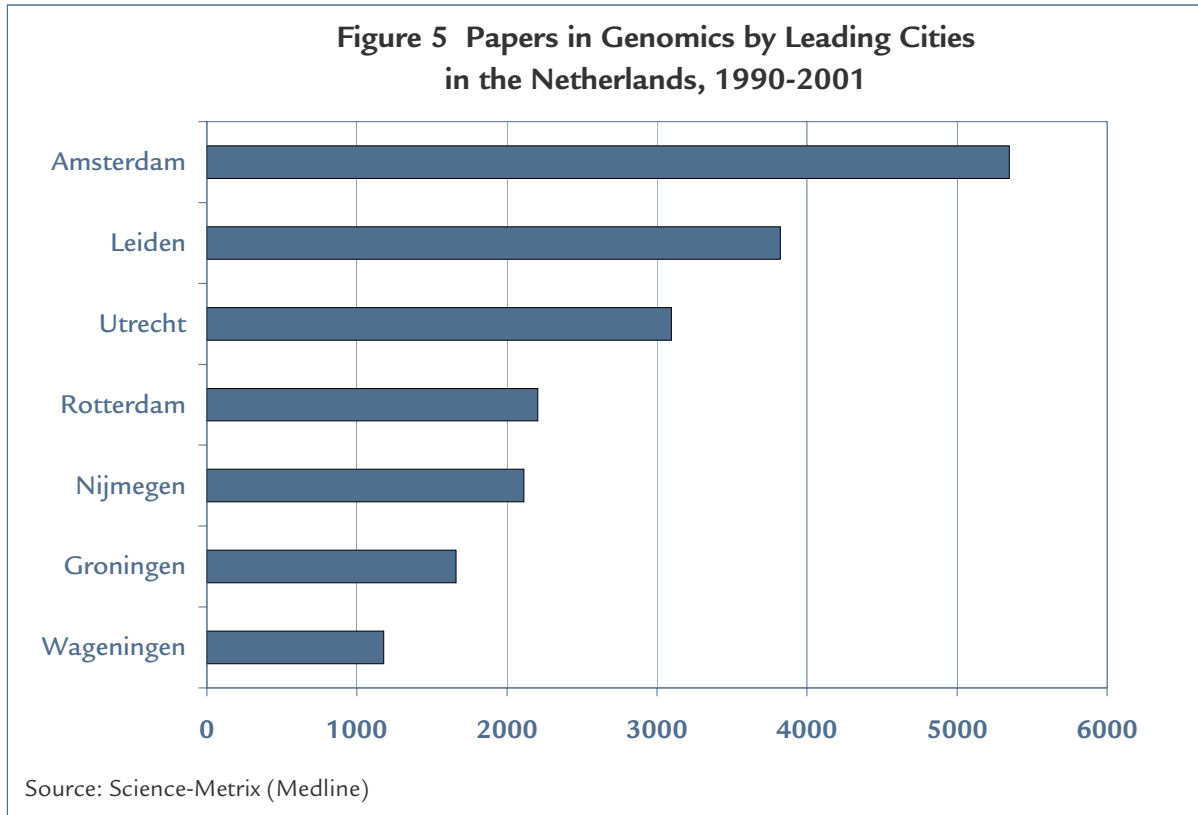
**Table 6 Ranking of Leading Enterprises in Genomics in the Netherlands.
Number of Papers by City, 1990-1999**

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
Total			114	83	60	34	28	22	22	15	11	44	433

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

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

Source: Science-Metrix (Internet)

Dutch University Hospitals Performing Research in Genomics

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

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

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
Internet: www.amtbv.com

Applied Biosystems

Hoogveenenweg 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

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
Internet: 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
Internet: 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
Internet: 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
Internet: 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
Internet: 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
Internet: 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
Internet: 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
Tel: +31 412 666 922
Fax: +31 412 666 980
Internet: www.organon.nl

PamGene (Life Sciences Partner)

P.O. Box 1345, 5200 BJ 's-Hertogenbosch
Burgemeester Loeffplein 70A
5211 RX 's-Hertogenbosch
The Netherlands
Tel: +31 73 615 80 80
Fax: +31 73 615 80 81
Internet: www.pamgene.com

Pepscan Systems B.V.

P.O. Box 2098
8203 AB LELYSTAD
The Netherlands
Tel: +31 320 237200
Fax: +31 320 238120
Email: p.vandijken@pepscan.nl
Internet: www.pepscan.nl

Pharming Group N.V.

P.O. Box 451
2300 AL Leiden
The Netherlands
Tel: +31 71 5247 400
Fax: +31 71 5216 507
Email: pharming@pharming.com
Internet: www.pharming.com

Philips In- en Externe Betrekkingen Nederland

Postbus 90050
5600 PB EINDHOVEN
The Netherlands
Tel: +31 40 2780278
Fax: +31 40 2782763
Email: pers.nl@philips.com
Internet: www.philips.nl/werken

Plant Research International

P.O. Box 16
6700 AA Wageningen
The Netherlands
Tel: +31 317 47 70 17
Fax: +31 317 41 80 94
Email: info@plant.wag-ur.nl
Internet: www.plant.wageningen-ur.nl

Primagen

Meibergdreef 59
1105 BA Amsterdam
The Netherlands
Tel: +31 20 566 85 69
Fax: +31 20 566 90 81
Email: e.derooy@primagen.com
Internet: www.primagen.com

Rhein Biotech N.V. (Berna Biotech)

MECC Office Building
Gaetano Martinolaan 25
6229 GS Maastricht
The Netherlands
Tel: +31 43 356 7890
Fax: +31 43 356 7899
Email: general@rheinbiotech.com
Internet: www.rheinbiotech.nl

Sanbio B.V.

P.O. Box 540
5400 AM Uden
The Netherlands
5405 PB Uden
The Netherlands
Tel: +31 413 251 115
Fax: +31 413 266 605
Email: sanbio@sanbio.nl
Internet: www.sanbio.nl

Shell Research and Technology Centre

P.O. Box 38000
1030 BN Amsterdam
The Netherlands
Tel: +31 20 6309111
Fax: +31 20 6308025

Solvay Pharmaceuticals

C.J. van Houtenlaan 36
Postbus 900, 1380 DA Weesp
The Netherlands
Tel: +31 294 47 93 57
Fax: +31 294 43 11 64
Email: mailto:gerard.dijkstra@solvay.com
Internet: www.solvaypharmaceuticals.com

SynCo Bio Partners

Paasheuvelweg 30
1105 BJ Amsterdam
P.O. Box 22620
1100 DC Amsterdam
The Netherlands
Tel: +31 20 7503600
Fax: +31 20 7503601
Email: info@synco-biopartners.com
Internet: www.synco-biopartners.com

Syngenta Mogen B.V.

P.O. Box 628
2300 AP Leiden
The Netherlands
Tel: +31 71 525 82 82
Fax: +31 71 522 14 71

Torex-Hiscom Nieuwegein

Nevelgaarde 4
3436 ZZ Nieuwegein
The Netherlands
Tel 030 60 38 797
Fax 030 60 38 492
Email: info@torex-hiscom.nl
Internet: www.torex-hiscom.nl

Unilever N.V.

PO Box 760
3000 DK
Rotterdam
The Netherlands

Westburg B.V.

P.O. Box 214
3830 AE Leusden
The Netherlands
Tel: +31 33 495 00 94
Fax: +31 33 495 12 22
Email: info@westburg.nl
Internet: www.westburg.nl

Xendo Laboratories B.V.

L.J.Zielstraweg 1
9713 GX Groningen
The Netherlands
Tel: +31 50 304 8004
Fax: +31 50 318 3441
Email: office@xendo.nl
Internet: www.xendo.nl