Infection and Immunity

General Information

Deans:

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Participating main research programs:

- Immunology and Infectious Diseases (I&I; UMC Utrecht)
- Strategic Infection Biology (SIB;FVM-UU)
- Risk Assessment of Toxic and Immunomodulatory Agents (RATIA; FVM-UU[1])

Scientific core of the focus area

Scientific background:
Understanding, preventing and finding cures for (re)emerging infections and chronic inflammatory diseases, in the broader context of public and environmental health issues, constitutes the core of the focus area of "Infection and Immunity". At Utrecht University, this focus area is covered by the combination of three highly-related, but complementary, research programs of the UMC Utrecht, the FVM-UU, and the faculty of Science, respectively. These programs, that each are major and strategic components of the research policy of the participating faculties as specified in the recent institutional "more focus and critical mass" reports, are designed to discover principles of infection and chronic inflammatory disease at the cellular, organ, host, and population level with the strategic goal to develop novel infection intervention and prevention tools and, hence, to increase animal and human health.

Coherence and contribution to the field:
To illustrate the coherence of the participating programs within the focus area, and to explain their contribution to the developments in the field, details about the individual main research programs are presented below.

Immunology and Infectious Diseases (UMC Utrecht)
The impact of infectious diseases and disorders of immunity on society is enormous, with both serious health and economical aspects. Hence, the mission of the program is to understand, prevent and cure (re)emerging infections and chronic inflammatory diseases, and to train graduate students in the broad field of "Infection and Immunity" within a high quality multidisciplinary scientific environment. Immunity research in the UMC Utrecht "Immunology and Infectious diseases" program is a well balanced mix of fundamental and translational research aimed to find solutions for prevention and treatment of immunological disorders, including hypo- and hyper-reactivity of the immune system. Research on hyporeactivity concentrates on immune deficiencies in children and patients after bone marrow transplantation. Research on hyperreactivity is mainly aimed at chronic inflammatory disorders which are studied in man and appropriate animal models. Immunotoxic and allergic effects from environmental and nutritional sources are also studied. A central theme of several groups is the investigation of the different types of defense against bacteria and viruses and how it is evaded by the pathogens. Innate immunity research is well represented in both the "infection" and "immunity" research lines of the program, in relation with autoimmune diseases, microorganisms or inflammatory damage to the host. Next to mechanisms of development of drug resistance, there is a major interest in the kinetics of chronic inflammatory diseases, in particular the switch to chronicity: from adaptive immunity in the (semi)acute phase to innate immunity in the chronic phase.

Strategic Infection Biology (FVM-UU)
Infectious diseases form a continuous threat to human, animal, and economic health. Control of the (re-) emergence and persistence of infectious agents requires detailed knowledge of all aspects of the entire infection chain, i.e. genome plasticity and virulence potential of infectious agents, cellular infection mechanisms, innate and adaptive host defense, and infection dynamics. The overall aim of this research program is to unravel principles of infection at the individual and community level to facilitate targeted development of novel infection intervention and prevention tools. The program may also open new avenues to exploit infectious agent derivatives to human and animal health benefit. In general, infection cycles involve contact with and adaptation of infectious agents to distinct niches in the host, breaching of

[1] The RATIA program includes the research programs of the Institute of Risk Assessment Sciences (IRAS), which is supported not only by the FVM-UU but also by the UMC Utrecht and the Faculty of Science.

tissue barriers, multiplication, (temporary) evasion of the innate and adaptive host defense, and spread to a new host. Development of novel targeted infection intervention and prevention strategies thus requires detailed knowledge of the pathogen, its host, the interplay between pathogen and host, and the interaction of the host with the environment, including other hosts. Unraveling of principles of infection and the associated pathology requires a multidisciplinary approach involving microbiology, immunology, cell biology, biochemistry, pathology, animal health, and epidemiology. This program exploits and integrates this expertise, providing the optimal setting to achieve our goals. The fact that this research program is focused on infectious agents that have zoonotic potential and/or pathogens that are anticipated to constitute a major threat for (future) veterinary-, clinical- and economic welfare, underlines the high socio-economic relevance of the program.

Risk Assessment of Toxic and Immunomodulatory Agents (FVM-UU)

The program Risk Assessment of Toxic and Immunomodulatory Agents (RATIA) aims at the development and further improvement of the scientific basis for assessment of risks (to human, animal and ecosystem health) of exposure to environmental agents. Specifically, the program focuses on: 1) veterinary public health issues related to food safety, and allergies to domestic, laboratory and farm animals 2) human and environmental health issues such as risks of exposure to biological, physical and chemical agents, and vaccines 3) occupational health issues such as risks to health of workers in concentrated animal feeding operations (CAFOs) and the animal feed industry, and veterinarians, and 4) ecosystem health issues such as endocrine disruption effects of various contaminants on animal wildlife. The overall impact of this program for human health is highlighted by the notion that veterinary public health includes not only microbial food safety, but also potential positive as well as negative health consequences through environmental and occupational exposure to non-infectious agents including bacterial endotoxins, allergens, environmental contaminants, residues of antibiotics and anti-neoplastic agents and naturally occurring hormones that can be transferred to humans through dairy products and meat.

Focus area "Infection and Immunity"

As outlined above, all multidisciplinary expertise required for state-of-the-art infection biology research is represented in this cluster of highly complementary research programs. Importantly, despite the great similarity in general focus, each of the participating faculties and research groups contributes to the program from their own perspective thus ensuring, up-to-date and continued, high quality of the respective research disciplines. Over the past few years, strong coherence between the participating research groups has been achieved mainly by the bundling of knowledge and expertise within the theme "Infection and Immunity" of the Academic Biomedical Centre Utrecht (ABC) and within the Eijkman Graduate School for Immunology and Infectious diseases.

Recently, prompted by the process of "more focus and critical mass" and the subsequent identification of focal areas of research, each of the individual faculties has assigned main research programs that fit with the institutional research policy and have sufficient focus and critical mass to boost high quality research and overall academic performance. As the next step, the process of "more focus and critical mass" will be urged even further by bringing together several related main research programs of different faculties within one focus area. The forthcoming years, the research leaders will have to make forward looking choices in order to further narrow down the present research areas. It is anticipated that by combining the aforementioned research programs, it will be possible to achieve even more focus and synergy, and, hence, to create an area of focus that will significantly contribute to the scientific excellence and competitiveness of Utrecht University in the field of "infection and Immunity".

Main research activities and ongoing (multidisciplinary) collaborations:

Since the establishment of the ABC in 2000, "Infection and Immunity" has been one of the four major, disease-oriented, themes. In line with the philosophy of the ABC to try and define common research goals and to foster interdisciplinary collaboration, e.g. by creating expertise centres and a unique set of shared high-tech research facilities for advanced proteomics, metabolomics, genomics, structural biology, and vaccine research, many fruitful collaborations have been established between the FVM, the UMC Utrecht and the faculty of Science, respectively. More specifically, where the focus area of "Infection and Immunity" is concerned extensive collaborations exist with research groups participating in focus area "5. Molecular Life Sciences and Bioinformatics" and focus area "9. Drug Innovation". The collaboration with research group in focus area 5 concerns the research on molecular processes from the atomic to cellular level and the research of biocomplexity and bioinformatics. Research results of these groups, as well as their technological and methological expertise, are essential for the focus area "Infection and Immunity'. In this respect, collaborative research with the groups of Prof.dr. J. Tomassen, Prof.dr. P. Gros, and Prof.dr. R.J. de Boer is especially noticeable. Research groups in the focus area "Drug Innovation" and the focus area "Infection and Immunity" have close collaboration as well. A very intensive interaction is that with Prof. dr. A.J.R. Heck, the director of the Netherlands Proteomics Center and researchers in focus area "Drug Innovation". The interaction with focus area 3. "Growth and Differentiation" is lucidly illustrated by the fact that 'clinical stem cell transplantation' is one of the leading research themes of Prof.dr. P.J. Coffer of the division of pediatrics UMC Utrecht. Finally, the focus area "Infection and Immunity" is strongly linked to focus area 4. "Epidemiology" in which the epidemiology of "infection and

immunity" is one of the central themes of focus. The excellent research environment provided by the ABC serves as a permanent crossover for research groups in the focus area "Molecular Life Sciences", "Drug innovation" and "Epidemiology", on the one hand, and the more disease-orientated, biomedical focus area's on the other.

Overview of strategic impulses and incentives policy:

Human Resources Management (HRM):

- The appointment of professors is the most important instrument for fostering innovation and safeguarding the quality of research. Therefore, personnel policy plans of both faculties are completely tuned to attract high-qualified researchers to hold chairs and tenured track positions. Moreover, HRM activities have a strong emphasis on the selection and scouting of young scientific talent. Since the appointment of professors is the most important instrument in HRM measures for promoting research, the board of directors (UMC Utrecht) and the dean (FVM-UU) not only make the final decision which candidate will be proposed to the University Board for an appointment, but they are also actively involved in the scouting of talent and the selection of good candidates
- The regular chairs are assigned to divisions (UMC Utrecht) or departments (FVM-UU), based on their performance in patient care, education, but predominantly in research. In addition, a significant part of the chairs in UMC Utrecht and FVM-UU is assigned based on strategic decisions made by the board of directors (UMC Utrecht) or the dean (FVM-UU). Finally, next to these chairs, there are some chairs specially intended for young, talented researchers, who are appointed for a period of 5 years. In this way, they have a chance to prove themselves for a period of 5 years. If they function well, they can proceed to a regular professorship afterwards.
- The FVM-UU recently reassessed its research program and focused its research activities by further clustering of its activities in thematic, cross-departmental programs and reallocated its chairs and research budget accordingly. It is anticipated that the implementation of these changes will further stimulate the integration of preclinical and clinical research and will contribute to the high quality of research by improving the international visibility, the viability and the earning capacity of the research programs within the FVM-UU.
- Besides the appointment of professors, the appointment of qualified postdoctoral researchers in tenured track positions is of utmost importance for the quality of research. In both the UMC Utrecht and the FVM-UU, the criteria considered obligatory for the appointment to a tenured track position include publishing in top international journals, obtaining competitive external funding, and participation in international networks.
- As mentioned above, to be considered for promotion to a tenured track position, post-docs are encouraged to bring in prestigious grants. Examples are the "Innovational Research Incentives scheme" of the Netherlands Organization for Scientific Research (NWO) and the so-called "high potential program" of Utrecht University. For some of these prestigious grants, an internal procedure is first carried out to select and improve the proposals to be submitted. An internal committee, consisting of members of the scientific staff, selects the candidates most likely to succeed in the national competition, and advises them on how to improve the quality of their application. This has proven very successful. In addition, post-docs are encouraged to spend some time abroad to build their networks, and well-qualified post-docs from abroad are actively recruited to spend time in the UMC Utrecht or FVM-UU. Although this kind of interchange occurs on a regular basis, it is our intention to further promote international exchange.
- In both faculties, newly appointed professors are generally supported by grants for PhD or postdoctoral projects to further their research. In general, the research projects of these professors dovetail with the faculty's focus areas.
- In both faculties, research groups and their leaders are recruited and evaluated based on quality and competence criteria. A three year window is generally maintained for evaluation.

Strategic (infrastructural) investments:

- The Academic Biomedical Centre Utrecht (ABC): In 2000, the Deans of the faculties of Medicine, Veterinary Medicine, and the former faculties of Chemistry, Biology and Pharmaceutical sciences (now comprising the faculty of Science) settled a strategic alliance and allocated a substantial part of their annual research budget to create the Academic Biomedical Centre Utrecht (www.abc.uu.nl). Since then, this partnership, which was established with the goal to strengthen the biomedical and biotechnology profile of Utrecht University in the fields of education, research and entrepreneurship, has proven to be an important factor in the current success of the Life Sciences in Utrecht.
- The ABC "matrix" philosophy: The combination of a well-considered selection of research programs that are either disease-orientated or merely orientated towards the development of sophisticated methodology and expertise has been one of the firmly rooted and leading principles of the ABC matrix philosophy. The interdisciplinary collaboration thus obtained has led to added value in both knowledge and expertise and has already resulted in a steady flow of high-quality and competitive research output that, as such, created the foundation for further strategic research alliances, either with academic or industrial partners. Over the last 6 years the ABC, which also incorporates the KNAW-

NIOB Hubrecht laboratory (www.niob.knaw.nl), has invested approximately 25 M€ to create several shared facilities (e.g., microarray facility, SNP facility, protein-expression facility, and MRI imaging facilities) and expertise centres that are all readily accessible for ABC members. Along with the strategic appointment of so-called ABC-professors, to again foster interdisciplinary education and research within the Life Sciences, it also permitted the foundation of three large internationally renowned knowledge centers within our campus. These centres that can be truly qualified as 'centres of excellence' include the Genomic Center Utrecht, the Netherlands Proteomic Centre, and the Metabolomics Centre Utrecht. As far as the focus area "infection and immunity" is concerned, the ABC has thus provided excellent opportunities for vaccine-, drug-, and translational research and, hence, has markedly contributed to the overall visibility of Utrecht University within this focus area.

Strategic funding and research organization / management

- In 2004, the UMC Utrecht decided to concentrate and stimulate research on the cross roads of disease- and methodologically-oriented programs with "Immunology and Infectious diseases" being designated as one of the four major disease-oriented programs.
- Over the last few years, the board of the UMCU has repeatedly assigned strategic funding to further strengthen research in a particular area. Extra funding relevant for the focus area is listed below.
    - 5 M€ (1 M€/yr for 5 years) was invested by the WKZ Fund to improve the international research position of the Wilhelmina Children's Hospital. With this budget, three large programs (Biomedical Genetics, Neurosciences and Immunology and Infectious Diseases) within the UMC Utrecht were promoted with 1.3 M€ each.
    - 10 M€ (1 M€/yr for 10 years) were invested by UMC Utrecht and ABC together (5 M€ each) in the establishment of the Genomic Center Utrecht (GCU; www.genomicscenter.nl), an interdisciplinary research center of UMC Utrecht and Utrecht University where scientists study the relationships between genes and diseases. The main research themes are Cancer Biomedical Genetics, NeuroBiomedical Genetics, Cardiovascular Biomedical Genetics and ImmunoBiomedical Genetics. The Center has extensive expertise in the fields of DNA micro-array analysis, gene expression, bioinformatics as well as functional biomedical genetics. The Genomics Center aspires to become 'the place to be' for excellent research in different fields of biomedical genetics, where methods and techniques are developed and directly applied to basic research as well as to clinical problems.
- As of January 2006, the research budgets for the FVM-UU's thematic research programs are task-oriented. Specific targets on the program focus, research output, earning capacity, international visibility and staffing of the program have been set to reinforce the FVM-UU's thematic research programs. The steering on these targets, as recently implemented, may lead to changes in the research budget meaning that excellent performance will be coupled to financial incentives for that particular research group. In contrast, poor performance will ultimately result in a reduction in personnel and means.

Position

The focus area "Infection and Immunity" constitutes an important niche within the Life Sciences that deals with important issues relevant to animal and human health. The programs involved are generally designed to understand, to prevent and cure (re)emerging infections and chronic inflammatory diseases and related public and environmental health issues. The multidisciplinary infection biology expertise that is created by the joint expertise of the participating programs accommodates the highly needed integration of fundamental and applied research in the field of infectious and chronic inflammatory diseases and has sufficient mass to 'make a difference' both in the national and international research arena.

Strategic position of the focus area in a national perspective:

- In respect to the focus area "Infection and Immunity", the position of Utrecht University is unique in that it is home to the only faculty of Veterinary Medicine in the Netherlands. Given the intimate relationship between animal and human health, as exemplified not only by the zoonotic potential of pathogens studied (emerging infections usually originate from wildlife or animal populations) but also by issues related to livestock welfare and food-safety, the joint research programs of both the FVM-UU and the University Medical Center constitutes a unique centre of excellence. The added value of the FVM-UU is one of the major assets that justifies the claim that Utrecht University has a very strong, if not, ultimate strategic position to outperform in the focus area of "infection and immunity".
- All participating research groups have a longstanding tradition in the field of "infection and immunity" and have an excellent academic reputation, as evidenced by the high impact of the scientific output, the participation in national and international scientific networks, and the strong track records and earning capacity of the individual scientists.
- The FVM-UU, which is the only one in the Netherlands, has a particularly strong reputation. As recently stated by an international review committee the FVM-UU is - based on the quality of its research - ranked as the number 1 of all veterinary faculties within Europe and belongs to the top-5 veterinary faculties world-wide. This picture is recently underscored by an independent survey performed by the renowned Thomson/ISI institute indicating that in the fields of "Veterinary Science", "Veterinary Medicine", and "Animal Health", the FVM-UU holds the fourth position in the list of most-frequently cited veterinary research institutions world-wide (Science Watch 2005 16:1-2). Of note, the FVM-UU is the only European institution in the top-10 list.
- The UMC Utrecht has a strong position within the Netherlands as shown, inter alia, by the bibliometric analysis performed by the CWTS (Centre for Science and Technology Studies at Leiden University). In this analysis the average journal impact (JCS/FCS) of all 4,626 publications produced by UMC Utrecht in the time period 1998-2002 has been calculated to be 1.34, which is the highest when compared to the score of all UMC's in the Netherlands (ranging from 1.07 – 1.34). In addition, the average citation score (CPP/FCS) of all these publications has been calculated to be 1.55. This means that the articles of UMC Utrecht are cited 55% more often than the world average. Compared to the average citation score of all Dutch scientific publications (1.25) and the average citation score of all UMCs (1.33, ranging from 1.08 to 1.55) the citation score of UMC Utrecht is very high. The CWTS bibliometric analysis was also performed at the level of the research programs. Based on data collected over the years 1998-2002, the UMC Utrecht research program "Infection and Immunity" performed extremely well with a citation score above 1.60. Data including the years 2003-2005 have recently become available also and are presented farther down under "past performance".
- Thomson ISI 'Essential Science Indicators' has recently performed an analysis on the topic of Air Pollution over the period 1995-2005. Their results show that the work at IRAS (Environmental and Occupational Health (EOH) division) of the last 10-15 years in this area has secured the number one position inside Europe, measured by the number of cites. Only the Harvard School of Public Health, John's Hopkins Bloomberg School of Public Health and Brigham Young University have a better score (http://www.esi-topics.com/airpoll/authors/b1a.html).
- The ABC offers the largest concentration of high-level biomedical infrastructure and expertise in the Netherlands. Being fully embedded in the ABC, researchers within the joint program thus have access to a unique combination of technical expertise and infrastructure that would normally not have been available or only to a lesser extent. For example, the ABC has recently been very instrumental in stimulating vaccine research which clearly benefits from the presence of the participating centers of excellence dedicated to e.g., advanced NMR, functional genomics, proteomics, structural biology (crystallography), drug-delivery (drug innovation) and epidemiology.
- The RATIA program has the advantage of having a WHO Collaborative Centre included. Thus, The IRAS, which forms part of the RATIA program, was selected on the basis of specific expertise as "WHO Collaborative Centre for Research on environmental Health Risk Assessment". This position and status foster international collaboration, and hence, contribute significantly to the overall strategic position of the program.
- The department of Infectious diseases and Immunology of the FVM-UU is recognized as "OIE reference laboratory for *Campylobactor fetus* (bovine genital Campylobacteriosis) and *Campylobacter jejuni/coli* "

- Besides its outstanding scientific performance and its unique and well-defined position, the strategic position of the joint program is strengthened further by the fact that the FVM-UU and the UMC Utrecht are located in close proximity to numerous internationally renowned research institutes that are also operative in the areas of infectious diseases and human and veterinary health, including the National Institute of Public Health and the Environment (RIVM), and the Netherlands Vaccine Institute (NVI). In addition to collaborations with other academic institutions within the Netherlands, extensive collaborations exist with some pivotal institutes that are relevant for the focus area, namely the Center for Infectious diseases Control (CIDC) Lelystad, the Animal Sciences Group of Wageningen University, TNO Life Sciences (TNO Nutrition and Food Research Institute of the Netherlands Organization for Applied Scientific Research), and the Animal Health Service (GD, Deventer).

Taken together, from a national point of view, Utrecht University holds the ultimate position to foster highly competitive and innovative research in the area of "Infection and Immunity".

Strategic position and embedding within the European research arena:

- By joining the research programs of both the FVM-UU and the UMC Utrecht and by building extensive collaborations with ongoing research programs of the faculty of Science that are focussed on structural biology, bioinformatics and drug innovation, an extremely valuable centre of excellence for "Infection and immunity" has been created that is unique not only for the Netherlands but also in Europe. An important asset of this cluster is the fact that it covers almost every aspect of this focus area, ranging from fundamental cell biology, immunology, infection biology, proteomics, immunogenetics, bioinformatics, risk assessment, and epidemiology to translational research and clinical studies in animals and humans. To our knowledge, the level of interaction of the fundamental and clinical (veterinary) sciences with the molecular Life Sciences in the faculty of Science, in combination with the presence of such a prestigious faculty of Veterinary Medicine (the FVM-UU is the only European institution in the top-10 list as published by Thomson/ISI institute), is unprecedented and unrivalled within Europe.

In conclusion, taken into account the individual strength and unique expertise of the partners involved, together with the recent advances made through the successful implementation of the ABC-philosophy with substantial investments in expertise centers and state-of the art research infrastructure, it is expected that by further clustering of research activities in the focus area "Infection and Immunity" a sound and stable foundation can be created that will allow Utrecht University to grow into one of the leading institutes for "Infection and Immunity" research within Europe.

Valorisation and Technology transfer

Participation in (international) research consortia and networks:
All research lines of this program have a strong national and international visibility as evidenced by a variety of national and international collaborations. As listed below, these collaborations can roughly be divided into partnerships within research consortia, strategic alliances with governmental institutions or industrial partners, and collaborations with academic partners.

Research Consortia:

- Researchers within the focus area do all participate and share their expertise in the Eijkman Graduate School for Immunology and Infectious diseases (EGS; www.eijkmanschool.org). The EGS was founded in 1994 and also accredited in this year by the Royal Netherlands Academy of Arts and Sciences (KNAW). The accreditation was renewed in 1999 and again in 2004 for a period of six years (2004-2009). More than forty research groups are actively participating in the EGS. They origin from the Faculties of Pharmaceutical Sciences, Veterinary Medicine and Biology for the Utrecht University but also from the national Institute of Public Health and the Environment (RIVM), Netherlands Vaccine Institute (NVI) and the Animal Sciences Group (ASG) from Wageningen University (WUR) (formerly ID-Lelystad).
- The European Union in the framework of Networks of Excellence (GA2LEN (allergy and asthma)) or Integrated Projects (ECNIS and INTRASE (both in the field of risk assessment), GABRIEL (genetics of asthma and gene-environment interactions)
- NGI (Netherlands Genomics Initiative)/VIRGO consortium: Genomics of host-respiratory virus interactions: towards novel intervention strategies.
- Knowledge Chain Animal Infectious Diseases (Kennisketen Infectieziekten Dier): FVM-UU, Animal Sciences Group of Wageningen-UR, Center for Infectious Diseases Control Lelystad (CIDC) and Animal Health Service Deventer(GD B.V.). In September 2006, this consortium received 15 M€ for their proposal "Impuls veterinair Aviaire Influenza Onderzoek Nederland" that was successfully submitted for subsidization in the framework of the 'Fonds Economische Structuurversterking' (FES).
- EU KP6 & special calls:
    - Healthy Poultry (special call for Avian Influenza): The Epidemiology of avian influenza in the Netherlands (2003)
    - SARSTRANS (special call for SARS): Modelling the spread and control of emerging respiratory infections
    - EDEN (integrated project): Effects of climate change on emerging vector-borne infections in Europe

Strategic alliances with governmental institutions:

- TNO (Netherlands Organization for Applied Scientific Research), TNO Life Sciences (two collaborative centers, 'Risk Assessment in the Work Environment' and 'Food Allergy')
- RIVM (National Institute of Public Health and the Environment): Centre for Infectious disease control (CIb). The RIVM is poised to further intensify its links with and investments in the UU RATIA program.
- The RATIA program has also the advantage of having a WHO Collaborative Centre (Environmental Health Risk Assessment) included.
- The SIB program hosts the OIE Collaborative Center on Campylobacter.

Strategic alliances with industrial partners:

- The Netherlands Vaccine Institute (NVI); Sanquin Amsterdam; Intervet International BV; Numico NV; Crucell NV; Pfizer Ltd; GenMab BV

Collaboration with academic partners:

- National collaborations exist for example with: Erasmus University Rotterdam, University Medical Center St. Radboud Nijmegen, University of Amsterdam (UVA), Vrije University in Amsterdam (VU), Academic Medical Center Amsterdam (AMC), Leiden University, Wageningen University, and others.
- Most, if not all, of the investigators at the UMC Utrecht and the FVM-UU collaborate intensively with colleagues both nationally and internationally. Interestingly, it could be clearly documented with the last CWTS analysis of the output of both the UMC Utrecht and the FVM-UU that collaboration, and international collaboration in particular, leads to scientific publications in higher impact journals with much higher citation scores.
- Current international partners of both faculties include e.g., NIOSH USA, EPA USA, NIPH Oslo Norway, University of Aarhus, etc.

Opportunities for valorization and critical factors involved:

- Given the enormous socio-economic impact of immunological and infectious disease in animals and man, and taking into account the risks of zoonoses and their impact on food safety, there is a great need for valorization and technology transfer activities particularly in the focus area of "Infection and Immunity". Thus, valorization and technology transfer in the focus area will contribute substantially to

the well-being of society in that the generated knowledge and products are of critical use for such important issues like: preventing and/or controlling pandemic outbreaks of life-threatening diseases, vaccine safety and production, microbiological food-safety and quality, negative health consequences through environmental and occupational exposure, and fighting bioterrorism.
- Valorization and Technology transfer activities will generally be directed to the development of diagnostic tests, (improved) vaccines, and medication. In general, the commercial potential and economic value of successfully developed and registered products in the focus area is high.
- Utrecht University and the UMC Utrecht encourage researchers to valorize their research outcomes. To this end, two holding companies – the UU Holding BV and the UMC Utrecht participations -, have been established aimed amongst others to assist and fund start-up companies. Over the last few years, the holdings had major success in founding new start-up companies that are active in the focus area of "infection and immunity", with Pepscan systems, AM-Pharma, and Crucell as the most prominent examples.
- In line with the province of Utrecht being now considered to be the most prominent center for scientific research and development of commercial activity in the field of infectious diseases and immunity in the Netherlands', Utrecht is also home to a significant number of companies active in this area, including Genmab and national subsidiaries of leading pharmaceutical companies including GlaxoSmithKline and Roche.
- The participation of the immunopharmacology and pharmacoepidemiology programs of the Utrecht Institute for Pharmaceutical Sciences (UIPS) in the ABC is worth mentioning with respect to the opportunities of valorization and technology transfer.
- Utrecht University is participating, either as founding member or participant, in many projects granted by TI Pharma in the field of "Infection and Immunity": e.g., CXC chemokine receptors: potential targets for chronic inflammatory diseases (Kraneveld); Glucocorticoid-induced insulin resistance (Bijlsma); Pheno- and genotyping of local and systemic inflammation from "healthy smokers" to severe COPD (Koenderman); Antibodies against Klebsiella pneumoniae as an alternative (Strijp); Design of predictive models, drug delivery, and live-virus Malaria vaccines for the developing world (Hennink); Vaccine delivery: alternatives for conventional multiple injection vaccines (van Eden; Hennink); Exploitation of Toll-like receptors in drug discovery (Pasterkamp); Transition of systemic inflammation into multiorgan pathology (Koenderman); Immune modulation and tolerance induction, prevention and inhibition of inflammatory diseases (van Eden), New antibodies to fight antimicrobial resistance (Liskamp, Pieters, Breukink).
- In June 2006, within the Randstad-Noordvleugel a consortium was formed with academia (University Utrecht, UMC Utrecht, AMC Amsterdam, VuMC Amsterdam, Animal Science Group University Wageningen), governmental research institutions (e.g., RIVM, CIDC), and local provincial governments (Utrecht, Flevoland, Noord-Holland, Amsterdam, Utrecht city) as participating partners. This consortium, that gained ample support from both local start-ups, medium-sized companies, and multinationals active in the field of infectious diseases, has successfully submitted a grant proposal entitled "Immunovalley: research & valorisation of emerging infectious diseases" for the 'Pieken in de Delta' program of the Dutch Ministry of Economic Affairs.

Taken together, it is anticipated that the combined strengths of the research programs involved together with their embedding within the framework of the ABC, makes this cluster an attractive partner for both academic and industrial partners, hence providing ample opportunities for valorisation in the area of both veterinary and human health.

National and international funding opportunities:
Based on the past performance of the participating research groups it can be expected that future funding will be obtained from the following organizations:

National
- NWO (the Netherlands Organisation for Scientific Research): ZonMW, STW, CW, ALW, and WOTRO
- Dutch Ministry of Education, Culture and Science (OCW)
- Dutch Ministry of Health, Welfare and Sport (VWS)
- Dutch Ministry of Social Affairs and Employment (safety and health) (SzW)
- Dutch Ministry of Economic Affairs (EZ)
  - EZ: Smart-Mix
  - EZ: Pieken in de Delta (PiD)
  - EZ: TI Pharma (also see under "opportunities for valorization")
  - EZ: "Innovatie in Dialoog" focus traject "Life Sciences & Health"
  - EZ: WBSO "Wet Bevordering Speur- en Ontwikkelingswerk"
- Netherlands Genomics Initiative (NGI; 2nd round)
- Centre for Translational Molecular Medicine (CTMM)
- Stakeholders: the Netherlands Asthma foundation, the Heart Foundation, the Cancer Foundation.
- Industrial partners

International:

- EU 6th and upcoming 7th Framework Programs
- Industry, CEFIC
- Welcome trust
- US Health Effects Institute

Key figures (2001-2005)

Participating Research groups:

I&I : UMC Utrecht
SIB : FVM-UU
RATIA : FVM-UU, UMC Utrecht and faculty of Science

Past performance:

UMC Utrecht and I&I:
Recently, a bibliometric trend analysis was performed by the CWTS at Leiden University to assess the citation scores and numbers of publications of the 5 research institutes of the UMC Utrecht. These results are based on data collected over the years 1998-2005 and indicated that the average journal impact (CPP/FCSm) of all 9,152 publications amounted to 1.58 (for I&I: Number of publications = 2,142; CPP/FCSm =1,69).

SIB/RATIA:
In 2006 a new organizational structure has been adopted that crosses the classical disciplinary boundaries to accommodate the growing coherence within the departmental research program. Thus, the FVM-UU has recently focused its research activities by further clustering of its activities into five thematic, cross-departmental programs including the SIB and RATIA programs. These programs are all headed and managed by top-scientists recruited from those research groups and research lines that received scores of 4 and higher (on a five-points scale with "5" being excellent and "4" very good) in the last peer-reviewed evaluation report that was published in March 2006. For the former programs IVR3 (IRAS) and IVR6 (Infectious diseases and Immunology) the overall score was 5. On the basis of past performance and the individual track-records, some individual scientist were selected additionally to participate in the newly formed main research programs in order to safeguard specific (veterinary) expertise and/or to follow and distinct research ambitions as determined by the ABC.

Faculty (number of chairs/professorships):

I&I: n=20; Prof.dr. J.G.J. van de Winkel; Prof.dr. F. Miedema; Prof.dr. P.J. Coffer; Prof.dr. J. Verhoef; Prof.dr. M.J.M. Bonten; Prof.dr. A.I.M. Hoepelman; Prof.dr. C.A.F.M. Bruijnzeel-Koomen; Prof.dr. J.W.J. Bijlsma; Prof.dr. J.J. Heijnen; Prof.dr. F. van Bel; Prof.dr. J.L.L. Kimpen; Prof.dr. W. Kuis; Prof.dr. E.A.M. Sanders; Prof.dr. A.B.J. Prakken; Prof.dr. L. Koendermans; Prof.dr. J.W.J. Lammers; Prof.dr. A. Rothova; Prof.dr. A.W. Hoes; Prof.dr. Th.J.M. Verhey; Prof.dr.Ir. B. Brunekreef.

SIB: n=12; Prof.dr. J.P.M. van Putten; Prof.dr. P.J.M. Rottier; Prof.dr. W. van Eden; Prof.dr. H.P. Haagsman; Prof.dr. J.B. Helms; Prof.dr. W. Stoorvogel; Prof.dr. A. Gröne; Prof.dr. J.A.P. Heesterbeek; Prof.dr. A.G.M. Tielens; Prof.dr. A. Stegeman; Prof.dr. J.A. Wagenaar; Prof.dr. W. Gaastra.

RATIA: n=8; Prof.dr. M. van den Berg; Prof.dr.Ir. D.J.J. Heederik; Prof.dr. W. van Eden; Prof.dr.Ir. B. Brunekreef; Prof.dr. F. van Knapen; Prof. dr. W. Seinen; Prof.dr. W. Slob; Prof.dr. T. Willemse.

In the focus area "Infection and Immunity" a total number of n=38 chairs is implicated.

Current Academic Staff (fte scientific staff, with % of total):

Academic staff	2005-2006	
	Direct funding (fte; as % of total)*	External funding
I & I	51 (21)	64
SIB **	40 (34)	39
RATIA **	17 (15)	38

* The number of fte (direct funding) in the research programs of the faculty of veterinary medicine and the UMC Utrecht amounts to 163 and 238 fte, respectively. Percentages shown refer to total number of fte per individual faculty.

** The number of fte's appointed by direct- and external funding is estimated on the basis of the current Metis data for 2006 (FVM-UU).

Individual funding (KNAW and NWO vernieuwingsimpuls/NWO Innovational Research Incentives Scheme):

VENI:
Dr. L.H. Ulfman (2002), Dr. J.A.M. Borghans (2002), Dr. M.L. Boes (2003), Dr. K.U. Birkenkamp (2004), Dr. R. Wubbolts (2004), Dr. A. Vroon (2005), Dr.Ir. B.J. Bosch (2005), *Dr. S.H.M. Rooijakkers (2006), Dr. U. Gehring (2006), Dr. H. Schmitt (2006).*

VIDI:
Dr. A.B.J. Prakken (2002), Dr. P.J. Coffer (2002), Dr. C.P.M. Broeren† (2001), Dr. C.A.M. de Haan (2004), Dr. M.M.S.M. Wösten (2005), *Dr F.M. Reggiori (2006).*

VICI:
Prof.dr. J.A.P. Heesterbeek (2004)

NWO-Aspasia:
Dr. L. Meyaard (2001)

NWO-Meervoud:
Dr. D.V. Kaloyanova (2004), Dr. E.J.A.M. Sijts (2005)

Utrecht University 'High-Potential' program:
Mw. dr. D. van Baarle (2006; with Dr. C. Keşmir), Dr. C.A.M. de Haan (2006; with Dr. F.M. Reggiori), Dr. F.M. Reggiori (2006; with Dr. C.A.M. de Haan)

Preference strategic partners (national):

1-3. RIVM (CIb, NVI)
AMC
WUR (ASG, CIDC)
4. TNO
5. Erasmus UR