



Hubrecht
Institute

Developmental Biology
and Stem Cell Research

Report by the directors



Site visit Hubrecht Institute
10-11 November 2014

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The Hubrecht Institute 2014: evaluation by the Directors

Before a site visit, the Royal Netherlands Academy of Arts and Sciences (KNAW) requires that the Institute Director presents his or her own vision on the current state of the institute, and plans for the future. Here follows a brief summary of his views on behalf of the board of directors of the Hubrecht Institute.

Mission statement and research areas

The Hubrecht Institute performs basic research in the field of developmental biology, with an emphasis on the biology of stem cells. The institute aspires to be a world leader in this field. The institute currently ranks as one of top institutes worldwide in the field of developmental biology and stem cell research. This is reflected by the citation impact score of 2.86, which puts the Hubrecht at the top of the list of all institutes and universities in the Netherlands. Internationally, this score is also impressive and is comparable to the EMBL Heidelberg (2.98), Harvard (2.40), and MIT (2.45).

To maintain and improve this position we implement the following strategy:

1. We use an international recruitment strategy focusing strictly on excellence.
2. We have a tenure-track system for junior group leaders with a flat organizational structure; group leaders have full scientific freedom and receive all the positive and negative consequences of such responsibility. Currently approximately half of the junior group leaders receives tenure after 6 years. The evaluation procedure is transparent and is based on external referees.
3. The institute is equipped with the most advanced equipment (microscopes, cell sorters, DNA sequencers) managed from a well-embedded facility support.
4. We aim at increasing the critical mass of the institute by active national and international grant recruitment (including donations from foundations and wealthy individuals) and by closely collaborating with UMC Utrecht.
5. We collaborate with the best national and international groups in the field of stem cell biology and developmental biology.

Researchers at the Hubrecht Institute study a variety of biological processes, mainly concerning the developmental biology of animals. Developmental biologists are interested in the mechanism by which an organism grows from a single fertilized egg into a fully formed adult. This encompasses many areas, from basic (pre-)embryonic processes, such as the establishment of a body plan, to the specifics of organ growth in adult animals. Closely linked to developmental biology is stem cell research. Embryonic, fetal, adult and cancer stem cells are all studied. Deregulation of developmental processes can lead to cancer, which is also a key theme of research within the institute. Knowledge and expertise gained within the Hubrecht will be beneficial for prevention and treatment of diseases and therefore for the quality of life.

Even though research at the Hubrecht Institute focuses mostly on the fundamental aspects of developmental and stem cell biology, it has direct implications for translational and clinical applications. For example, the recently established Foundation Hubrecht Organoid Technology (HUB) aims to use organoid technology, developed at the Hubrecht Institute, for translational and clinical applications. Another example is Cergentis, a company established in 2012, based on the structural genomics technology of Wouter de Laat developed at the Hubrecht Institute. Cergentis uses Targeted Locus Amplification (TLA) as a DNA diagnostics tool that enables high-resolution identification of genomic rearrangements.

Organizational structure of the Hubrecht Institute

The Hubrecht Institute is one of five life science institutes under the umbrella of the Royal Netherlands Academy of Arts and Sciences. As such it has no primary teaching duty, and no obligations to perform applied research. Researchers at the Hubrecht can devote all of their attention to fundamental biomedical research and are committed to pursue excellence in their research.

At present over 280 people (200 fte) are working at the Hubrecht (appendix 3), spending a total budget of 20 M€ (appendix 4) and producing about 120 papers a year (appendix 5).

Between 2008 and 2014, a number of significant changes were realized at the organizational level. In 2012 a new managing director, Mariëtte Oosterwegel, was recruited to the institute replacing Jos Koelman. When Hans Clevers accepted the position of president of the Royal Netherlands Academy of Arts and Sciences in 2012, Alexander van Oudenaarden became the institute director. The current board consists of Mariëtte Oosterwegel (managing director), Jeroen den Hertog (deputy director research), and Alexander van Oudenaarden (institute director).

During the last 6 years the overall organizational structure of the institute was further simplified, contributions of facilities were scrutinized, as were individual scientists and support staff. The resulting organization is described in the attached organogram and table (Appendix 2). In brief, the institute director holds responsibility for the entire institute and he is also a group leader. The managing director is in charge of the non-scientific service departments. The deputy director research is responsible for the research infrastructure and he is also a group leader. The 18 senior and junior group leaders fall directly under the director. Group leaders are responsible for their group finances and hiring, and are scientifically fully independent. Junior group leaders are offered 5-6 year contracts and are supported with a PhD student (once) and a technician. A senior group leader is appointed as buddy for each junior group leader for advice in practical and strategic matters. Senior group leaders are tenured and supported by a technician. When a senior group leader earns a Professor position at a university (either at Utrecht University or elsewhere in the Netherlands) the institute provides the senior group leader with an additional graduate student. Some bench fee is provided for each person in the group. More importantly, the institute strives to provide cutting-edge research facilities at low cost for the individual research groups. A nominal fee is charged for animal care and sequencing. Histology, imaging and cell-sorting services are free. All research facilities are attached to one of the existing research groups.

In weekly meetings, the director discusses all scientific and non-scientific issues with the managing director Mariëtte Oosterwegel and the deputy director research Jeroen den Hertog. During the last two years Stefan Schulte-Merker, who represented the group leaders, often attended this meeting. The managing director is directly responsible for the IT-, finance and personnel department, as well as for the technical and domestic service, general facilities (media kitchen, canteen, security, reception, cleaning) and communication. The deputy director research is directly responsible for the animal facilities, research infrastructure, coordination of master and PhD students and Intellectual Property and he serves as scientific sparring partner. A single, monthly consultation with all group leaders serves as the main, formal communication forum with the scientific staff. Additionally we have a monthly meeting with the group leaders during which one of the group leaders presents the future scientific goals for his/her group. We feel these meetings are instrumental to collectively contribute to the quality of our research program and to stimulate complementary collaborations within the institute.

Formal communication with our directors of the Royal Netherlands Academy of Arts and Sciences (KNAW) occurs twice yearly. In addition, the supervisory board of the affiliation of the Hubrecht Institute with UMC Utrecht, which consists of two board members of the KNAW and two board members of UMC Utrecht, meets at least twice a year and the directors of the Hubrecht Institute join these meetings as observers. Moreover, there is frequent informal contact, whenever needed, on issues such as the building activities, fundraising, biotech activities, animal rights etc.

Every Thursday, there is a lunch meeting in our auditorium during which all academic scientists (staff members, postdocs, graduate students and technicians) are present. Two postdocs or graduate students each present a half hour seminar on their ongoing research. These meetings are well attended and appreciated. Our lecture hall is used several times per week for seminars by international speakers. Seminars are typically co-organized with the graduate school Cancer, Stem Cells, and Developmental Biology (CS&D with UMC Utrecht and Utrecht University).

Various meetings are organized to enhance general collaboration within the institute. Four times a year a group leader presents a layman's talk to the service department and vice versa we recently introduced presentations by our service departments (several presentations per year) to better educate our employees on what our facilities can provide for our scientists. Additionally we started a non-scientific seminar series on 'career-related issues' organized by Catherine Rabouille. During these seminars topics such as 'balancing family and work' and 'finding an ideal post-doc lab' are discussed.

The director also has monthly meetings with post-docs and graduate students to inform them about developments at the institute, but more importantly for them to provide feedback to him on how to further improve the Hubrecht Institute as a workplace. During such a meeting about 15 graduate students or post-docs attend, which means that on a yearly basis the institute director will be able to meet all graduate students and post-docs in our building.

Both research groups and the personnel committee initiate monthly social events. The board of directors aims to celebrate professional and personnel highlights with the whole institute to improve community feeling. For example, once a year at the end of New Year's speech of the institute director, 5 of our employees are awarded the Embryo award. This award is given to PhD students, post-doctoral students, scientific staff or non-scientific staff, who demonstrated extraordinary commitment to make the Hubrecht Institute a great place to work.

PhD training

The Hubrecht Institute has hosted approximately 50 PhD students at any given time since 2008 and on average, 10 PhD students have defended their thesis each year. All PhD students at the Hubrecht Institute are enrolled in the Cancer, Stem Cells and Developmental Biology (CS&D) graduate school (until 2013 known as Cancer Genomics and Developmental Biology, CGDB). For each PhD student a PhD committee is installed, consisting of a professor who acts as the thesis supervisor, the direct supervisor (if distinct from the thesis supervisor) and two members, at least one of which is not employed at the Hubrecht Institute. The committee convenes with the PhD student once per year to discuss progress of the project and to check whether the theoretical requirements (in total 14 weeks of courses/seminars over the 4-year period) are met.

A brief description of organizational and personnel changes (2008-2014)

New group leaders

In 2008 the Hubrecht Institute became affiliated with the UMC Utrecht (see below), which included a 40 M€ investment over 10 years. This financial boost allowed us to significantly expand the number of groups in our institute:

- Wouter de Laat (biomedical genomics): recruited as senior group leader in 2008.
- Catherine Rabouille (secretion regulation): recruited as senior group leader in 2008.
- Alyson MacInnes (zebrafish cancer models): newly recruited as junior group leader in 2008, did not receive tenure in 2013.
- Johan de Rooij (cell adhesion): newly recruited as junior group leader in 2008, did not receive tenure in 2013.
- Jacco van Rheenen (cancer biophysics): newly recruited as junior group leader in 2008, tenured in 2012.
- Daniele Guardavaccaro (ubiquitin biology): newly recruited as junior group leader in 2008. Will be evaluated for tenure in 2015.
- Niels Geijsen (stem cells and reprogramming): recruited as senior group leader in 2010.
- Eelco de Koning (diabetes): recruited as senior group leader in 2010.
- Menno Creyghton (neuro epigenetics): newly recruited as junior group leader in 2011. Will be evaluated for tenure in 2015.
- Puck Knipscheer (DNA damage): newly recruited as junior group leader in 2011. Will be evaluated for tenure in 2015.
- Alexander van Oudenaarden (single-cell biology): newly recruited as senior group leader and director in 2012.
- Eva van Rooij (molecular cardiology): newly recruited as junior group leader in 2013. Will be evaluated for tenure in 2018.
- Catherine Robin (embryonic hematopoiesis): newly recruited as junior group leader in 2013. Will be evaluated for tenure in 2018.
- Jop Kind (single-cell genome structure): newly recruited as junior group leader in 2014. Will be evaluated for tenure in 2019.
- Geert Kops (cancer cell biology): newly recruited as senior group leader in 2015.

Leaving group leaders

- In 2008 Christine Mummery left to head the Department of Anatomy and Embryology at the Leiden University Medical Center.
- In 2009 Marcel Tijsterman moved to the Department of Toxicogenetics at the Leiden University Medical Center.
- In 2010 Frits Meijlink retired as a group leader.
- In 2012 Dana Jongejan-Zivkovic retired as a group leader
- In 2012 Rene Ketting became a Director of the Institute of Molecular Biology (IMB) in Mainz.
- In 2012 Eugene Berezikov moved to the European Research Institute for the Biology of Aging (ERIBA) at the University Medical Center Groningen.
- In 2013 Johan de Rooij did not receive tenure and moved his lab to the UMC Utrecht.
- In 2013 Alyson MacInnes did not receive tenure and moved her lab to Sanquin in Amsterdam.
- In 2014 Stefan Schulte-Merker moved to Münster University to become a Full Professor (W3) for cardiovascular organogenesis and regeneration.

Financial future of the Hubrecht Institute

In 2013 the annual budget of the Hubrecht comprised of 20 M€, of which the KNAW provides 5.6 M€ lump sum. This annual lump sum of the KNAW has not changed during the last 14 years, but has in fact decreased due to budget cuts of the Ministry Education, Culture and Science (OC&W). In 2008 an affiliation with the UMC Utrecht was initiated by former Hubrecht director Hans Clevers and the former chairman of the UMC Utrecht board, Geert Blijham in order to expand the Hubrecht to an internationally leading research institute. This affiliation led to an investment of 40 M€ by the UMC Utrecht to be spent during the period 2008-2018. The UMC Utrecht contribution therefore increased the core budget by about 70%. This financial injection allowed the Hubrecht Institute to effectively grow by 10 more groups during the last 6 years. However, our long-term budget shows that by the end of 2018 both the UMC budget and our own general reserve will be completely spent. The estimated costs for 2016 to run the institute including the new laboratory building are 13.5 M€, whereas the KNAW lump sum is only 5.6 M€. We are currently discussing with the UMC Utrecht and the KNAW how to continue this collaboration after 2018. It is our hope that the KNAW will increase our lump sum in the future, which would enable us to continue our present constellation and exploit our new building, which is expected to be fully functional in September 2015.

Embedding within Utrecht campus

About half of our group leaders have formal professor appointments at the UMC Utrecht (van Rheenen, Clevers, Cuppen, de Laat, van Oudenaarden, Kops) and at Utrecht University (Geijsen, Korswagen, van Oudenaarden). Jeroen Bakkers is in the last formal stage to obtain a professorship at the UMC Utrecht. Two of our group leaders have professor positions at Leiden University (de Koning, den Hertog). Therefore the majority of our group leaders have professor positions in the Netherlands.

Importantly, three of our most recent recruits (Catherine Robin, Eva van Rooij, Geert Kops) were recruited in close collaboration with the UMC Utrecht and have part-time appointments at the UMC Utrecht. Edwin Cuppen and Catherine Rabouille also have part-time appointments at the UMC Utrecht. These dual appointments further stimulate collaborations and improve the exchange of knowledge, expertise and sharing of equipment.

Many scientific collaborative projects exist between the Hubrecht Institute and groups at the UMC Utrecht and Utrecht University in several different areas. An example is the extensive collaboration with the Institute for Molecular Medicine (led by Hans Bos), which led to the recruitment of major international (Stand up to Cancer) and national funding (NWO Gravity Project). Additionally, there are several collaborations between the Netherlands Proteomics Centre (led by Albert Heck) and the Hubrecht Institute.

In addition, together with the UMC Utrecht and Utrecht University, the Hubrecht Institute played a major role in the creation of the Graduate Program CS&D (Cancer, Stem Cells, and Developmental Biology) as part of the Graduate School of Life Sciences (GS-LS). The Hubrecht as a whole and individual Hubrecht group leaders actively participate in the CS&D school by yearly organizing multiple graduate courses,

including the 'developmental biology' and 'zebrafish in development and disease' courses.

At national level, the Hubrecht Institute is active in several consortia. An example is the recently awarded NWO Gravity program (CancerGenomiCs.nl). Internationally, the Hubrecht Institute operates in many European and international projects. Recently, a close collaboration between the Hubrecht Institute and the Skolkovo Center for Stem Cell Research, the Whitehead Institute for Biomedical Research (Cambridge, MA, USA), and the UMC Groningen was initiated. The Hubrecht Institute will work with this international team to set up a new stem cell institute in Russia.

The affiliation of the Hubrecht Institute with the UMC Utrecht has led to new collaborations and strengthened existing partnerships. One striking example is the recently established Foundation Hubrecht Organoid Technology (HUB), which aims to use organoid technology, developed at the Hubrecht Institute, for translational and clinical applications. The organoid technology also formed the basis of a successful collaboration between the Hubrecht Institute and the UMC Utrecht in the field of cystic fibrosis. This project has led to new insights into the treatment of cystic fibrosis and will hopefully lead to an improvement in the treatment of patients with cystic fibrosis. In the near future ties between the UMC Utrecht and Utrecht University will be further enhanced by the use of complementary talents in our organizations. By strengthening the complementary expertise within Utrecht, we offer a very attractive environment and research infrastructure for scientists, which will strengthen our national and international position.

Next to the academic achievements, the Hubrecht Institute has applied for 12 patents since 2008. Several of these patents were licensed to the HUB. Another patent laid the foundation for a spin-off company, Cergentis BV that was founded in 2012.

Recruitment of external research funds (2008-2014)

Our group leaders have been very effective in recruiting external research funding totaling approximately 10 M€/year (earning capacity is about 50% of total budget, appendix 3). These funds include many prestigious European Research Council (ERC) awards: ERC starting grants (Ketting, Tijsterman, Berezikov, de Laat), ERC consolidator grants (Robin, van Rooij), and ERC advanced investigator grants (Clevers, van Oudenaarden) as well as 4 of one of the most prestigious Dutch research awards, the NWO VICI award (Ketting, Cuppen, de Laat, van Oudenaarden).

Building activities (2008 – 2014)

Since the affiliation with UMC Utrecht in 2008, there is a need for additional space. The KNAW has recognized this need, which has led to three phases of building activities:

The first phase was to build an extension to the fish facility. The courtyard between the Hubrecht Institute and the Fungal Biodiversity Center has been turned into a new fish facility and it includes some lab space, which will be used for microinjections in the future, but has temporarily housed one to two research groups since it was built in 2010.

The second phase was an extension of the rodent facility, which was finished in 2013. This extension doubled the size of the mouse house and includes a multifunctional area that can be used as an extension of the fish facility or of the mouse facility, depending on what type of space is most needed. In the course of the building process it became evident that we needed some space for *Xenopus* for the Knipscheer-group and a frog-room was quickly included in the plans. Moreover, it became evident that the van Oudenaarden lab was moving into the Hubrecht Institute and the multifunctional area was turned into temporary lab and office space.

The third phase is the extension of the laboratory building, which is in full swing now and is scheduled to be finished in August 2015. This extension will provide a 60% increase in lab and office space, as well as an increase in the number of meeting rooms. Moreover, this extension will provide a larger canteen with sufficient capacity to accommodate all occupants of the building complex and space in the lobby for outreach activities. The extension will be connected to the current building at all levels by hallways to ensure that the Hubrecht will remain a single entity. Two additional floors will be added (fourth and fifth

floor) that will be rented to UMC Utrecht. On these two floors, UMC Utrecht will house research groups that are interested in regenerative medicine, which will eventually lead to intensified interactions between the Hubrecht Institute and UMC Utrecht, which is in line with the affiliation that was initiated in 2008.

Outreach activities (2008 – 2014)

The Hubrecht Institute is increasingly involved in public media (newspapers, popular magazines, TV) and other community engagement activities and recently recruited a part-time communication officer to coordinate all these activities. A few recent examples are:

EuroStemCell, an ambitious program that unites 33 partner institutions cross Europe to build trust and provide high quality information via online media and direct stakeholder engagement with stem cell research and regenerative medicine, aimed at European citizens at all educational levels.

Debating European Science Issues (DESI), a dynamic debating competition in 7 European countries, which invites young people to engage in debate on cultural, societal and ethical implications of advances in biomedical science. The goal of the DESI project is to encourage young people to take active interest in biomedical science, to learn think critically on scientific information and to engage with contemporary research. The Hubrecht Institute coordinates the project nationally in collaboration with societal organizations and private partners.

Group leaders of the Hubrecht are often invited speakers by national civil society organizations such as the Association foundations for rare diseases (VSOP), Cystic Fibroses foundation (NCFS), Dutch Cancer Society (KWF), and Dutch Heart Foundation (NHS).

The Hubrecht frequently hosts (inter)national visitors of the Utrecht Science Park (USP), participates in local events (Festival De Beschaving), collaborates on talent workshops with Utrecht Life Sciences (ULS), is going to be involved in the U-talent program from the Junior College Utrecht for secondary schools to nurture talent, provides information for exhibitions in the University Museum Utrecht ('Down to the bone') and is engaged in lunch seminars at Studium Generale (Cuppen, 'Pimp your mind'; Clevers 'Playing with genes', 'Building with cells').

In addition, the Hubrecht is represented in various fund raising events organized by the Foundation Friends of the Hubrecht Institute (service clubs, JFK gala).

Strengthening interdisciplinary research

Due to the lack of space in our current building it is currently impossible to attract more group leaders. When the new building will be ready at the end of 2015 we will resume the recruitment of new group leaders (expected one junior group leader per year). The long-term goal is to integrate the stem cell and developmental biology groups together with more quantitative sciences (such as the physical and technical disciplines). New interdisciplinary group leaders are expected to work closely with the current group leaders. The current director has accumulated experience with interdisciplinary research during his time at MIT (2000-2012), where he has trained graduate students and post-docs with backgrounds in physics, biology, biophysics, engineering, computer science, and systems biology. Interdisciplinary groups or cross-disciplinary collaborations between groups can attack scientific problems that cannot be solved by groups of researchers with a uniform background. Similar initiatives in the United States have been a great success: for example: Harvard Systems Biology; the Princeton Center for Quantitative Biology; the California Institute for Quantitative Biosciences. The Max Planck Institutes in Dresden (MPI Molecular Biology & Genetics and MPI for the Physics of Complex System) provide a good example in Europe.

Implementation recommendations of previous site visit in 2008

During the site visit in 2008 the Hubrecht Institute was evaluated as excellent with regards to quality, productivity, relevance, and vitality/feasibility. The committee made five recommendations.

First it was suggested to have a transparent mechanism for future recruitments and appointments to tenure. We started a recruiting committee chaired by the institute director. The members of this committee are several senior group leaders from UMC Utrecht and the Hubrecht Institute. For one opening typically several candidates visit the Hubrecht Institute for 2 days. All candidates are interviewed by the members of the committee and most of the group leaders of the Hubrecht Institute. Based on the feedback of the recruiting committee and the Hubrecht group leaders, the board of directors decides on making an offer to the candidate.

Junior group leaders are initially appointed for a period of six years. After about 4-5 years the institute director sends out 15-20 letters to international experts in the field of the junior group leader. Additional advice is asked from the Scientific Advisory Committee (SAC) chaired by René Medema. The board of directors will decide on tenure based on the advice of the international experts and the SAC. We are striving for excellence. Currently 1 out of 2 junior group leaders receives tenure after 6 years. Recently we also organized an afternoon during which all our junior group leaders present their progress to the SAC. This meeting takes place at the Hubrecht Institute. This allows the SAC to provide advice and feedback to our junior group leaders long before they are evaluated for tenure.

In the second recommendation the committee stressed the importance of recruiting the best international candidates and efforts should be made to recruit more female group leaders. Since 2008 we recruited 5 female group leaders (two French, one American, two Dutch). Additionally, Alexander van Oudenaarden was recruited by Hans Clevers from MIT, where he was full Professor in Physics and Biology.

In the third recommendation the committee mentioned that based on scientific excellence and the expected expansion of the staff substantial expansion of the housing of the Hubrecht Institute would be required. This recommendation has been realized with the new laboratory building and the new animal facility.

The committee advised in the fourth recommendation to put in place a formal mentoring system for junior group leaders. This has been implemented by starting a buddy system in which each junior group leader is teamed up with a senior group leader who provides advice and mentoring. Additionally we invite the SAC to meet with our junior group leaders to provide the junior group leaders with advice (also see recommendation 1).

In the last recommendation the committee advised to strengthen the imaging facility at the Hubrecht Institute. During the last six years we significantly expanded the imaging facility (<http://www.hubrecht.eu/information/imagingcenter.html>). Currently this facility hosts 4 confocal microscopes, an intravital imaging microscope, a two-photon microscopy setup, a spinning-disk confocal microscope, and many epifluorescence microscope setups.

Closure

The Hubrecht Institute is a very dynamic and ambitious place to be, working on the frontiers of life sciences together with local, national and international collaborators. The Hubrecht is facing an exciting and challenging time with the opening of the new laboratory building. We are continuously trying to improve ourselves, both scientifically and in terms of business support, and will use the recommendations of this site visit to further improve our institute.

The board of directors of the Hubrecht Institute

Alexander van Oudenaarden
Jeroen den Hertog
Mariëtte Oosterwegel

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APPENDIX 1

SWOT analysis

Strengths

- Excellent quality research
- Tenure track system
- High quality research infrastructure
- (Inter)national embedding

Weaknesses

- Structural costs heavily depending on external money
- Lack of technology transfer expertise at KNAW

Opportunities

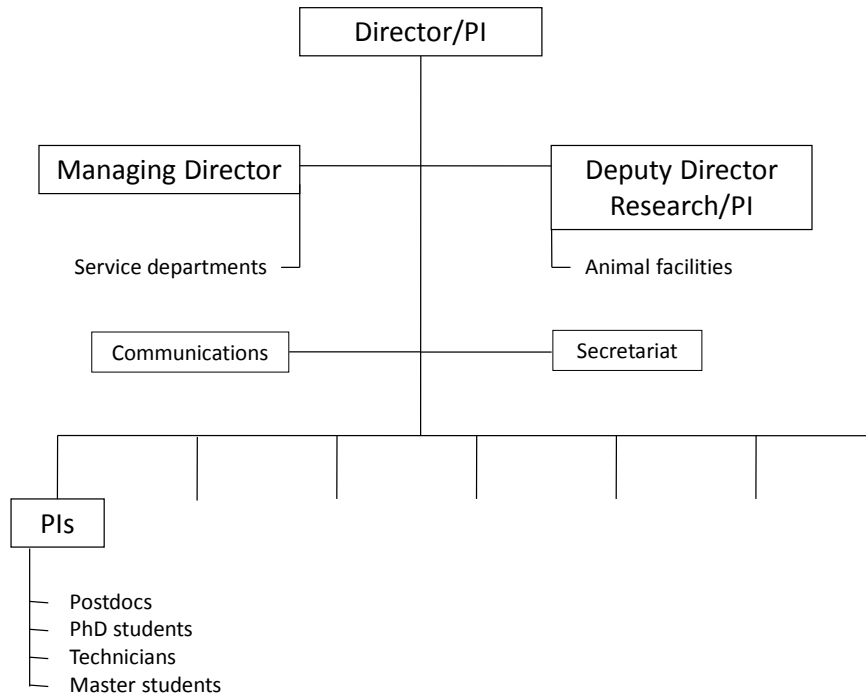
- Strengthening multidisciplinary research
- Intensify collaboration with UMC Utrecht
- Collaboration with HUB Foundation 'Hubrecht Organoid Technology'

Threats

- Collective labor agreement prohibit 6-9 year tenure track periods
- European regulations and accountancy control require time-consuming support
- Increasingly tight regulations of animal welfare committees
- Financial commitment of KNAW and UMC Utrecht after 2018 is uncertain

APPENDIX 2

Organogram



Director/PI

Alexander van Oudenaarden Quantitative biology of stem cells and development

Managing Director

Mariëtte Oosterwegel

Deputy Director Research/PI

Jeroen den Hertog Protein-tyrosine phosphatases in development

PIs

Jeroen Bakkers	Cardiac development and genetic
Hans Clevers	Lgr5 stem cells, Wnt signaling & cancer
Menno Creyghton	Neuro epigenetics
Edwin Cuppen	Genome biology and medical genetics
Eelco de Koning	Diabetes and islet neogenesis
Wouter de Laat	Biomedical genomics
Jacqueline Deschamps	Genetics of morphogenesis during axial elongation in the mouse embryo
Niels Geijsen	Stem cell modeling of human genetic disease
Daniele Guardavaccaro	Ubiquitin ligases and cancer
Jop Kind	Spatiotemporal regulation of genomic function
Puck Knipscheer	Molecular mechanisms and regulation of DNA repair
Rik Korswagen	Wnt signaling in development and disease
Catherine Rabouille	Secretion regulation
Catherine Robin	Hematopoiesis and stem cells during embryonic development
Jacco van Rheenen	Cancer biophysics
Eva van Rooij	Molecular Cardiology

APPENDIX 3

Number of staff at institutional level

	2008	2009	2010	2011	2012	2013
Research staff	46,41	57,4	62,2	67,8	65,64	65,31
PhDs	52,1	44,1	49	51	48	47
Research staff total	98,51	101,5	111,2	118,8	113,64	112,31
Technicians	42	40	41	41,4	42	45,33
Support staff	32,23	30	32,4	38,1	43,16	44,26
Grand total	172,74	171,5	184,6	198,3	198,8	201,9

APPENDIX 4

Funding and expenditure at institutional level (in K€)

	2008	2009	2010	2011	2012	2013
<i>Funding</i>						
Direct funding	5,421	6,029	7,348	8,288	8,059	7,576
Research grants	6,058	6,956	7,063	8,708	7,836	11,012
Industry funding	192	229	468	334	265	212
Other	2,003	2,102	1,264	1,326	2,660	1,875
Total	13,674	15,316	16,143	18,656	18,820	20,675

<i>Expenditure</i>						
Personnel	7,726	9,295	9,891	11,689	11,255	12,092
Other	5,360	5,975	6,639	6,715	7,796	8,875
Total	13,086	15,270	16,530	18,404	19,051	20,967

Funding and expenditure at institutional level (in %)

	2008	2009	2010	2011	2012	2013
<i>Funding</i>						
Direct funding	39.6%	39.4%	45.5%	44.4%	42.8%	36.6%
Research grants	44.3%	45.4%	43.8%	46.7%	41.6%	53.3%
Industry funding	1.4%	1.5%	2.9%	1.8%	1.4%	1.0%
Other	14.6%	13.7%	7.8%	7.1%	14.1%	9.1%
Total	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

<i>Expenditure</i>						
Personnel	59.0%	60.9%	59.8%	63.5%	59.1%	57.7%
Other	41.0%	39.1%	40.2%	36.5%	40.9%	42.3%
Total	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Notes

Direct funding: KNAW and UMC Utrecht
 Research grants: all funding like NWO, KWF, CGC, CBG, EU, fundraising etc.
 Industry funding: contract research
 Other: non-grant-related income like University Utrecht, ICIN, graduate school etc.

APPENDIX 5

Aggregated results of the institute

2008	2009	2010	2011	2012	2013
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<i>Academic publications</i>						
In refereed journals	87	89	82	117	121	118
Book chapters	1	4	2	2	1	2

<i>PhD theses</i>						
Internal	8	10	13	9	7	9
External	2	0	0	2	0	0
Total	10	10	13	11	7	9

APPENDIX 6

Number of staff at group level (fte)

		2008	2009	2010	2011	2012	2013
Bakkers group							
research staff	research staff excl. PhD	1	4	4	3	3	4
	PhD	1	1	1	2	2	2
research staff Total		2	5	5	5	5	6
technicians	technicians	0.8	0.8	0.8	0.8	0.8	0.8
technicians Total		0.8	0.8	0.8	0.8	0.8	0.8

Clevers group							
research staff	research staff excl. PhD	9	10	11	12.5	16.2	15
	PhD	6	6	7	4	3	1
research staff Total		15	16	18	16.5	19.2	16
technicians	technicians	3.5	3.5	3.5	6	6.7	10
technicians Total		3.5	3.5	3.5	6	6.7	10

Creyghton group							
research staff	research staff excl. PhD	N.A.	N.A.	N.A.	1	2	2
	PhD	N.A.	N.A.	N.A.	1	1	1
research staff Total					2	3	3
technicians	technicians	N.A.	N.A.	N.A.	1	1	1
technicians Total					1	1	1

Cuppen group							
research staff	research staff excl. PhD	2.8	2.8	4.8	3.5	2.5	4.5
	PhD	2	2	4	2	2	4
research staff Total		4.8	4.8	8.8	5.5	2.5	8.5
technicians	technicians	4.2	6.2	7.2	6.4	5.4	4.2
technicians Total		4.2	6.2	7.2	6.4	5.4	4.2

de Koning group							
research staff	research staff excl. PhD	N.A.	N.A.	N.A.	1	1	1
	PhD	N.A.	N.A.	N.A.	1	1	1
research staff Total					2	2	2
technicians	technicians	N.A.	N.A.	N.A.	2	1	3
technicians Total					2	1	3

de Laat group							
research staff	research staff excl. PhD	4	6	6	7	6	6
	PhD	3	5	5	5	6	6
research staff Total		7	11	11	12	12	12
technicians	technicians	2	1	1	1.6	2	2.9
technicians Total		2	1	1	1.6	2	2.9

den Hertog group							
research staff	research staff excl. PhD	3	3	2	3	3	3
	PhD	1	2	3	2	3	2
research staff Total		4	5	5	5	6	5
technicians	technicians	1	1.84	1.84	1.2	2.84	1.84
technicians Total		1	1.84	1.84	1.2	2.84	1.84

Deschamps group							
research staff	research staff excl. PhD	1	1	1	1	2	2
	PhD	2	2	3	4	2	2
research staff Total		3	3	4	5	4	4
technicians	technicians	1	1	1	1	2	2
technicians Total		1	1	1	1	2	2

Geijsen group							
research staff	research staff excl. PhD	N.A.	2	2	2	2.63	2
	PhD	N.A.	0	1	1	1	2
research staff Total			2	3	3	2.63	4
technicians	technicians	N.A.	1	2	3	3	3
technicians Total			1	2	3	3	3

Guardavaccaro group							
research staff	research staff excl. PhD	1	1	1	1	1	1
	PhD	0	2	4	4	4	2
research staff Total		1	3	5	5	5	3
technicians	technicians	0	0	1	1	0	0
technicians Total		0	0	1	1	0	0

Knipscheer group							
research staff	research staff excl. PhD	N.A.	N.A.	N.A.	2	3	3
	PhD	N.A.	N.A.	N.A.	1	1	2
research staff Total					3	3	5
technicians	technicians	N.A.	N.A.	N.A.	1	1	1
technicians Total					1	1	1

Korswagen group							
research staff	research staff excl. PhD	2	2	2	2	1	1
	PhD	1	4	4	3	3	3
research staff Total		3	6	6	5	4	4
technicians	technicians	1	1	1	1	1	1
technicians Total		1	1	1	1	1	1

Rabouille group							
research staff	research staff excl. PhD	N.A.	N.A.	2.8	3.8	1.8	0.8
	PhD	N.A.	N.A.	1	2	1	2
research staff Total				3.8	5.8	2.8	2.8
technicians	technicians	N.A.	N.A.	0	0.8	0.8	0.8
technicians Total				0	0.8	0.8	0.8

Robin group							
research staff	research staff excl. PhD	N.A.	N.A.	N.A.	N.A.	N.A.	4
	PhD	N.A.	N.A.	N.A.	N.A.	N.A.	1
research staff Total							5
technicians	technicians	N.A.	N.A.	N.A.	N.A.	N.A.	1
technicians Total							1

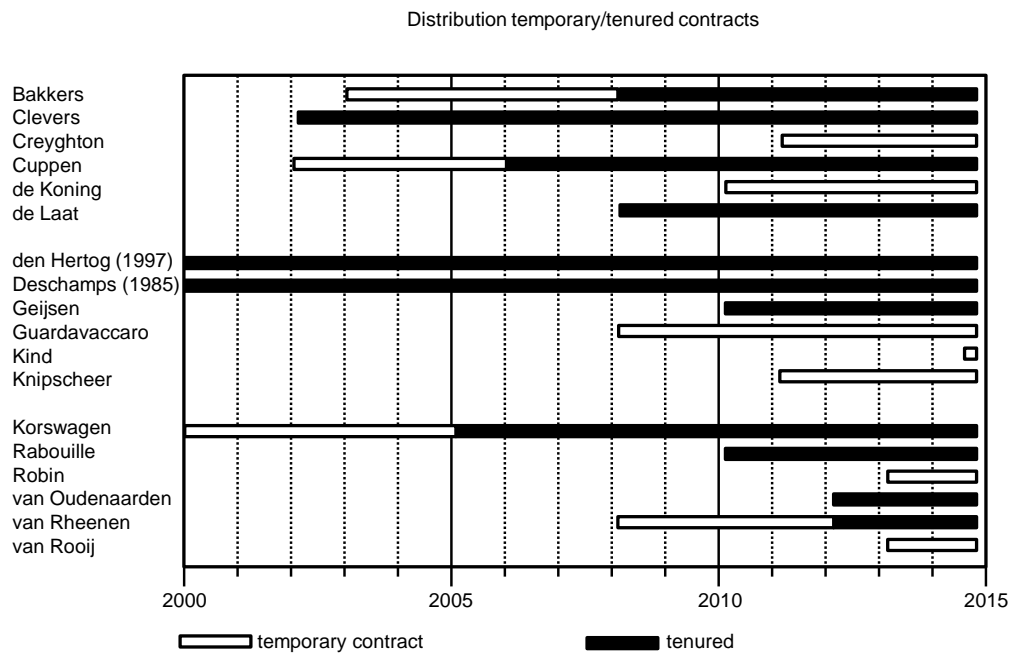
van Oudenaarden group							
research staff	research staff excl. PhD	N.A.	N.A.	N.A.	0	4	4.8
	PhD	N.A.	N.A.	N.A.	2	4	5
research staff Total					2	8	9.8
technicians	technicians	N.A.	N.A.	N.A.	0	0	1
technicians Total					0	0	1

van Rheenen group							
research staff	research staff excl. PhD	1	1	1	3	3	4
	PhD	0	1	3	3	3	4
research staff Total		1	2	4	6	6	8
technicians	technicians	2	2	2	2	2	2
technicians Total		2	2	2	2	2	2

van Rooij group							
research staff	research staff excl. PhD	N.A.	N.A.	N.A.	N.A.	N.A.	1
	PhD	N.A.	N.A.	N.A.	N.A.	N.A.	2
research staff Total							
technicians	technicians	N.A.	N.A.	N.A.	N.A.	N.A.	1
technicians Total							1

APPENDIX 7

Figure: temporary/tenured contracts PIs



APPENDIX 8

Draft program site visit Hubrecht Institute

Sunday 9 November 2014		
	Committee members: arrival at hotel	Apollo Hotel Utrecht City Centre
19.00-21.30	Committee members: dinner	Oudaen, Oudegracht 99, Utrecht

Monday 10 November 2014		
08.30-08.45	Arrival and coffee/tea	Board room
08.45-09.15	Alexander van Oudenaarden - General introduction	Board room
	<i>Presentations group leaders 10 minutes; Q&A/discussion 10 minutes</i>	
09.15-09.35	Alexander van Oudenaarden - Quantitative biology of development & stem cells	Board room
09.35-09.55	Catherine Robin - Hematopoiesis and stem cells during embryonic development	Board room
09.55-10.15	Jacco van Rheenen - Cancer biophysics	Board room
10.15-10.30	Break	Board room
10.30-10.50	Eelco de Koning - Diabetes and islet neogenesis	Board room
10.50-11.10	Jacqueline Deschamps - Genetics of morphogenesis during axial elongation in the mouse embryo	Board room
11.10-11.30	Edwin Cuppen - Genome biology and medical genetics	Board room
11.30-11.50	Wouter de Laat - Biomedical genomics	Board room
11.50-13.05	Lunch / Opportunity for site visit team to evaluate	Board room
13.05-13.25	Rik Korswagen - Wnt signaling in development and disease	Board room
13.25-13.45	Puck Knipscheer - Molecular mechanisms and regulation of DNA repair	Board room
13.45-14.05	Daniele Guardavaccaro - Ubiquitin ligases and cancer	Board room
14.05-14.20	Break	Board room
14.20-15.20	Opportunity for site visit team to talk to junior group leaders and to visit the laboratories	Board room & institute
15.20-16.05	Opportunity for site visit team to talk to a number of PhD students and postdocs	Board room

16.05-16.15	Break	Board room
16.15-16.45	Opportunity for site visit team to talk to Frank Miedema, dean and vice president executive board UMC Utrecht	Board room
16.45-17.15	Opportunity for the site visit team to talk to René Medema, chairman of the scientific advisory board & chairman board of directors Netherlands Cancer Institute (NKI)	Board room
17.15-18.00	Opportunity for site visit team to talk to representatives from societal relevant organizations (Jacqueline Noordhoek, Cystic Fibrosis Foundation (NCFS) & Mariëtte Driessens, Association Foundations for Rare and Genetic Diseases (VSOP) and Mariëtte Oosterwegel on outreach	Board room
19.30-	Dinner	Den Draeck, Oudegracht 114, Utrecht

Tuesday 11 November 2014		
08.45-09.00	Arrival and coffee/tea	
	<i>Continuation presentations group leaders</i>	
09.00-09.20	Jeroen den Hertog - Protein-tyrosine phosphatases in development	Board room
09.20-09.40	Eva van Rooij - Molecular cardiology	Board room
09.40-10.00	Catherine Rabouille - Secretion regulation	Board room
10.00-10.20	Menno Creyghton - Neuro epigenetics	Board room
10.20-10.55	Break	Board room
10.55-11.15	Niels Geijssen - Stem cell modeling of human genetic disease	Board room
11.15-11.35	Jeroen Bakkers - Cardiac development and genetics	Board room
11.35-12.00	Alexander van Oudenaarden - Future perspectives	Board room
12.00-12.20	Hans Clevers - Lgr5 stem cells, Wnt signaling & cancer	Board room
12.20-13.00	Lunch	Board room
13.00-13.30	Meeting site visit team with directors	Board room
13.30-15.30	Preparation of draft report	Board room
15.30-16.00	Presentation of preliminary conclusions to directors and group leaders. Theo Mulder will be present too	Board room or auditorium
16.00-17.00	Drinks/informal meeting with Hubrecht employees	Canteen



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