

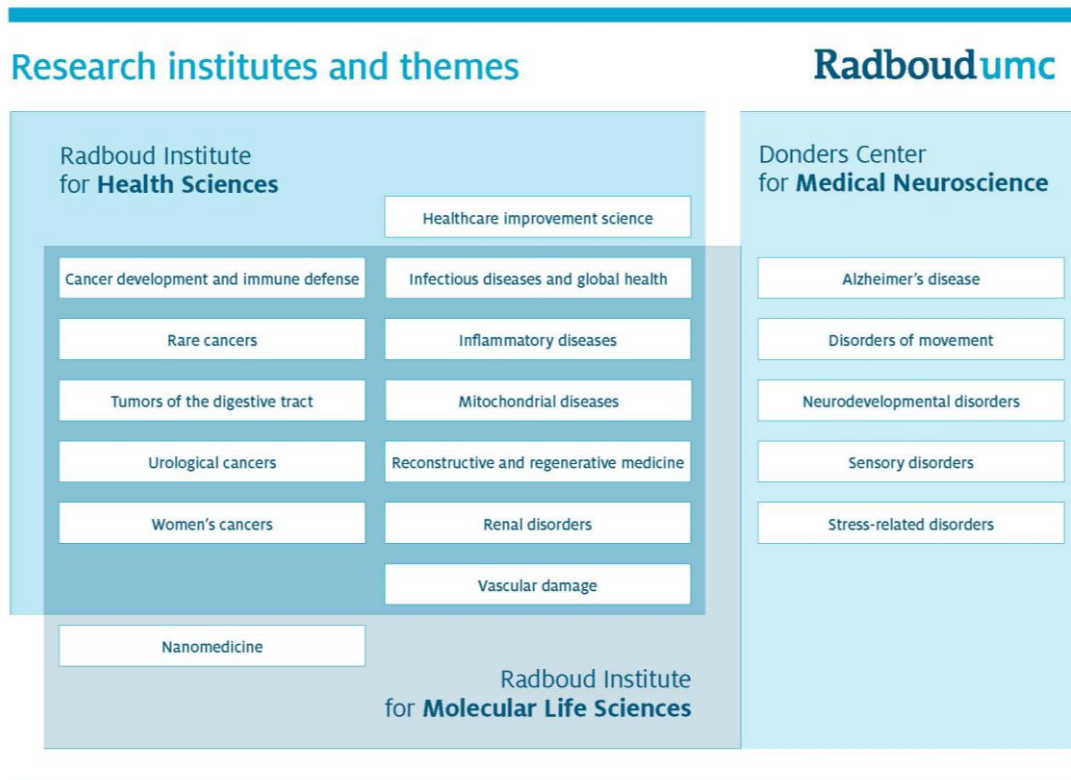
Annual report 2017

Radboud Institute for Health Sciences (RIHS)

Institute for Health Sciences
Radboudumc

Research in Radboudumc

High-quality research has always been a corner-stone of the Radboud university medical center (Radboudumc). We have concentrated our research in three excellent research institutes, each with a dedicated Graduate School, covering research from molecule to man to population. These research institutes interact closely and operate internationally to have a significant impact on healthcare across disciplines. Together, they cover eighteen focused and interactive research themes each aiming at developing tools for individualizing preventive, diagnostic and treatment strategies under the umbrella of “Personalized Healthcare”. Research programs at the molecular level are done in cooperation with the Faculty of Science and those at the population level with the Faculty of Social Sciences.



RIHS research comprises 12 themes, which are described briefly below.

Healthcare improvement science

Theme leader: Prof. Gert Westert

The main focus is on the structure, process and outcomes of healthcare in daily practice, with the aim of improving performance and delivery from the perspective of the patient. Researchers study existing and new interventions at the micro and macro level. Their aim is to explore which interventions or structures work in what circumstances. Immediate value for patients is paramount.

Cancer development and immune defence

Theme leader: Prof. Joop Jansen

Researchers working in this theme investigate resistance to therapy, the tumour micro-environment, cancer-cell trafficking and the interaction between the immune system and cancer. This basic knowledge is translated into novel forms of therapy that target tumour cells. Strategies are also developed for expanding and manipulating immune cells for clinical use, exploiting and boosting the power of the immune system. For the translational part of this work, researchers carry out phase I, II and III clinical trials.

Rare cancers

Theme leader: Prof. Carla van Herpen

Despite the rarity of each of the 'rare' cancers (*i.e.* an incidence <6/100,000 per year), they represent in total about 22% of all cases of cancer. Due to their low frequency, rare cancers pose particular challenges. The main aim is to improve diagnosis and prognosis and to perform personalized clinical studies and translational bench-to-bedside research in patients with rare cancers. This is performed in a national and international collaborative setting and in relationship with patient advocacy groups, where applicable.

Tumours of the digestive tract

Theme leader: Prof. Iris Nagtegaal

Research in this theme is designed to improve the prognosis and treatment of patients with tumours of the digestive tract, with a focus on sporadic and hereditary forms of colorectal, esophageal and pancreatic cancer. The aim is to achieve better prevention of cancer in high-risk patients and develop and implement new diagnostic tools for staging and therapy response. In addition, researchers are developing treatment innovations, ranging from improved surgical techniques to immunotherapy.

Urological cancers

Theme leader: Dr Tom Scheenen

Research involves identifying and evaluating the usefulness of new biomarkers and imaging techniques for risk, diagnostic, prognostic and predictive assessment in prostate, bladder and kidney cancer. In addition, new and existing prevention and treatment modalities in these types of cancer are evaluated. Synergistic multidisciplinary research collaboration – from molecular life sciences to population sciences – ensures a focus on 'utility' for patients and public health.

Women's cancers

Theme leader: Prof. Leon Massuger

The goal of this theme is to improve the patient-centred quality of care in women's cancers (breast, ovary, cervix, vulva, endometrium and pregnancy-related cancer) in partnership with patients through prevention, early diagnosis or implementation of new management strategies supported by a better understanding of carcinogenesis and tumour development, paying special attention to hereditary causes, preservation of fertility and individual post-treatment care.

Infectious diseases and global health

Theme leader: Prof. David Burger

Researchers within this theme aim to have a significant and global impact on the control, treatment and elimination of infectious diseases. The theme combines cutting-edge research in immunology, microbiology, pharmacology and novel 'omics' methodology with translational and implementation research in immunology and infectious diseases. There are two research lines: Infectious diseases & host defence, and poverty-related infectious diseases.

Inflammatory diseases

Theme leader: Prof. Irma Joosten

Chronic inflammation is currently among the leading causes of morbidity and mortality in the Western world. Researchers working within this theme aim to translate results from the molecular and population level to the individual patient in order to improve diagnosis, disease management and the treatment of (chronic) inflammatory disorders such as rheumatoid arthritis, chronic obstructive diseases and psoriasis.

Mitochondrial diseases

Theme leader: Prof. Jan Smeitink

The mission within this theme is to better understand the cellular bio-energetics in health and disease at all levels of complexity. Knowledge thus gained will enable the development of preventive measures and help to make substantial contributions to the development of rational treatment strategies for mitochondrial diseases.

Reconstructive and regenerative medicine

Theme leader: Prof. Wout Feitz

The focus within this theme is on the development and clinical translation of innovative diagnosis and therapies, including regenerative medicine and nano-medicine, for personalized care and cure of patients needing reconstruction of lost or damaged tissues. This will be achieved through transdisciplinary research by leading research groups in medicine, dentistry, biochemistry, chemistry, biology and materials science.

Renal disorders

Theme leader: Prof. Joost Hoenderop

Current and future care of patients with renal and renal-related disorders can be considerably improved. To achieve this, researchers working on this theme aim to increase knowledge of the molecular and immunological basis of rare glomerular and tubular disorders; they develop biomarkers for optimal prediction of disease prognosis; and apply strategies for preventing and improving renal replacement therapy.

Vascular damage

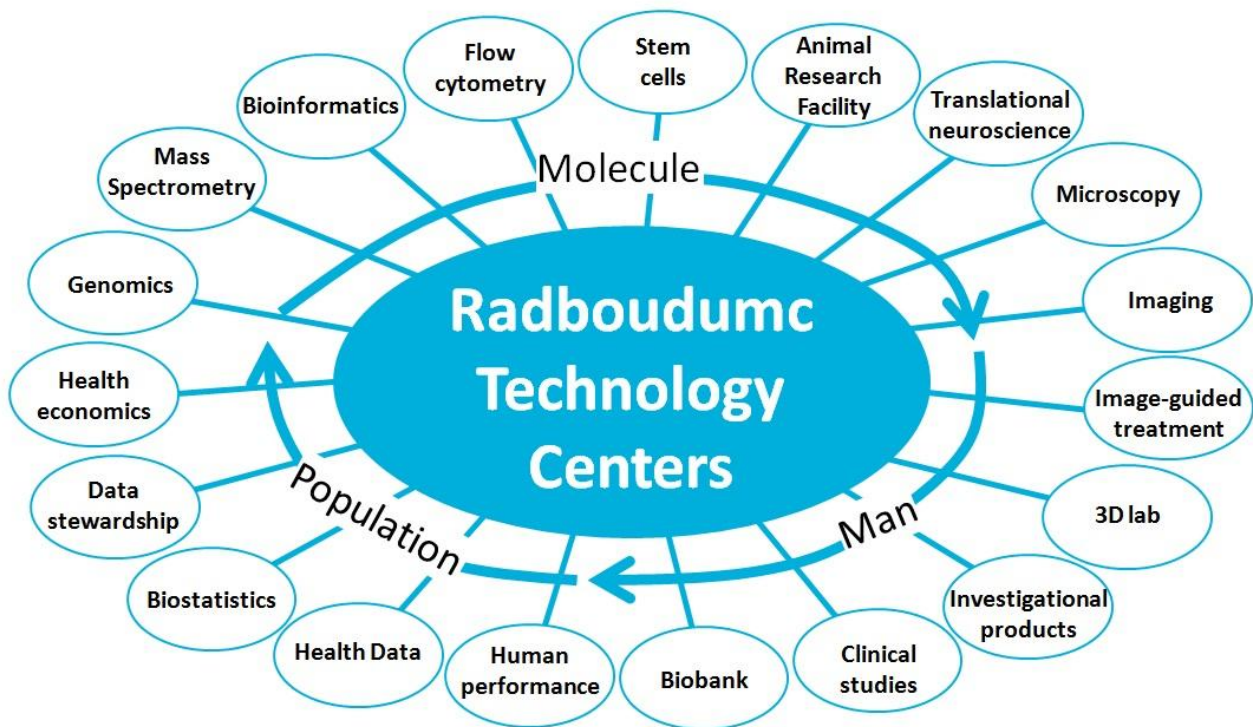
Theme leader: Prof. Gerard Rongen

In this theme the aim is to increase understanding of the causes and consequences of vascular injury and to translate this knowledge into improved personalized cardiovascular healthcare. Early detection of atherosclerosis, primary and secondary prevention of atherosclerosis, optimal treatment of atherosclerosis to preserve end-organ function, and implementation of effective diagnostics and therapies in practice are key focus areas.

Research facilities

World-class infrastructure and talented support staff are essential ingredients for high-quality research. We have well-integrated laboratories, extramural research facilities and nineteen state-of-the-art Technology Centers.

The Radboudumc Technology Centers (www.radboudumc.nl/research/technologycenters) offer research facilities for internal and external researchers and are linked to the Radboud University Research Facilities.



Radboud Institute for Health Sciences

A. Reflection and preview

1. Reflection

2017 was a successful year for RIHS: 89 PhD candidates defended their theses, more than 1400 scientific papers were published in international peer-reviewed journals and 6 researchers received a prestigious personal grant. The institute made an important step for public outreach on Saturday 7 October, when it organized an Open day in the Weekend of Science (“Weekend van de Wetenschap”), hosted by Diederik Jekel, science journalist and presenter. About 2000 visitors became a health scientist for one day and discovered how special healthcare research is (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=23246>). We also launched a new RIHS website (www.rihs.nl), fully integrated into the Radboudumc website.

In 2017 the governance of the Radboudumc Technology Centers (RTCs) was adjusted. Central RTCs are now placed under supervision of a research institute (for RIHS: Biobank and Statistics) and receive a tailor-made budget. The decentral RTCs annually receive €50.000 for the upcoming 3 years and their performance will be evaluated in 2019.

A closer collaboration within the region has been established by facilitating joint junior researcher positions with collaborating hospitals (CWZ, Rijnstate, JBZ and SMK).

2. Risks, threats and opportunities

The fact that researchers can only belong to a single research institute makes collaborations with other faculties challenging.

Success rates of health sciences related grant proposals are much lower than proposals from the molecular life sciences. The societal challenges program of Horizon 2020 is an opportunity for an institute like RIHS that has societal relevance as its aim. RIHS is glad with the new policy for the installation of special chairs as this is an important instrument for the connection with important stakeholders.

3. SEP evaluation

a) In 2018 RIHS and RIMLS, including their 13 themes, will be evaluated simultaneously by means of a site visit (2-4 December 2018) by an external independent committee according to the nationally-approved Standard Evaluation Protocol (SEP 2015-2021). Currently, the two research institutes together with their research themes are gathering all the necessary data and preparing the self evaluation report.

b) In 2011 the former NCEBP was evaluated. Many recommendations of the evaluation committee were already implemented: e.g., accreditation RIHS graduate school by the research school accreditation committee of the KNAW; formation Radboudumc Technology Centers and DRE; improved external communication of the societal impact of RIHS’ research by e.g., Open day and patient evening; creation visiting professor fund.

c) In 2018 RIHS will start with public lectures. Furthermore, collaborations with other RU faculties and international research institutes will be further explored and we are working on a training for supervisors.

d) The previous SEP evaluation committee advised to give more financial responsibility to the research institutes, because the integral responsibility of the 51 department chairs prohibits efficient

leadership of the institutes. This has not been implemented yet but is currently discussed in the Radboudumc Executive Board.

4. Mission and vision

The mission of the RIHS is to improve clinical practice and public health. It does so by providing evidence of the efficacy and efficiency of existing and new tests, treatments and policies as well as innovative modes of health care delivery, by training young researchers in methodologies for obtaining such evidence and by developing new methodologies for improved research programmes in this field.

The Institute's focus is on developing methodologies that optimize personalized healthcare and on the application of these tools in disease-oriented research themes. In line with the Radboudumc's mission of having *a significant impact on healthcare*, the Institute aims to bridge the gap between science and society. Societal impact is at the core of the Institute's ambitions.

Very recently we discussed our mission, SWOT and strategy together with a small group of prominent RIHS senior researchers. Currently we are revising our mission, trying to make it more proactive (in agreement with the Radboudumc mission) and including the patient's perspective.

B. Quality of research output

Some research highlights are listed below:

- Jeroen van der Laak (Women's cancers) and colleagues published in JAMA (IF=44.4) about AI for the identification of cancer in tissue images: Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer (<https://www.radboudumc.nl/en/news-items/2017/computer-herkent-kanker-in-weefselbeelden>).
- Radboudumc's Primary healthcare was listed second best of the world after Oxford in the international ranking of Primary Health Care as compiled by the Center for World University Rankings (CWUR). An exceptional position for a Dutch department (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=22943>).
- According to Web of Science 12 papers of Jelle Barentsz (Urological cancers) and his group on prostate MRI are among the top 1% of the published papers in the specialty of urology or radiology. One is among the 0,1% (hot paper in the field) (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=23391>).
- Teun Bousema (Infectious diseases and global health) and coworkers highlighted in Nature Communications the importance of older age groups in the maintenance of transmission of malaria and identified likely thresholds for diagnostics to limit transmission (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=23348>). Bousema also received the prestigious Eijkman medal for his special work on malaria epidemiology (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=22236>).
- Vincent Aengevaeren and Thijs Eijsvogels (Vascular damage) assessed the association between lifelong exercise volumes and indicators of coronary atherosclerosis. Their results were published in Circulation (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=21773>).
- Maroeska Rovers (Urological cancers) en Nico Verdonschot (Reconstructive and regenerative medicine) were elected as members of the Academia Europaea (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=22951>).
- Nico Verdonschot was awarded to present the 2017 Erwin Morscher Honorary Lecture (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=22111>).

C. Societal impact

Much – if not most – RIHS research has direct societal impact and is implemented in clinical care or public health. Research results are shared with the professional and lay community through contributions to guidelines or protocols, professional and popular publications, newspaper and radio, board membership of national and international societal advisory groups (e.g., Dr Eddy Adang, Prof. Maria Hopman, Prof. Bart Jan Kullberg and Prof. Gerhard Zielhuis are members of the Health Council of the Netherlands) and policy institutes, outreach activities and public-private collaborations.

Some highlights in 2017 were:

- RIHS organized a successful *Open day* (see above).
- Together with the television program “De kennis van nu”, Monique Steegers (Healthcare improvement science) and Esmeralda Blaney Davidson (Inflammatory diseases) performed an online study (“*Groot national Pijnonderzoek*”) on pain sensitivity in the Dutch population (<https://www.radboudumc.nl/en/news/2017/women-are-more-sensitive-to-pain-than-men>).
- Rob Baltussen (Infectious diseases and global health) initiated a citizen panel on making choices in health care (burgerforum ‘keuzes in de zorg’). In September and October 24 participants debated about the coverage of medical treatments in the basic benefit package in The Netherlands, including the underlying values and principles they find important. The initiative was extensively covered in the national news (<https://www.radboudumc.nl/projecten/burgerforum>).
- With the shift from intravenously to orally administered drugs in modern oncology, drug absorption often limits the full potential of these drugs. In the "Volkskrant" Nielka van Erp (Urological cancers) explained that intake with food can reduce gastro-intestinal toxicity, improve patients comfort and save drugs (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=21484>).
- Merel Ritskes (Reconstructive and regenerative medicine), professor of evidence-based laboratory animal science and founder of SYRCLE (Systematic Review Center for animal Experimentation), was awarded one of the first Cochrane-REWARD prizes for reducing waste in research (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=21906>).
- A collaboration of nephrologists nationwide led to a new treatment guideline which in the end enables tailored therapy with the orphan drug eculizumab and a considerable cost reduction. The nationwide study CUREiHUS, initiated by the Radboudumc and led by Nicole van de Kar and Jack Wetzels (Renal disorders) is one of the hallmarks of this new national approach and acquired a lot of (inter)national attention (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=22790>).

D. Acquisition

Grant type	Title	Researcher(s)	Theme	Awarded
Personal grants				
NWO Vidi	Personalizing BCG immunotherapy in bladder cancer: a novel approach using germline and acquired DNA variants	Sita Vermeulen	Urological cancers	€800k
NWO Veni	Building a digital pathologist for improved treatment of prostate cancer	Geert Litjens	Urological cancers	€250k
NWO Veni	Posterior Urethral Valves: Causes and prediction of future kidney function	Loes van der Zanden	Renal disorders	€250k
ERC Proof of Concept	BioMechMeniscus: A biomechanically driven, patient specific pre-planning and surgical tool to optimize placement of a novel meniscus prosthesis	Nico Verdonschot	Reconstructive and regenerative medicine	€150k

Senior Dekker - Dutch Heart Foundation	Sitting Interruption Treatment as a novel eHealth Secondary prevention Strategy	Thijs Eijvogels	Vascular damage	€400k
Dekker - Dutch Heart Foundation	Measuring Athletes Risk of Cardiovascular Events: a follow-up study (MARC-II)	Vincent Aengevaeren	Vascular damage	€130k
Large Horizon 2020 grants				
H2020	MyLeg	Nico Verdonshot (consortium)	Reconstructive and regenerative medicine	€4,5M
H2020	EPTRI – European Paediatric Translational Research Infrastructure	Saskia de Wildt (consortium)	Renal disorders	€3,1M
H2020	c4c (Collaborative Network for European Clinical Trials For Children)	Saskia de Wildt (consortium)	Renal disorders	€130M
H2020	EQIPD (European Quality In Preclinical Data)	Kim Wever (consortium)	Vascular damage	€4,5M
Other grants (not complete overview)				
ZonMw-TOP	Host response to Lyme disease	Bart Jan Kullberg / Leo Joosten	Infectious diseases and global health	€900k
ZonMw	PRO-SWAP	Heiman Wertheim (Consortium)	Infectious diseases and global health	€577k
ZonMw	Cost-effectiveness of psychosomatic therapy for patients frequently attending primary care with medically unexplained symptoms	Pim Assendelft	Healthcare improvement science	€235k
ZonMw	Evaluation of two vaginal, uterusparing surgical methods for pelvic organ prolapse reconstruction: modified Manchester operation (MM) and sacrospinal hysteropexy (SSH)	Kirsten Kluivers	Reconstructive and regenerative medicine	€490k
ZonMw	Cost-effective diagnostic evaluation of patients with symptomatic breast disease; ultrasound as accurate initial imaging technique	Ritse Mann	Women's cancers	€408k
ZonMw	Landelijke Farmacotherapie Eindtoets Medicatieveiligheid; 'voorkomen is beter dan genezen'	Kees Kramers	Healthcare Improvement Science	€150k
ZonMw	CUREIHUS	Jack Wetzels (consortium)	Renal disorders	€319k
ZonMw	CMyLife e-clinics	Nicole Blijlevens	Rare cancers	€200k
ZonMw	4 projects in program "Palliantie"	Yvonne Engels/ Jeroen Hasselaar / Marieke Groot / Stef Groenewoud	Healthcare Improvement Science	€1,6M
NWO	Citius Altius Sanius	Maria Hopman / Thijs Eijvogels (consortium)	Mitochondrial diseases / Vascular damage	€4,0M
NWO	Efficient deep-learning systems	Jeroen van der Laak / Henkjan Huisman	Women's cancers/ Urological cancers	€255k

STW	Further development of Anatomy Projector	Stefan Hummelink	Women's cancers	€150k
KWF	Nationwide implementation of standardized structured reporting to support optimal treatment decisions	Rosella Hermens	Women's cancers	€265k
KWF	Lifestyle factors and urinary bladder cancer: etiologic and prognostic heterogeneity by tumour stage and molecular subtype	Alina Vrieling	Urological cancers	€576k
KWF	Anakinra: safety and efficacy in the management of Fever during neutropenia and mucositis in patients with multiple myeloma receiving an autologous hematopoietic stem Cell Transplantation after high-dose melphalan (AFFECT)	Nicole Blijlevens	Rare cancers	€617k
Bill & Melinda Gates Foundation	P. falciparum infection dynamics and transmission to inform elimination (INDIE)	Teun Bousema (consortium)	Infectious diseases and global health	€5,3M
MRC / Wellcome Trust	Cluster randomized trial of ivermectin for malaria elimination	Rob Baltussen / Teun Bousema	Infectious diseases and global health	€202k

E. PhD policy

- The RIHS Introduction course was revised. In 1,5 day PhD candidates are now provided with insights, tips and tricks at the start of their PhD track (<https://www.radboudumc.nl/en/education/courses/rihs-introduction-course-for-phd-candidate>).
- New Radboudumc guidelines have been developed for the PhD thesis and for assessing cum laude promotions.
- Activities RIHS PhD council:
 - Successful PhD retreat with BMJ chief editor Fiona Godlee and former minister Ronald Plasterk (<https://www.radboudumc.nl/en/news/2017/over-100-phd-candidates-attended-the-retreat>)
 - Introduction Peer 2 Peer meeting with starting PhD candidates
 - Start organisation Discussion and Drinks about diverse topics (The impact of the elections on healthcare costs and medical research, Going abroad during or after your PhD?, Forensic epidemiology)
 - Visit to ZonMw
- More than 170 new Training and Supervision Plans (TSP) were submitted in 2017. To give feedback in time the RIHS TSP committee now monthly meets to discuss the new TSPs.
- A career workshop was organized for PhD candidates and postdocs, aiming to provide insight into the next steps in their career and to give them practical tools to successfully make this next step.
- Many RIHS PhD candidates are medical doctors who combine their PhD research with clinical tasks. Meetings were organized with this group to learn from their experiences.
- On the new Radboudumc website we nicely organized the information for PhD candidates per stage of the PhD track (start, current, finish). (<https://www.radboudumc.nl/en/research/academic-and-scientific-training/level-of-experience/phd-candidates/registration-checklist/orientation>)
- A survey was sent out to all Radboudumc full professors to ask for their opinion about PhD tracks and the (role of the) graduate schools.
- A successful Midsummernight event was organized for all Radboudumc PhD candidates (<http://www2.rihs.nl/news/RIHSNewsitem?newsid=22746>)

- RIHS contacted some alumni PhD candidates to form a group of RIHS ambassadors.
- RIHS offered 6 junior researcher positions. Four of the projects were proposed by a RIHS researcher together with an international partner. PhD candidates, once appointed, carry out at least one year of the research abroad.

F. Academic integrity

In a new Research Code, the JCI (Joint Commission International) working group Research has described ten core qualities that are characteristic for scientific researchers in the Radboudumc.

All second year PhD candidates participate in a compulsory two-day course, which deals with academic integrity issues. All Radboudumc (junior) Principal Investigators participate in this course in turn. Every course is evaluated to further improve it.

In case of problems, PhD candidates can contact their mentor or the contact persons appointed by the research institutes. The contact persons annually report about the cases they encountered.

The assurance of data management, which is extremely important for the integrity of research, took shape in 2017 in the Digital Research Environment (DRE).

G. Research data management (RDM)

The Radboudumc and private parties co-developed the Digital Research Environment (DRE). The idea is that, once research data are collected, all data manipulations and analyses take place within this web-based secure environment. Through this, it is secured that there are trails of different versions of both data and programs, that a 'third user' can be invited to the data without transferring data, that pseudonymization takes place of identifiable data, and that data can be made accessible according to the FAIR criteria. A team of data stewards has been appointed that will help investigators switch to the DRE. It is aimed that 100% of all researchers will use the DRE before 1/7/2018. Researchers are allowed not to use the DRE if the functionality of the DRE is insufficient (which is still the case with high performance computing) or if they can prove that they arranged the same functionality in an alternative way.

The RU Steering Group RDM has reviewed the RDM policy of the RIHS and the institute is now working on the Steering Group's recommendations. In communication with the Steering Group, we are working on a template page describing FAIR for inclusion in PhD theses.