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Mission statement

The mission of GRIAC is the multidisciplinary translational study of obstructive airway and pulmonary diseases and healthy ageing

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Introduction

The Groningen Research Institute for Asthma and COPD (GRIAC) is dedicated to research on obstructive and pulmonary diseases on the edge of clinical and fundamental research. The main theme of GRIAC is unravelling the underlying mechanisms of the development, progression and remission of airway obstruction, allergy and airway hyperresponsiveness, their mutual interactions, and their relevance to treatment. These phenomena are important risk factors for the development of asthma and COPD and crucial characteristics in their clinical pictures.

GRIAC operates within the research framework of the University Medical Center Groningen, which has a central focus on healthy ageing and the Faculty of Science of the University of Groningen, which has a focus on molecular life and health. GRIAC is part of the governmentally accredited organization GUIDE (Groningen University Institute for Drug Exploration) which is embedded in the Groningen School of Medical Sciences (GSMS).

Participating departments

The multidisciplinary and translational research of GRIAC is the result of an intensive collaboration between the researchers of GRIAC, consisting of our members from different disciplines. The disciplines involved are allergology, experimental pulmonology and inflammation research, epidemiology, general practice, molecular pharmacology, pathology, paediatric pulmonology and paediatric allergology, pulmonology and respiratory insufficiency. GRIAC recently added new members from the department of Clinical Pharmacy and from ERIBA, the European Research Institute for the Biology of Aging. Collaboration is based on freedom, equivalence and consensus. Extensive collaboration exists with Departments of Genetics, Pharmaceutical Technology and Biopharmacy, and the Groningen Transplantation Center. Furthermore, collaboration exists with the Department of Analytical Biochemistry (University Center for Pharmacy).
Research program

GRIAC defines ‘obstructive airway and pulmonary disease’ in relation to healthy ageing, as its main topic, which is reflected in our mission statement. Research projects have to fit within this research topic, describing the projects in their mutual cohesion. The tuning of projects and development into a program is the responsibility of the program leaders of GRIAC, in exchange with the Scientific Board of the Institute. GRIAC operates within the University Medical Center Groningen (UMCG) and its overarching research theme “Healthy Ageing”, and partially within the Groningen Research Institute of Pharmacy (GRIP), with a focus on Molecular Life and Health. Research within GRIAC focuses on the main challenges of obstructive airway and pulmonary disease, as well as pulmonary fibrosis:

- Identifying risk factors for the development, progression and remission of disease
- Identifying disease-related genes, gene pathways, gene functionality and gene regulation and their relation to specific phenotypes of obstructive airways disease and pulmonary fibrosis
- Unravelling the pathophysiology of allergen-, environmental- and smoke- induced disease, in humans, animal models, and in vitro cell systems
- Unravelling the effects of disease-related inflammation on lung function, hyperresponsiveness and remodeling of large and small airways
- Defining new targets for personalized (drug and device) intervention and evaluation of intervention strategies, which includes the development of novel approaches in preventive medicine
- Development of noninvasive or less invasive tools to assess severity of disease and effects (and side effects) of treatment.

Scope of research

These challenges are investigated particularly in asthma and COPD, resulting in integrated subprograms on:

1. Epidemiology and genomics
3. Clinical Medicine: Assessment, modulation of and intervention in disease severity, progression and remission

Epidemiology and genomics

The longstanding expertise in identifying risk factors and the availability of large, prospective, long-term follow up of patient-based and population-based cohorts (such as LifeLines) and the collaboration with the Department of Genetics enables extensive sub-programs, including exposomics, (epi)genome-wide association, genome-wide interactions and transcriptome sequencing studies. This has resulted in identification of numerous novel genetic loci related to asthma and COPD onset and progression. Proteomic and lipidomic research has led to identification of disease susceptibility and progression markers. GRIAC has a longstanding collaboration with the proteomics facility, and recently incorporated its first member from the European Research Institute on the Biology of Ageing (ERIBA), strengthening its focus on bioinformatic analyses of integrated genomic datasets.

Molecular medicine

GRIAC is actively engaged in studies linking clinical outcomes to pathophysiology, also on a molecular basis. Often based on outcomes from and also involving omics studies, the functionality of genes and proteins in disease is studied using molecular approaches in cells and tissues from patients, in cell lines and in animal models. In vivo and in vitro silencing and overexpression of genes are now established techniques that are operational at the UMCG and GRIP, including the development of knock out and transgenic mouse models, and the
use of RNA interference and pharmacological modulation of cells and tissue slices. Fundamental to this line of research is the exploration of intracellular and intercellular pathways and interactions relevant for tissue repair, disease development, progression and remission, as well as for the exploration of novel drug targets.

**Clinical medicine**

Patient-centered research is at the heart of GRIAC. Our translational research approach includes large-scale clinical management in primary care, clinical and intervention studies in allergy, food allergy, asthma and COPD. Because it is moving towards precision medicine (predictive, preventative, personalized, and participatory) in obstructive and pulmonary disease, GRIAC is in an excellent position to incorporate genomic markers in intervention studies. GRIAC is actively engaged in the development of clinical questionnaires for disease diagnosis and monitoring of disease control. Pulmonary rehabilitation and novel, personalized bronchoscopic intervention techniques are evaluated for the treatment of COPD.

**How we collaborate**

Every two weeks GRIAC organizes research meetings for the whole institute in which both internal and external speakers are invited to venture new ideas and to challenge the audience. This constitutes also the forum in which different types of research are being presented to all members of GRIAC. Members of GRIAC participate in very different aspects of asthma and COPD research, ranging from epidemiology, clinical allergology, pulmonology, pharmacology, and general practice to basic research in genetics, proteomics, tissue studies, cell cultures and animal models. Lively discussions always take place. To enhance collaboration and stimulate new areas of research, GRIAC organizes twice yearly a research retreat and monthly “brainstorm sessions” on a specific topic. These brainstorm sessions are used to stimulate novel ideas for multidisciplinary research, and to discuss publication ideas for high impact journals.

During the GRIAC retreat members of the Board of directors, scientific staff and post-docs of GRIAC discuss future perspectives and new developments in research and explore potential new collaborations within their research, based on international developments in the field. During and after the research meeting investigators can discuss their grant proposals with the staff members, who are expert in a particular field.

Finally, there are weekly meetings for junior researchers and staff members. At these meetings there is ample time for discussion on choosing the appropriate study design, the set-up of research protocols, analyses and interpretation of results of research, and for preparation and improvements in concepts of abstracts, and oral and poster presentations at international meetings. Introductory lectures are provided in lung function measurements, laboratory techniques, genetic research and so on. We aim to make our PhD students familiar with these research techniques. These weekly GRIAC meetings aim to teach the understanding of different aspects of the approach towards research on asthma and COPD in the various disciplines involved in GRIAC in order to improve the level of interdisciplinary research. PhD courses in epidemiology, statistics and genetic data analyses are being organised for members of GRIAC and others interested as well.

**Organisation**

Two program leaders lead the Institute. They have the following tasks:

- Representatives in GSMS and GUIDE
- Contacts with the UMCG
- Contacts with the University of Groningen
- Policy preparation for KNAW, FMW, UMCG and University of Groningen
- Preparing propositions for research development
The coordinators are advised extensively by the Board of GRIAC, consisting of senior members of the participating departments, who all have their own specific expertise. This board advises in all aspects of research. The board meets once monthly to exchange ideas and prepare policies.
Perspectives

Asthma and COPD research takes place in a lively and rapidly changing field. New developments will encompass the functional genomics (including exposomics, lipidomics and proteomics) of asthma and COPD. We envisage that integration of the – omics techniques will provide novel insight into the disease networks that lead to these obstructive airway diseases.

Within each sub-program, specific research goals are complemented with an overarching emphasis on healthy ageing, (personalized) drug development, societal impact and the relevance of infrastructure. As listed below, this GRIAC approach has resulted in important achievements in past years and in new targets to work on for the future.

The strategic sub-programs
• Epidemiology and genomics: Study approaches integrating epidemiological and genomic techniques are customary at GRIAC. Epidemiological studies encompassing endogenous, environmental and lifestyle risk factors, in general and patient-based population and from the prenatal phase to mature age. Genomic studies are performed at the level of genetics, epigenetics, gene expression and function, molecular mechanisms and gene-gene and gene-environment interactions in disease development, progression, remission, and severity, as well as disease intervention (pharmacogenomics), and these are integrated with proteomic approaches.
• Molecular Medicine: The focus here is on role of allergens, smoking and other lifestyle factors in pathophysiology and pathogenesis of environment-induced diseases including asthma, COPD, and pulmonary fibrosis. In vivo studies in humans and animal models (including transgenerational models) using mice and unrestrained guinea pigs are used to identify disease mechanisms and drug targets. Investigations include lung function techniques and studies of blood, tissues and/or cells derived from airways or lungs. Furthermore, in vitro studies assess cellular activation, adhesion and interactions with other cell types and with their environment, including the extracellular matrix. Signaling pathways and the function of susceptibility genes that were identified in the epidemiology and genomics subprogram are studied in cells and tissue explants (e.g. lymphocyte subsets, epithelial cells, fibroblasts, intact airway and smooth muscle preparations). Interactions between different cell types are studied by using cells obtained from sputum induction and nasal brushings as well as airway wall and lung tissue obtained by bronchoscopy, surgical biopsy or surgical resection.
• Clinical Medicine: Assessment, modulation and intervention in disease severity, progression and remission: Disease outcome assessment is being studied with techniques such as exhaled breath analyses, nasal epithelial gene expression, and small airway dysfunction. In addition, validated questionnaires on quality of life, drug side effects, hyperresponsiveness and symptoms are developed for diagnostic purposes as well as outcome assessment. Interventions can be at the level of cell cultures, animal models and clinical studies with targeted therapy.

Output, visibility and (external) funding

Productivity of GRIAC is at present overall very good and recently, GRIAC was assessed by the Standard Evaluation Protocol (SEP, see ‘special topics’ for more details). Results in internal medicine and basic science have been published in top peer reviewed journals and patents have also been filed. GRIAC members have been urged to focus on publication strategy and brainstorm sessions have been organized to even further improve the impact of scientific output. Asthma and COPD are highly prevalent in the general population, and thus focussing on these two syndromes is appropriate and has a high societal relevance. At
current the priority of the institute is ranging from cellular models to the underlying disease models to the clinic (translational research) with transdisciplinarity as a major feature.

The national and international academic reputation of the senior GRIAC members can be weighted at its merits judging the invitations to address international congresses and their prominent roles in various national and international research and professional societies and working groups in addition to their role in EU collaborations. In 2014, the Expertscape Website graded GRIAC amongst the top institutes in Europe in relation to asthma and COPD. Moreover, since several of these GRIAC members are relatively young and proven to develop their high potential in their specific research field (e.g. epidemiology, pediatric and adult pulmonology, and molecular pharmacology), GRIAC can face its future with confidence.

We will continue to invest in the training of young scientists in the field of obstructive airways and pulmonary disease, with a focus on multidisciplinary translational research. Given the true interdisciplinary nature of the institute, we feel confident that ongoing close collaboration of GRIAC members who share their in-depth knowledge of specific research fields in asthma, COPD, and pulmonary fibrosis will keep the institute at the internationally acknowledged level of excellence in the future, and that they will be able to generate sufficient resources to finance this research. We have shifted our focus from smaller (University Medical Centers) towards larger (inter)national and interdisciplinary research grants (Lung foundation consortium grants, NWO TOP grants, European funding) as well as personal grants (VENI, ViDi, VICI and ERC grants). Within the U4 collaboration of the Universities of Groningen, Ghent, Göttingen and Uppsala, international collaborations are ongoing for PhD students to stay at 2 or 3 of these universities for an international PhD project.
The year 2016 in review

All contributions to the scientific work in GRIAC are important and highly appreciated. It cannot be stressed enough that all the scientific output and results obtained are only possible due to the contribution of every single person who works within our research institute. Nevertheless, without disrespect to the work of members who are not specifically mentioned, we like to highlight some topics that drew particular attention in 2016.

Highlights

In relation to the thesis defences of Dr. R. Hoffmann and Dr. D. van Hemelen minisymposia were organized. Speakers at these symposia were national and international leading researchers.

On September 23, 2016 the Children’s Allergy & Asthma Center in the UMCG was officially opened with a symposium. See ‘special topics’ for more details.

Prof. Dr. G.H. Koppelman received a Lung Foundation Netherlands consortium grant together with researchers from the Academic Medical Center Amsterdam and the Erasmus Medical Center Rotterdam. See ‘special topics’ for a short description of the project.

W. van Geffen, MD, received an European Respiratory Society Short-Term Fellowship to acquire new insights into pulmonary physiology at the Royal Brompton Hospital in London.

Dr. A. Faiz received a 2-year junior investigator grant from the Lung Foundation Netherlands for his research proposal entitled: Understanding the genetic and epigenetic drivers of cigarette smoke susceptibility in COPD. See ‘special topics’ for a short description of the project.

Prof. Dr. P.J. Wijkstra had his inaugural lecture entitled ‘Chronische beademing: een adembenemende ontwikkeling’ (English: “Chronic Ventilation: a breathtaking development”) on December 13th.

Three GRIAC researchers retired in 2016: Prof. D.S. Postma (April 1), Prof. A.E. Dubois (April 15), and Prof. H. Meurs (December 9). To celebrate this, retirement symposia were organized. Speakers at these symposia were national and international leading researchers. See ‘special topics’ for more details.

Prof. Dr. H.M. Boezen was awarded as Fellow of the European Respiratory Society.

Prof. Dr. M. Schmidt was awarded as Fellow of the British Pharmacological Society.

Prof. Dr. D.S. Postma obtained the COPD10 UK award for scientific contribution to the field.

On March 24, Prof. Dr. I.H. Heijink hosted a visit by donors of the Lung Foundation Netherlands to the EXPIRE lab. The feedback was very positive.

Prof. Dr. B.N Melgert obtained a fellowship for the innovation of teaching from the University of Groningen.

Dr. J.F.M. van Boven will be representing GRIAC in the junior board of the “Dutch FDA” (College ter beoordeling van geneesmiddelen).
Prof. Dr. I.H. Heijink organized the NRS-symposium ‘Lung Repair and Regeneration’ on November 11 in Amsterdam in collaboration with Dr. R.J. Rottier from Erasmus MC, Rotterdam. Approximately 70 participants attended the meeting.

**Prizes/Awards**

Dr. M. de Vries won an international trainee scholarship from the American Thoracic Society.

D. van der Plaat, MSc, won an abstract scholarship from the American Thoracic Society.

A.I.R. Spanjer, MSc, won the Translational Research Prize from the Federation of European Pharmacological Societies (EPHAR) and the European Association for Clinical Pharmacology and Therapeutics (EACPT).

M. Ketelaar won a travel grant for best oral abstract at the International Severe Asthma Forum 2016 (ISAF).

W. van Geffen, MD, won the Young Researcher Grant from the European Respiratory Society.

Dr. L.E.M. Kistemaker won the best young investigator abstract award of assembly 5 (Inflammatory Airways Diseases and Clinical Allergy) of the European Respiratory Society.

Dr. M. Duiverman won the best abstract award in noninvasive ventilatory support of the European Respiratory Society.

M. Ketelaar received a Talent Grant from the Ubbo Emmius-Junior Scientific Masterclass (UEF-JSM Talent Grant, University of Groningen).

Dr. L.E.M. Kistemaker won the Netherlands Respiratory Society Swieringa Thesis Award.

Prof. Dr. H.M. Boezen was awarded as Fellow of the European Respiratory Society.

Prof. Dr. M. Schmidt was awarded as Fellow of the British Pharmacological Society.

Prof. Dr. D.S. Postma obtained the COPD10 UK award for scientific contribution to the field.

**Visitors**

Prof. Dr. I. Adcock, Imperial College London, UK. February 29, 2016.

Dr. R.C.J. Langen, Maastricht University, Maastricht. February 29, 2016.

Prof. Dr. E.C. de Jong, Academic Medical Center, Amsterdam. February 29, 2016.

Prof. Dr. L. Koenderman, University Medical Center Utrecht, Utrecht. February 29, 2016.

Prof. Dr. C. Taube, Leiden University Medical Center, Leiden. March 23, 2016.

Prof. Dr. R. Penn, Thomas Jefferson University, Philadelphia, USA. March 31 & Dec 9, 2016.

Prof. Dr. S.T. Holgate, Southampton General Hospital, UK. April 1, 2016.

Prof. Dr. S.T. Weiss, Harvard Medical School, Boston, USA. April 1, 2016.
Prof. Dr. P.J. Sterk, Academic Medical Center, Amsterdam. April 1, 2016.

Prof. Dr. E. Bleecker, Wake Forest University, Winston-Salem, USA. April 1, 2016.

Dr. H. de Groot, Reinier de Graaf Hospital, Delft. April 15, 2016.

Dr. Y. Meijer, University Medical Center Utrecht, April 15, 2016.

Prof. Dr. M. Peters-Golden, University of Michigan, USA. April 28, 2016.

Dr. K. Affleck, GlaxoSmithKline, UK. July 7-8, 2016.

Dr. A. Yeo, GlaxoSmithKline, UK. July 7-8, 2016.

Dr. J. Betts, GlaxoSmithKline, UK. July 7-8, 2016.

Dr. Prakash, Mayo Clinic, Rochester, USA. December 1, 2016.

Dr. S. Kelada, University of North Carolina, USA. November 14-15, 2016.

Prof. Dr. K. Racké, University of Bonn, Germany. December 9, 2016.

Prof. Dr. A.J. Halayko, University of Manitoba, Canada. December 9, 2016.

Prof. Dr. A. Stewart, University of Melbourne, Australia. December 9, 2016.

Prof. Dr. J. Hourihane, University College Cork, Ireland. December 12, 2016.
Special Topics

Special topic 1

Retirement of Professors Postma, Dubois and Meurs from GRIAC in 2016

2016 marked a great change within GRIAC with three renowned GRIAC investigators retiring from their scientific positions, and new young GRIAC investigators joining the board. To celebrate the scientific careers of these investigators, retirement symposia were organized, which featured many local, national and international speakers.

On April 1st, Prof. Dr. Dirkje Postma retired at the UMCG. It is nearly impossible to sum up everything that Dirkje did for respiratory research, health care and education in Groningen, the Netherlands and internationally. Dirkje is one of the founding chairs of the Groningen Research Institute for Asthma and COPD (GRIAC). She managed to bring together a large number of respiratory researchers from different disciplines, with focus on clinical, basic and/or translational science and across all research areas of asthma and COPD.

Dirkje put asthma genetics on the map with her landmark paper in the New England Journal of Medicine in 1995. A group of researchers, led by Dirkje, described the linkage between bronchial hyperresponsiveness and genetic markers on chromosome 5q31-q33. Dirkje has contributed over 800 scientific papers to date, is/was a mentor of more than 85 PhD students and many more fellows, post-docs and PIs. She had a leading role in the foundation of the Netherlands Respiratory Society (NRS) and the national programme of lung research. She was a valued physician by her patients and a valued educator by all her trainees. In all respects and by objective standards, Dirkje is the most successful respiratory researcher in the Netherlands to date (quote Peter Sterk).

At the symposium several scientists that played key roles in her scientific career, took the stage to (often from a historical perspective) review the field to which they, mostly in collaboration with Dirkje and others, contributed. They provided personal perspectives on both science as well as working with Dirkje. Many, many beautiful moments were described. An impressive 380 people visited the symposium, from all across the country, and abroad.

The celebration of her work was reinforced by several prizes and recognitions during the ceremony:

- Dirkje received the Thomassen à Thuessinkpenning for her exceptional contributions to the University Medical Center Groningen.
- Dirkje was declared NVALT (Dutch Society for Physicians for lung diseases and tuberculosis) honorary member.

- The establishment of a “Dirkje Postma Talent award” by the Longfonds. A 200,000 € award will be awarded to a young researcher.

On April 15th, 2016 Prof. Dr. Ewoud Dubois, internist-allergologist at the University Medical Center Groningen, said farewell to the Beatrix Children's Hospital. To thank his great commitment to pediatric allergology, a symposium was organised to honor his farewell, entitled “the identity of pediatric allergy”. The speakers of this symposium addressed the developments in allergy research in recent years. In addition, attention was paid to the many studies and PhD students that Prof. Dubois has supervised. We also looked forward to the promising future of the pediatric allergology in Groningen. With many interested parties, and even a special contribution of young patients and a musical contribution, it certainly was a special day. Prof Dubois has been very important in the past 25 years for the pediatric allergology within the University Medical Center Groningen and will be succeeded by Dr. Aline Sprikkelman. He will still be involved in various scientific studies in the coming years.

In honor of the retirement of Prof. Dr. Herman Meurs, a farewell symposium was organized on December 9th, 2016 to celebrate the scientific achievements Herman has made during his career. The symposium featured many close scientific collaborators of Herman, who made it all the way from overseas to join Herman on this wonderful day: Prof. Alastair Stewart (Melbourne, Australia) with whom Herman did his sabbatical, Profs. Raymond Penn (Jefferson University) and Andrew Halayko (University of Manitoba), and Prof. Harm Maarsingh (Palm Beach Atlantic University), former PhD student of Herman.

Herman contributed several key findings to the scientific literature and was best known for his work on the mechanisms of airway hyperresponsiveness. Key findings include the role of muscarinic receptors and their cross-talk with beta receptors, and the role of nitric oxide metabolism and the enzyme arginase. The scientific lectures presented at the symposium were centered around these scientific themes, and were followed by an inspiring tour though Herman's life as scientist and mentor, presented by Herman himself.

On behalf of all members of GRIAC, we thank everyone for making these events enjoyable and memorable. Most importantly, we thank Professors Postma, Dubois and Meurs for all their valuable contributions they have made to GRIAC over the past years.
Excellent assessment of the research program of GRIAC: Opportunities ahead

Gerard Koppelman and Reinoud Gosens


In 2015, the research institutes of the University Medical Center Groningen and the University of Groningen were assessed using the Standard Evaluation Protocol 2015 – 2021, which is the protocol for Research Assessments in the Netherlands. In 2016, after a round of rebuttal, the final report was published. The three main topics for this research assessment were research quality, societal relevance and viability, and this was scored at 1 (World leading/excellent); 2 (very good); 3 (good); and 4 (unsatisfactory).

What were the conclusions of the review committee?

Research quality: Score : 1 out of 4
GRIAC is a large, mature, research group. The research undertaken by GRIAC is of very high quality and internationally competitive (potentially in the top 3% of respiratory research worldwide). The reasons for this include: the focus on expression of asthma and COPD in the natural setting across the life course, the establishment of disease cohorts, the infrastructure for deep phenotyping, the strong translational activities, cross fertilization of specialties within GRIAC, high performing and effective pathology laboratory, strong collaboration and networking and investments in disease stratification. GRIAC has a rich and diverse publication output of top quality. A proportion of the publications needs to be in specialized more practical journals that do not attract the greatest impact but yet are crucial for promoting translational research. It is important to note that GRIAC is ranked 3rd out of 300 research centers in Europe and number one in the Netherlands (source Expertscape). A strong input by patients into discussing research priorities and individual projects has been achieved by incorporating a Patients’ Forum into GRIAC.

Relevance to society: Score: 1 out of 4
GRIAC is a real beacon of success for its outreach activities. Indeed, this is among the most remarkable distinguishing features of this research grouping. The effectiveness of their ability to move research into practical settings becomes very clear when looking at indices of activity such as: leadership in professional societies, advisory boards, roles in local/national government; active promotion of their research to healthcare professionals, patients and the public at large; production of educational materials; strong interaction with companies, patent applications and setting up of a spin-off company. In all areas the team shows an impressive creativity and enthusiasm for developing policy and practice.

Viability: Score: 2 out of 4
The performance of the group on all indicators bodes well for its continued success and viability and there can be no doubt that their current activity will continue to produce high quality results. With a change in leadership there is an opportunity to create a visionary plan
for its future development to take full advantage of the technology revolution and the population and patient disease cohorts. The SWOT analysis gives some insight into issues that will need to be addressed in a forward looking strategy. First of all, the task of the new and ambitious leaders following in the footsteps of the retiring, a world class and charismatic leader, in April 2016 will be a challenge. Other challenges are: acquiring national and EU funding to enable multidisciplinary research (e.g. in consortia); pushing the bar higher in securing more grants to enable talented individuals to become leaders in their own right; framing some challenges in lung disease such as stratifying airways disease along causal pathways and develop therapeutics accordingly with GRIP; applying novel technology platforms such as imaging, biosensors, biomarker exploration; using multi-omics approaches in addition to genomics (systems approaches); developing relationships with the diagnostic devices and imaging industries e.g. to explore remote monitoring the exposome to explore gene/environmental interactions; considering interfacing with other disease areas, where appropriate (e.g. COPD/lung cancer and asthma/other allergic diseases).

**GRIACs response: Opportunities ahead**

GRIAC has welcomed the assessment of the committee. In board meetings, the GRIAC retreat as well as in a brainstorm session with principal and young investigators, we have discussed our challenges ahead based on this assessment.

We found strong support of our multidisciplinary, translational approach. We acknowledge that a proportion of the publications are necessarily in specialized, more practical journals that do not have the highest impact but are still crucial for disseminating translational research. We aim to continue our method of collaboration within GRIAC, which is aimed at stimulation multidisciplinary research.

Regarding our outreach activities, we would like to thank the patients from our patient advisory board for their advices and notice that GRIAC sets an example for patient participation in research. For the next years, we intend to generate a possibility for patients and the general public to communicate with researchers at GRIAC, by supporting and generating interactive webpages at the GRIAC website. In addition, we advise the possibility of webpages within the individual research institute’s domains containing general information for the public in lay Dutch.

We acknowledge that we can take our integrative genomic approach in translational science to a next level. This would require the establishment of GRIAC core facilities in new technology application and bioinformatics. The integration of GRIP within GRIAC allows for opportunities to direct our integrative genomics approach towards identification of drug targets and subsequent drug discovery. This topic was clearly prioritized by GRIAC members, and future investments in GRIAC translational multi-omics would include equipment (robotics for sample preparation of patient samples for genomics analysis, including epigenomics and single cell sequencing), IT-infrastructure and continuous bioinformatics staff support. We will also build on our world-leading position in implementing lung devices in COPD. Furthermore, to enhance our viability we strongly support new young scientists in obtaining personal grants (i.e. 3 grants in 2015) and started a postdoc mentoring system to help talented researchers become leaders in their fields.
Special topic 3

Patient participation to improve quality of research and health care within GRIAC

Machteld Hylkema

GRIAC highly values the contribution from patients to improve clinical study design and research grant proposals and help in choosing priority areas. Since a few years now, GRIAC has a board of 10-12 patients with asthma and COPD that meets 4 times per year. They review studies at an early stage of project development, through to hearing final reports of completed studies. The patients’ input helps with ensuring the research is relevant and the outcomes are clearly communicated to the end users. Last year, the following project updates and proposals were presented and discussed (table 1). Besides that, patients and researchers were trained in two separate meetings by dr. Truus Teunissen from the Lung Foundation Netherlands, on what criteria are being used by the Lung Foundation Netherlands for evaluation of patient participation in project proposals.

Table 1. Project reports and proposals in 2015/2016

<table>
<thead>
<tr>
<th>Project report</th>
<th>Researcher</th>
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<tbody>
<tr>
<td>A pro-inflammatory role for the Frizzled-8 receptor in chronic bronchitis.</td>
<td>Anita Spanjer, Molecular Pharmacology</td>
</tr>
<tr>
<td>A new proteogenomic approach to identify unique patient-specific protein</td>
<td>Corry-Anke Brandsma, Pathology</td>
</tr>
<tr>
<td>variants and causal pathways important in development of COPD.</td>
<td></td>
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<tr>
<td>Oxidative stress inhibits lung regeneration: mechanisms and new opportunties</td>
<td>Reinoud Gosens, Molecular Pharmacology</td>
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<td>for therapy</td>
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<td>The sweet taste of tolerance: a new vaccin against allergens for sustained</td>
<td>Martijn Nawijn, Medical Biology</td>
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<tr>
<td>suppression of allergic asthma.</td>
<td></td>
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<tr>
<td>The use of ICS/laba during complaints in mild asthma.</td>
<td>Jan Willem Kocks, General Practice</td>
</tr>
<tr>
<td>To stop unnecessary use of inhalation corticosteroids in COPD.</td>
<td>Jan Willem Kocks, General Practice</td>
</tr>
<tr>
<td>Epigenetic reprogramming of basal-like lung stem cells to treat chronic</td>
<td>Machteld Hylkema, Pathology</td>
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<td>mucus hypersecretion.</td>
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<tr>
<td>Nasal high-flow therapy for the treatment of COPD exacerbations.</td>
<td>Marieke Duiverman, Pulmonary Diseases and Home Mechanical Ventilation</td>
</tr>
<tr>
<td>The Puffin study for individual advise for children with asthma.</td>
<td>Gerard Koppelman, Pediatric Pulmonology and Pediatric Allergology</td>
</tr>
</tbody>
</table>
Special topic 4

The lung eQTL database and consortium: origin and history.

Wim Timens

It started all in 2007; Peter Paré and Yohan Bossé in interaction with Merck / Rosetta Inpharmatics developed an initiative for extensive GWAS and RNA-expression analysis of archival lung tissue that was extensively clinically characterized and annotated. In this early development phase I (WT) spent some time as visiting scientist in the iCapture Institute in Vancouver and this way was enabled to be involved in this initiative. This led to a research proposal to Merck Inc. in which the three academic participants (University of British Columbia, Laval University and UMCG) provided lung tissue with all extensive characteristics of about 1200 patients and MSD/ Rosetta performed all GWAS analysis and RNA expression analysis as well as all subsequent bio-informatics. This combined analysis led to a unique dataset including eQTL (expression quantitative trait loci): “genomic loci that contribute to variation in expression levels of mRNAs” . All raw data were made available to the participants. At the start the PI’s in this project were: Peter Paré (UBC), Yohan Bossé (Laval), and Wim Timens (UMCG) in collaboration with Gregory Opiteck, Jonathan Derry, David Nickle, and Christine Suver (Merck/Rosetta). Soon after the start Don Sin (UBC), Michel Laviolette (Laval) and Dirkje Postma (UMCG) joined as PI’s. After the formal project was finished, the collaboration continued as the “Lung eQTL consortium” with David Nickle and Ke Hao as Merck collaborators. After retirement of Michel Laviolette and Dirkje Postma, Philippe Joubert and Maarten van den Berge took their places.

The Lung eQTL database has proven an enormous asset for further research in the three University environments but also in numerous collaborations. These have led to date to more than 40 high level publications, up to 20 in progress and many more to be expected to rise from this initiative.

Key publication:

Special topic 5

Opening of Pediatric Allergy & Asthma Center in the UMCG

Aline Sprikkelman

The number of children with one or more allergic diseases continues to increase*. To generate the best, highly specialized care for these children, the UMCG has opened the Pediatric Allergy & Asthma Center. In the center, doctors, nurses and researchers from different departments will work together in the diagnosis and treatment of children with (suspected) allergic diseases and asthma. The center is part of the Beatrix Children's Hospital of the University Medical Center Groningen and was officially opened with a symposium on September 23rd, 2016.

The Pediatric Allergy & Asthma Center offers expertise in the field of diagnosis and treatment of allergic diseases of the respiratory tract, the skin and the gastrointestinal tract as well as food or drug allergy or allergy to insect venom. The focus is on complex care for children who have severe several allergies at once, or children who develop a severe allergic reaction to drugs used for the treatment of cancer or arthritis. Such an allergic reaction can be expressed by a reaction of the skin, eyes or respiratory tract, but also by the cardiovascular tract or gastrointestinal tract.

Where, for example hay fever will trigger irritated eyes and problems with the upper respiratory tract, a food or insect venom allergy can give a very serious and life-threatening reaction, such as anaphylactic shock. In such a shock, the airways can swell dangerously, blood pressure can drop severely and organ failure may occur. In that case, direct administration of adrenaline is important to stop the reaction. Without treatment, a severe allergic reaction be fatal. But there are also less severe acute reactions. An allergic reaction to a cancer treatment, for which no alternative is available, can be life-threatening as well.

Care for these complex patients will be designed in close cooperation and coordination with the health care providers and hospitals in the region. In addition to patient care the center offers tailored education and research activities. The center brings together nurses, doctors and researchers from different departments, such as (pediatric) allergy, (pediatric) pulmonology, dermatology and ENT specialists.

* It is expected that 50% of people in the European Union has an allergic condition in 2025. Of these, some 100 million people have allergic rhinitis, 70 million people have asthma, and 17 million people have a food allergy. Of these, 3.5 million children will suffer from food allergy.
Chronic obstructive pulmonary disease (COPD) is the third leading cause of death in the world and is characterized by impaired pulmonary function and progressive airway obstruction.\(^1,2\) There are multiple risk factors for developing COPD (Figure 1), among others, exposure to cigarette smoke (passive or \textit{in utero}), occupational exposure to dusts and chemicals (such as vapors, gases, dusts, fumes (VGDF), and pesticides); indoor and outdoor air pollution; chronic asthma or bronchitis; history of lower respiratory-tract infections and/or pulmonary tuberculosis; poor nutrition and poor socioeconomic status.\(^1-3\) Cigarette smoke exposure is considered the most important risk factor and about 13% of the smokers develop COPD.\(^4,5\) On the other hand, there is a considerable proportion of COPD patients (25-45\%) that do not have smoking as underlying cause of their disease.\(^14\) In developing countries this proportion is higher compared to developed countries, but even in the Netherlands approximately 16\% of the COPD patients are never-smokers.\(^6\)

Figure 1: Risk factors for COPD (Adapted from Global Initiative for Chronic Obstructive Lung Disease (GOLD): \textit{Global Strategy for the Diagnosis, Management, and Prevention of COPD}(\textit{7}))

COPD is usually the result of an interplay between poor lung development and lung growth, (long-term) exposure to noxious particles or gases and, (epi-) genetic susceptibility.\(^8\) The diagnosis of COPD is largely based on the presence of airway obstruction, which is commonly diagnosed based on the spirometry measurements of forced expiratory volume in one second (FEV\(_1\)) and its ratio to forced vital capacity (FEV\(_1\)/FVC).\(^4\) Unfortunately, relatively little is known about underlying mechanisms of COPD in never-smokers, since usually this group is excluded from analysis or there is no special focus on this group.\(^9\) Common
genetic variants underlying lung function (FEV₁, FVC and FEV₁/FVC) or COPD have been identified by several genome-wide association (GWA) studies.(10-14) Among others, the Nicotinic Cholinergic Receptor (CHRNA3/5), Family With Sequence Similarity 13 (FAM13A) and hedgehog-interacting protein (HHIP) were reported. However, these studies were performed in only ever-smokers or population based studies including both ever- and never-smokers.

We have performed several GWA studies in specifically never-smokers using data from three Dutch population based cohort studies, i.e. the LifeLines study (n=5,070), the Vlagtwedde-Vlaardingen study (n=432) and the Rotterdam study (n=1,126). We assessed the association between single nucleotide polymorphisms (SNPs) and lung function (FEV₁, FEV₁/FVC and FEF₂₅₋₇₅) or airway obstruction. The information from these studies may ultimately contribute to the understanding of cellular and molecular pathways involved in lung function impairment and the development of COPD.

First, we were able to replicated associations between FEV₁/FVC and two SNPs annotated to the well-known COPD genes HHIP and FAM13A in never-smokers.(15) The two SNPs were also associated with gene expression levels of HHIP and FAM13A in lung tissue. In addition, the genetic risk score analysis showed that the combined effect estimate for the two independent SNPs accounted for a 2.4% lower FEV₁/FVC level, a credible clinically relevant effect (Figure 2).

![Figure 2. Genetic risk score (GRS) analysis of the risk alleles in FAM13A and HHIP on FEV₁/FVC level in the identification cohort. Genetic risk scores where created by adding up the number of alleles (risk alleles) for both HHIP and FAM13A SNPs associated with a lower FEV₁/FVC level. A value of 0 means no risk alleles for both SNPs, and a value of 4 means a subjects is carrying all four risk alleles of both SNPs. The mean FEV₁/FVC levels and 95% CI are given for each GRS based on a median age and a mean height.](image)

Of interest, a substantial proportion of our study population, i.e. 6%, was carrying all four risk alleles. HHIP is known to play an important role in fetal lung branching development and silencing of HHIP was shown to lead to differential expression of about 300 genes enriched for cell growth, lung extracellular matrix and genes associated with COPD.(16) FAM13A may play a role in emphysema development and loss of FAM13A resulted in increased cell proliferation and activation of b-catenin signaling.(17) We concluded that the genes HHIP and FAM13A confer a risk for airway obstruction in general that is not driven exclusively by
cigarette smoking. Moreover, these two genes might have an impact on the prevalence of COPD worldwide, especially in countries where COPD due to smoking is less prevalent.

Next, we performed a GWA study on small airways obstruction using the spirometric measurement of forced expiratory flow at 25%-75% of forced vital capacity (FEF25–75). The risk allele of the same SNP annotated to HHIP was genome-wide associated with a 98 mL/s lower FEF25–75 level. In the sensitivity analysis excluding subjects with predominantly large airways obstruction, a SNP annotated to Mitochondrial Trans-2-Enoyl-CoA Reductase (MECR) was genome-wide significant, and in addition associated with gene expression levels of MECR and Erythrocyte Membrane Protein Band 4.1 (EPB41). MECR is involved in mitochondrial fatty acid synthesis and over-expression of MECR increases Peroxisome proliferator-activated receptor alpha (PPARα) activity, which might play a role in emphysema progression. This study therefore provided novel insights into the role of the well-known COPD gene HHIP in both the small and large airways and showed supportive evidence for the role of the novel gene MECR in specifically small airways obstruction.

The last GWA study was on airway obstruction, which can be defined as either FEV1/FVC<70% or FEV1/FVC<lower limit of normal (LLN). There is a considerable controversy about which definition should be used in research and clinical practice, since both may lead to misclassifications. Only few genetic regions were overlapping between previous GWA studies, due to the usage of different airway obstruction definitions and populations. We therefore aimed to assess the genetic overlap between the two definitions of airway obstruction in the same never-smoking individuals of our Lifelines cohort. We expected a reasonable overlap in associated SNPs between the two definitions, since based on either definition 96% of the never-smokers were classified into the same group (either having or not having obstruction). Surprisingly, only 4% of the SNPs were overlapping between the two definitions at p<10^{-4} and 26% at p<0.05 (Figure 3).

![Figure 3. Venn diagrams showing the overlap between the two definitions of airway obstruction for the number of subjects classified as having airway obstruction and the number of identified SNPs with p<10^{-4}.](image)

This implies that the definition of airway obstruction and the strategy (discovery-replication design) have a substantial influence on the GWAS results, and thus on which variants are
selected for replication. Finally, our results also suggest that genes $FABP7$ and $NFCY(-AS1)$ could play a role in the pathogenesis of airway obstruction in never-smokers.

In conclusion, we identified several SNPs associated with lung function or airway obstruction in specifically never-smokers. The genes $HHIP$, $FAM13A$, $FABP7$ and $NFCY$ are susceptibility genes for the development of airway obstruction and showed to have an effect regardless of exposure to cigarette smoking. $HHIP$ is involved in the development of both small and large airways and our data suggests that $MECR$ plays a role in specifically small airways obstruction. In addition, the definition of airway obstruction had a substantial influence on which genes were associated with airway obstruction and therefore it is important for future studies to use the same definition or to focus more on specific COPD subtypes.

References


Special topic 7

Granted projects in 2016

De-implementation of unnecessary Inhaled Corticosteroids use in COPD - Dr. Jan Willem Kocks (UMCG), Dr. Job van Boven (UMCG), Dr. Tjard Schermer (Radboud MC)

Granted by Citrien Fund, sponsored by ZonMW via the 'Nederlandse Federatie van Universitair Medische Centra' (NFU).

Both asthma and COPD are prevalent chronic obstructive lung diseases that cause, among other things: cough and shortness of breath. Inhaled Corticosteroids (ICS) are indicated for the treatment of asthma but only to a limited extent in the treatment of COPD. Only for those COPD patients that experience 2 or more exacerbations per year or are treated in hospital for at least 1 exacerbation and for those COPD patients that also suffer from asthma is a treatment with ICS indicated.

Even though limited indication for ICS in COPD has been incorporated in Dutch treatment recommendations for general practitioners for several years, no reduction in ICS prescriptions in patient groups that are not indicated for use has been seen.

In addition to increasing health care costs the use of ICS is also associated with side-effects. Both local (e.g. oral thrush, hoarseness and dysphonia) and systemic (e.g. increases the chance of pneumonia, cataract and osteoporosis). Stressing the need to restrict the use to only the indicated patients.

This study's primary aim is reducing ICS prescriptions by educating both GP's and pharmacists on the optimal use of ICS in COPD. GP and pharmacists regularly organize pharmacotherapy meetings during which new developments are discussed (FarmacoTherapeutisch Overleg, FTO). The project will use these meetings to present the newest developments in the field of ICS use in COPD patients. At the end of the meeting the GP’s receive an A4 paper sheet with decision tree for the correct indication per individual patient. Patients are selected from pharmacy dispensing records and patients that received oral steroid courses are excluded.

GP’s are requested to study the list and proceed with discontinuation in those patients that qualify. Additionally, education is given via publications in the professional and public media. The study is considered successful if 10% of this group has stopped using ICS 12 months after the intervention.

This study's features several secondary aims, among which:

- Identifying barriers and facilitators in the process of starting and stopping with ICS. Both from the perspective of the professional as well as from the perspective of the patient. This is achieved via focus groups.
- Assess medical costs before and after the intervention.
- Assess exacerbation rates before and after the intervention.
**Understanding the genetic and epigenetic drivers of cigarette smoke susceptibility in COPD** - Dr. Alen Faiz (UMCG)

**From genetic profile to precision medicine in children with persistent asthma.**

*The PUFFIN trial (Pharmacogenetics Use For Further treatment Improvement in children)*. - Prof. dr. A.H. Maitland- van der Zee (AMC), PI, Prof dr GH Koppelman (UMCG), co-PI, , Dr M. W. Pijnenburg (Erasmus MC), co-PI.

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Chronic obstructive pulmonary disease (COPD) is a highly prevalent and debilitating respiratory disease, characterized by chronic inflammation leading to accelerated lung function decline. The major risk factor for COPD is inhalation of noxious particles and gases, particularly cigarette smoking in the developed world. Despite this fact, only a subset of 20-30% of smokers are susceptible and will ultimately develop COPD. This suggests that genetic factors also play an important role in the development of this disease. Interestingly, specifically in COPD, the inflammation associated with smoke exposure remains even after subjects have quit smoking. It is currently postulated that this may be caused by persistent epigenetic changes, e.g. DNA-methylation. I hypothesise that smoking susceptibility is determined by genetic variations affecting gene-expression in bronchial epithelium, the first line of defence against the inhaled toxins. Furthermore, I put forward that prolonged smoking in combination with genetic variations in susceptible individuals leads to DNA-methylation that persists after smoking cessation, leading to persistent inflammation.

I will assess the influence of genetic polymorphisms on the transcriptional response of the bronchial epithelium to smoke exposure. To this end, smoking-induced expression Quantitative Trait Loci (eQTLs) will be investigated in a unique cohort of subjects with and without COPD before and after smoking. Furthermore, I will investigate whether changes in DNA-methylation after smoking cessation are different in patients with COPD compared to asymptomatic smokers. Finally, I will validate these newly identified genetic variants and DNA-methylation sites in-vitro using cutting edge genome editing technology (CRISPR–Cas9). This study will allow early identification of susceptible subjects and provide new and important insights into the persistent epigenetic changes caused by smoking with the ultimate aim to provide new treatment targets for early intervention.

**From genetic profile to precision medicine in children with persistent asthma.**

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increased down regulation of the B2AR. Therefore, in these children LABA should be avoided and alternative step up treatment should be considered.

In this nationwide, multi-centre Randomized Clinical Trial (RCT) we aim to assess the value of a precision medicine (PM) approach: genotype-guided treatment in children with uncontrolled asthma despite ICS compared to non-genotype guided treatment. Participants will be randomized to ‘the control arm’ (n=150) or ‘precision medicine-guided treatment’ (n=150). In the precision medicine arm, children homozygous (estimated n=24) or heterozygous for the variant ADRB2 (estimated n= 75) will be treated with a double dose ICS, while children homozygous for the wild types will be treated with LABA. Children will be followed for 6 months. In the control arm, children will be randomized to LABA or double dosage of ICS. Primary outcome will be longitudinal changes in asthma control (Asthma Control Test scores) in the first three months of the trial. Cost-utility of the intervention (euro/QALY) will be assessed. (figure)

We hypothesize that genotype-guided treatment leads to better and faster symptom control in children with uncontrolled asthma despite ICS use, and decreases asthma related costs.

Full information on background, rationale and description of the trial was recently published in Vijverberg et al., The need for precision medicine clinical trials in childhood asthma: rationale and design of the PUFFIN trial. Pharmacogenomics. 2017 Mar;18(4):393-401. doi: 10.2217/pgs-2016-0174. Epub 2017 Feb 22.

**Children in the study will be randomized to precision medicine-guided treatment based on ADRB2 genotyping or usual care (control arm). In the control arm children will be randomized to add on treatment with a long-acting beta2-agonist (LABA) or doubling of the dosage of inhaled corticosteroids (ICS), the two most common add options in the Netherlands.**
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## International collaboration 2016
(As far as related to joint projects and publications in 2016)

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<td>Prof W. Windisch</td>
<td>Lungenklinik Merheim, Kliniken der Stadt Köln, Universität Witten/Herdecke</td>
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<td>Prof. G. Yimer</td>
<td>Addis Ababa University</td>
<td>Addis Ababa, Ethiopia</td>
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<tr>
<td>05-01-2016</td>
<td>L. Hesse Pathology &amp; Medical Biology, UMCG</td>
<td>Successful immunotherapy in a mouse model of allergic asthma</td>
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<td>19-01-2016</td>
<td>Prof. M. Idzko University of Freiburg Germany</td>
<td>Purinergic signalling: from bench to bed side and back again</td>
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<tr>
<td>02-02-2016</td>
<td>Dr. F. Greven GGD Groningen</td>
<td>Air pollution during New Year's fireworks and daily mortality in the Netherlands</td>
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<tr>
<td>16-02-2016</td>
<td>Dr. J. van Boven, E.I. Metting, M. Román Rodríguez</td>
<td>Inhaler technique, the past, the present and the future</td>
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<tr>
<td>01-03-2016</td>
<td>A. Spanjer Molecular Pharmacology UMCG</td>
<td>The role of WNT receptor Frizzled-8 in inflammation and remodeling in airway disease</td>
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<tr>
<td>15-03-2016</td>
<td>Dr. C. Xu Pulmonology &amp; Genetics UMCG</td>
<td>DNA methylation changes in childhood - relevance for asthma</td>
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<tr>
<td>05-04-2016</td>
<td>Dr. C.A. Brandsma Pathology UMCG</td>
<td>Genetic regulation of gene expression changes in COPD</td>
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<tr>
<td>10-05-2016</td>
<td>Prof. Dr. D. Ebo University of Antwerpen Belgium</td>
<td>Meer weten over allergiediagnostiek? Cannabis: een potent allergeen!</td>
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<tr>
<td>21-06-2016</td>
<td>B. Han Molecular Pharmacology UMCG</td>
<td>Novel strategies in the treatment of COPD: from oxidative stress to cyclic nucleotide compartments</td>
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<tr>
<td>20-09-2016</td>
<td>H. Tasena Pathology &amp; Medical Biology, UMCG</td>
<td>MicroRNA signature of Chronic Mucus Hypersecretion in COPD</td>
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<tr>
<td>04-10-2016</td>
<td>Dr. I. Sayers University of Nottingham UK</td>
<td>Translating lung function genome-wide association studies: New insights for lung biology and treatment opportunities</td>
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<tr>
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<tr>
<td>18-10-2016</td>
<td>Dr. A. Faiz</td>
<td>Functional validation of findings in GWAS studies</td>
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<td>Pulmonology, Pathology &amp; Medical Biology UMCG</td>
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<td>01-11-2016</td>
<td>E.I. Metting</td>
<td>Social implications of asthma and COPD</td>
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<td>15-11-2016</td>
<td>Dr. S.N.P. Kelada</td>
<td>Utilizing mouse genetic diversity to identify novel pathways in allergic airway disease</td>
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<td>University of North Carolina USA</td>
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<tr>
<td>06-12-2016</td>
<td>Dr. H. Baarsma</td>
<td>Non-canonical WNT-5A repairs endogenous lung repair in COPD</td>
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<tr>
<td>20-12-2016</td>
<td>J. Ong</td>
<td>Identification of transforming growth factor-beta regulated microRNAs and the microRNA-targetome in primary lung fibroblasts</td>
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<td>Pathology &amp; Medical Biology UMCG</td>
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<tr>
<td>05-01-2016</td>
<td>Maartje Nieuwenhuis Pulmonology</td>
<td>Genetics of the severity of bronchial hyperreponsiveness in asthma</td>
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<tr>
<td>12-01-2016</td>
<td>Tristan de Jong ERIBA</td>
<td>Transcriptome changes in model organisms</td>
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<tr>
<td>19-01-2016</td>
<td>Navessa Padma Tania Molecular Pharmacology</td>
<td>Endothelial Follistatin-like 1 regulates postnatal development of the pulmonary vasculature by modulating BMP/Smad signaling</td>
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<td>02-02-2016</td>
<td>Wilma Biek-vd Velde Pulmonology</td>
<td>The UMCG research toolbox and research register</td>
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<tr>
<td>09-02-2016</td>
<td>Frank Klont Analytical Biochemistry</td>
<td>Towards validation of promising protein COPD biomarker candidates</td>
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<td>16-02-2016</td>
<td>All</td>
<td>Discussion motivation letters ATS trainee scholarships</td>
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<tr>
<td>23-02-2016</td>
<td>Hataitip Tasena Pathology and Medical Biology</td>
<td>Identification of microRNAs that potentially regulate chronic mucus hypersecretion in COPD</td>
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<td>08-03-2016</td>
<td>Diana van der Plaat Epidemiology</td>
<td>Role of the gene HHIP in the large and small airways</td>
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<td>15-03-2016</td>
<td>Kai Imkamp Pulmonology</td>
<td>Being SMART in COPD lung attacks and more</td>
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<tr>
<td>22-03-2016</td>
<td>Eline van Dijk Molecular Pharmacology</td>
<td>Ex vivo elastase treatment disrupts parenchymal structure and enhances airway narrowing in precision cut lung slices</td>
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<tr>
<td>29-03-2016</td>
<td>Marlies Ketelaar Pediatric Pulmonology</td>
<td>The role of IL-33/IL1RL1 pathway in human asthma: a possible link between bench and bed?</td>
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<tr>
<td>05-04-2016</td>
<td>Jennie Ong Pathology and Medical Biology</td>
<td>The effect of TGF-β on the miRNA profile and targetome in primary lung fibroblasts</td>
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<tr>
<td>12-04-2016</td>
<td>Esther Metting General Practice</td>
<td>Observational study of the effect of ICS LABA combination in patients with steroid naïve asthma (GINA II)</td>
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<tr>
<td>29-04-2016</td>
<td>Laura Florez Sampredo Pharmacokinetics, Toxicology and Targeting</td>
<td>Elucidating the role of MIF in pulmonary fibrosis</td>
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<td>03-05-2016</td>
<td>All</td>
<td>ATS posters</td>
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<td>10-05-2016</td>
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<tr>
<td>24-05-2016</td>
<td>Corneel Vermeulen</td>
<td>DNA methylation profiles of bronchial biopsies in asthma remission</td>
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<td>31-05-2016</td>
<td>Dennis Kruk Pathology and Medical Biology</td>
<td>Mesenchymal stem cells in emphysema, finding the right niche for alveolar repair</td>
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<td>07-06-2016</td>
<td>Laura Hesse Pathology and Medical Biology</td>
<td>Successful immunotherapy in a mouse model of allergic asthma</td>
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<td>Maaik de Vries Epidemiology</td>
<td>Practice session on Veni interviewing</td>
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<td>14-06-2016</td>
<td>Alen Faiz Pathology and Medical Biology, Pulmonology</td>
<td>Genetics and epigenetics of corticosteroids</td>
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<td>21-06-2016</td>
<td>All</td>
<td>Evaluation and brainstorm of GRIAC research meetings</td>
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<tr>
<td>28-06-2016</td>
<td>Ana Julia de Faria Coimbra Lichtenfels Epidemiology</td>
<td>Air pollution and DNA methylation: association with lung function and COPD</td>
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<td>30-08-2016</td>
<td>All</td>
<td>ERS posters and oral presentations</td>
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<tr>
<td>13-09-2016</td>
<td>Reinoud Gosens/Gerard Koppelman Molecular Pharmacology/ Pediatric Pulmonology</td>
<td>Introduction to GRIAC</td>
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<td>20-09-2016</td>
<td>Jennie Ong Pathology and Medical Biology</td>
<td>Identification of TGF-β-regulated miRNAs and the miRNA-targetome in primary lung fibroblasts</td>
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<tr>
<td>27-09-2016</td>
<td>Claire Cox Pulmonology</td>
<td>Extra fine particle ICS compared to standard-sized particle ICS in smokers and ex-smokers with asthma</td>
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<tr>
<td>04-10-2016</td>
<td>Frank Klont Analytical Biochemistry</td>
<td>Who do we want/need an LC-MS assay for sRAGE?</td>
</tr>
<tr>
<td>11-10-2016</td>
<td>Hans Burgerhof Epidemiology</td>
<td>Value of the p-value</td>
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<tr>
<td>Date</td>
<td>Speaker</td>
<td>Title</td>
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<tr>
<td>18-10-2016</td>
<td>Eline van Dijk</td>
<td>Parenchymal disruption by ex vivo elastase treatment enhances airway narrowing in mice precision cut lung slices</td>
</tr>
<tr>
<td>25-10-2016</td>
<td>All</td>
<td>ATS abstracts</td>
</tr>
<tr>
<td>01-11-2016</td>
<td>Vera Otermann/Hester Hoving</td>
<td>Improving inhaler technique in asthma and COPD patients by combining the knowledge and experience of patients, scientists and health care professionals</td>
</tr>
<tr>
<td>15-11-2016</td>
<td>Navessa Padma Tania</td>
<td>Developmental and pathological roles of Follistatin-like 1 in the lung</td>
</tr>
<tr>
<td>22-11-2016</td>
<td>Hans Burgerhof</td>
<td>Lab statistics</td>
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<tr>
<td>29-11-2016</td>
<td>Victor Guryev ERIBA</td>
<td>Identification of smoke resistance markers in humans through RNA-sequencing data in various old world monkeys</td>
</tr>
<tr>
<td>05-12-2016</td>
<td>Nicole Dijk Pediatric Pulmonology</td>
<td>(Pharmaco)genetic effects of <em>IL1RL1</em> SNPs in ICS users</td>
</tr>
<tr>
<td>13-12-2016</td>
<td>Hataitip Tasena Pathology and Medical Biology</td>
<td>MicroRNAs: Regulators of chronic mucus hypersecretion in COPD?</td>
</tr>
<tr>
<td>20-12-2016</td>
<td>Laura Florez-Sampredo Pharmacokinetics, Toxicology and Targeting</td>
<td>Elucidating the role of the macrophage migration inhibitory factor in PF and COPD</td>
</tr>
<tr>
<td>Date</td>
<td>Initiator</td>
<td>Subject</td>
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<tr>
<td>26-01-2016</td>
<td>Prof. D.S. Postma &amp; Prof. H. Meurs, Pulmonology &amp; Molecular Pharmacology</td>
<td>How to achieve that GRIAC members receive more awards and prizes</td>
</tr>
<tr>
<td>23-02-2016</td>
<td>Dr. J.K. Burgess Pathology &amp; Medical Biology, UMCG</td>
<td>Regeneration of lung extracellular matrix microenvironment: a novel way forward for lung diseases?</td>
</tr>
<tr>
<td>26-04-2016</td>
<td>Dr. A.J.P. van den Brekel, Central Medical Library, UMCG</td>
<td>How to use PURE to register your scientific output</td>
</tr>
<tr>
<td>28-06-2016</td>
<td>Dr. M. van den Berge Pulmonology UMCG</td>
<td>Measurement of particles in exhaled air, a new small airways measurement. How can we use it for our research?</td>
</tr>
<tr>
<td>27-09-2016</td>
<td>I.M. Broeders Medical sciences RUG/UMCG</td>
<td>Access to LifeLines data. How can we use it for our research?</td>
</tr>
<tr>
<td>25-10-2016</td>
<td>Dr. D.O. Warmerdam Aging Biology UMCG</td>
<td>The Crispr Cas 9 technique. What is it and how can we use it for our research?</td>
</tr>
<tr>
<td>21-11-2016</td>
<td>Prof. G.H. Koppelman &amp; Prof. R. Gosens, Pediatric Pulmonology &amp; Molecular Pharmacology UMCG</td>
<td>GRIAC vision 2017 and beyond</td>
</tr>
</tbody>
</table>
Research projects 2016

Aimmune Therapeutics Inc., USA. The Palisade Study: Peanut Allergy Oral Immunotherapy Study of AR101 for Desensitization in Children and Adults. 2015–2016. Prof.dr.A.E.J.Dubois, Dr. J.N.G. Oude Elberink. MD/PhD-student: M.E. Pettersson

AstraZeneca; CARAT; identifying cutoff values. 2014-2017. Prof.dr. T. van der Molen, Dr. BMJ Flokstra – de Blok, Dr. C. de Jong.

AstraZeneca: risk to develop pneumonia in COPD: Comparing the effects of fluticasone propionate and budesonide on epithelial defense. 2015-2016. Prof. dr. I. Heijink, Prof. D.S. Postma, Dr. M. van den Berge. Technician: M.R. Jonker.

AstraZeneca/Mundipharma/Boehringer Ingelheim: Inhaler Research Workgroup (IRW) study. 2016-2019. Prof. dr. T. van der Molen, Dr. J.W.H. Kocks, E.I. Metting, Dr. S. Schokker, Dr. I Tsiligianni, PhD student: M. Román-Rodríguez


Boehringer Ingelheim International GmbH: The role of TRPA1 in neurogenic inflammation and airway hyperreactivity in asthma. 2016-2017. Dr. L.E.M. Kistemaker, Prof. dr. R. Gosens, Dr. M. van den Berge. Technician: S. Nijboer-Brinksma.


Brazil Science Without Borders: Genes and environments underlying COPD: genetic susceptibility to air pollution. 2015-2016. Prof.dr. H.M. Boezen, Prof.dr. T. Mauad (Sao Paolo, Brasil). Postdoc: Dr. A.J. de Faria Coimbra Lichtenfels.

CAPES/NUFFIC (Edital 68/2013): Activation of nuclear factor (erythroid-derived 2)-like 2 (Nrf2) & antioxidant response element (ARE) as therapeutic target for tissue repair in chronic degenerative lung disease. 2013-2017. Prof.dr. S. dos Santos; Prof.dr. L.C. de Moraes Sobrino Porto; Prof.dr. M. Schmidt

Chiesi: The role of small airways in asthma. Development of the SADT questionnaire. 2011-2016. Prof.dr. T. van der Molen, Prof.dr. D.S. Postma, Dr. M. van den Berge.


European Union/COST action (European Cooperation in the field of Scientific and Technical Research): Developmental Origins of Chronic Lung Disease. 2012-2016. Dr. M.N. Hylkema, Prof.dr. R. Gosens, Prof.dr. D.S. Postma


European Union (Horizon 2020): Advancing Care Coordination and TeleHealth Deployment (ACT@Scale II). 2016-2018. Prof.dr. T. van der Molen, Dr. J.W.H. Kocks, E.I. Metting, Dr. M.M.H. Lahr.


Genentech: Molecular Phenotyping of COPD Patients by Inhaled Corticosteroids (ICS) Response. 2015-2017. Dr. C.A. Brandsma, Prof.dr. W.Timens, Prof.dr. D.S. Postma, Dr. M. van den Berge.

GlaxoSmithKline: A better understanding of asthma remission: An integrative genomic approach for biomarker development. 2014-2017. Dr. M. van den Berge, Dr. N.H.T. ten Hacken, Prof.dr. W. Timens, Prof.dr. I.H. Heijink, Dr. C. Xu, Prof.dr. G.H. Koppelman, Dr. J.M. Vonk, Prof.dr. D.S. Postma. Post-doc: Dr. C. Vermeulen.

GlaxoSmithKline: Single cell sequencing of CD4+ lymphocytes to better understand the molecular mechanisms leading to asthma and its remission. 2015-2017. Dr. M.C. Nawijn, Prof.dr. D.S. Postma, Prof.dr. G.H. Koppelman, Dr. J.M. Vonk, Prof.dr. W. Timens, Prof.dr. I.H. Heijink, Dr. M. van den Berge.

GlaxoSmithKline: GOLD D Patients in Primary Care: A Group Whose Clinical Outcomes Can Easily Be Improved. 2015-2018. Prof.dr. T van der Molen, Dr. J.W.H. Kocks, Dr. C. de Jong.


Groningen Graduate School of Science (Ubbo Emmius PhD-position): Key role of A-kinase anchoring proteins in the pathophysiology of asthma. 2011-2016. Prof.dr. M. Schmidt, Dr. H. Maarsingh. PhD-student: B. Han.

Groningen Research Institute for Pharmacy (MPDI fellowship): Role of MIF in pulmonary fibrosis. 2015-2019. Prof.dr. B.N. Melgert, Prof.dr. G.J. Poelarends, PhD student: L. Florez-Sampedro

Groningen Research Institute for Pharmacy (Erik Frijlink Patents): Role of MIF in pulmonary fibrosis. 2016-2020. Prof.dr. B.N. Melgert, Prof.dr. G.J. Poelarends, Prof Dr P. Olinga. PhD student: S.S. Song


GSMS/University of Southampton: Functional characterisation of PCDH1, a novel gene for asthma and bronchial hyperresponsiveness. 2011-2017. Prof.dr. G.H. Koppelman, Prof.dr. J. Holloway, Dr. M.C. Nawijn, Dr. B.M. Willemse. PhD student: G. Faura Tellez

GSMS/University of Marburg, Germany. The role of mitochondrial SK channels in oxidative stress. 2014-2018. Dr. A.M. Dolga, Prof. dr. C. Culmsee. PhD student: B. Honrath

GSMS/Shantou University Medical College, China (Abel Tasman bursaal). Effect of toxic exposures during pregnancy on fetal immune and lung development. 2012-2016. Dr. M.N. Hylkema, Prof.dr. X. Huo. PhD student: J.J. Cao

GSMS/Shantou University Medical College. Genes, environment and respiratory health 2011-2016. Prof.dr. H. M. Boezen. PhD Student: X. Zeng


GSMS/UBC: Dysfunctional crosstalk between epithelial cells and fibroblasts contributes to abnormal tissue repair and remodeling processes in COPD. 2013-2017. Dr. C.A. Brandsma, Dr. I.H. Heijink, Prof.dr. W. Timens, Prof.dr. D.S. Postma, Dr. T.L. Hackett, Dr. S. Wadsworth. PhD student: E. Osei


GSMS/University of Newcastle (Australia): The role of β-catenin in the development of the asthmatic epithelial phenotype. 2016-2020. Prof. dr. I.H. Heijink, Dr. M.C. Nawijn, Prof. dr. D. Knight. PhD-student: V. Kuchibhotla.
GSMS/University of Sydney: Lung ageing and tissue remodeling in COPD. 2016-2020. Dr. C.A. Brandsma, Prof. dr. W. Timens, Prof. dr. I.H. Heijink, Dr. M. de Vries, Dr. M. van den Berge, Dr. P. Horvatovich, Dr. V. Guryev, Dr. B. Oliver. PhD.student: R. Woldhuis.

Holaira, USA: A Sequential Two Phase Multicenter, Randomized Study to Optimize Dose Selection and Evaluate Safety After Treatment with the Holaira™ Lung Denervation System in Patients with Moderate to Severe COPD, 2014-2018. The AIRFLOW-1 trial. Dr DJ Slebos, Dr J Hartman, K. Klooster.

International Primary Care Respiratory Group. UNLOCK: Uncovering and Noting Long-term Outcomes in COPD to enhance Knowledge. 2010-2018. Dr. N. Chavannes, Dr. I. Tsiligianni, Prof.dr. D. Price, Prof.dr. T. van der Molen.


IPCRG: Fresh Air Uganda: prevalence and burden of COPD in a rural area of sub-Saharan Africa. 2010-2017. Prof.dr. T. van der Molen, Dr. N.H. Chavannes, Dr. C. de Jong. PhD student: F.A. van Gemert

IPCRG: Fresh Air: Biomass fuel induced COPD, prevalence and pathophysiology. 2010-2018. Prof.dr. T. van der Molen, Dr. C. de Jong. PhD student: B.J. Kirenga


Lung Foundation Netherlands 3.2.09.055: Protocadherin-1 expression in airway epithelium: Investigations into a novel cause of bronchial hyperresponsiveness and asthma. 2009-2017. Prof.dr. G.H. Koppelman, Dr. M.C. Nawijn, Prof.dr. D.S. Postma.


Lung Foundation Netherlands 3.2.12.044: The functional relevance of microRNAs in COPD; elucidating their role in regulating pulmonary fibroblast function in COPD development. 2012-2017. Dr. C.A. Brandsma, Prof.dr. W. Timens, Prof.dr. DS Postma, Prof.dr. A. van de Berg, Dr. J. Kluiver. PhD-student: J. Ong


Lung Foundation Netherlands 3.2.12.079: Laminin α4 and α5 as regulators of airway inflammation and remodelling in allergic asthma. 2013-2017. Dr. B.G.J. Dekkers, Prof.dr. L.M. Sorokin, Prof.dr. H. Meurs. Post-doc: Dr. P. Prabhala


Lung Foundation Netherlands 4.1.13.007. Genes and exposures underlying COPD onset. 2013 – 2016. Consortium grant in collaboration with Erasmus Medical Center. Prof.dr. H.M. Boezen, Prof.dr. C.M. van Duijn, Dr. C.C. van Diemen, Prof.dr. D.S. Postma. Postdoc: Dr. K. de Jong. PhD students: D. van der Plaat, I. Nedeljković

Lung Foundation Netherlands 5.1.14.020 Identifying causal mechanisms of the inception of asthma through a novel experimental model for the interaction on the PCDH1 gene and environment. 2014 – 2017. Consortium grant in collaboration with University of Utrecht and University of Ghent. Dr. M. Nawijn, Prof. dr. G.H. Koppelman, Prof. dr. L. Bont , Prof. dr. B. Lambrecht


Lung Foundation Netherlands 4.1.15.002: Does high baseline oxidative stress attenuate macrophage function during exacerbations of COPD and asthma? 2015-2020. Prof.dr. B.N. Melgert, Dr. R. Lutter, Dr. F.O. Martinez, Prof.dr. H.A.M. Kerstjens; 2 PhD vacancies, 2 technician vacancies.

Lung Foundation Netherlands junior investigator grant 4.2.15.039JO: Neuronal remodeling: a novel perspective on airway hyperresponsiveness in asthma. 2016-2019. Dr. L.E.M. Kistemaker.
Lung Foundation Netherlands junior investigator grant 5.2.15.057JO: Treatment of chronic respiratory failure in COPD patients with Non-invasive ventilation: Starting at home and selecting the Right Patient; the RECONSIDER study. 2016-2020. Dr. M.L. Duiverman

MD/PhD/ALK: Epinephrine auto-injector prescription, compliance and quality of life. 2011 – 2016. Prof.dr. A.E.J. Dubois, Dr. B.M.J. Flokstra-de Blok. MD/PhD student: J. Saleh-Langenberg

MD/PhD: COPD in primary care and pulmonary rehabilitation: discovering the dynamics of the Minimal Clinically Important Difference (MCID) 2014-2018. Prof.dr. T van der Molen, Dr. C. de Jong. PhD student: H.J. Alma

MD/PhD: Insensitivity to glucocorticosteroid treatment in obstructive pulmonary diseases. 2009-2016. Dr. N.H.T. ten Hacken, Prof.dr. A.J.M. van Oosterhout, Dr. I.H. Heijink. MD/PhD student: J. Zijlstra

MD/PhD: Translating asthma associated genetic variation in IL33 and IL1RL1 into pathophysiology and clinical expression of asthma. 2013 – 2017. Prof.dr. G.H. Koppelman and Dr. M.C. Nawijn. MD/PhD student: M. Ketelaar

MD/PhD: Genetics of food allergy. 2013-2018. Prof.dr. A.E.J. Dubois, Prof.dr. G.H. Koppelman. MD/PhD student: C.D. van Ginkel

MD/PhD: Diagnosis, treatment and risk factors for therapy failure of Hymenoptera venom allergy. 2012-2016. Prof.dr. A.E.J. Dubois, Dr. J.N.G. Oude Elberink. PhD-student: B.J.P.R. Vos

MD/PhD: Severity of Anaphylaxis. 2015-2017. Prof.dr. A.E.J. Dubois, Prof.dr. G.H. Koppelman. MD/PhD student: M.E. Pettersson.

MRC: The roles of Pellino-1 in the control of airway viral infection. 2015-2016. Prof. Dr. Ian Sabroe, Prof. I. H. Heijink. Technician: M.R. Jonker.

National Health and Medical Research Council Australia APP1099569. Fibroblast Senescence as a driver of pulmonary fibrosis. 2016-2019. NHMRC research project in collaboration with University of Newcastle Australia. Prof.dr. D. Knight, Prof.dr J.K. Burgess, Prof.dr. G. Westall, Prof.dr. G. Laurent, Prof.dr. S. Mutsaers, Dr. C. Prele.

National Health And Medical Research Council Australia (NHMRC): Elucidation of the Aetiology of Airway Remodelling in COPD; 2016-2020. Dr. B. Oliver, Prof. dr. I. Adcock, Dr. C.A. Brandsma. PhD student: R. Woldhuis

Novartis: Effects of a combination of the beta-adrenoceptor agonist indacaterol and the muscarinic receptor antagonist glycopyrrolate on intrapulmonary airway constriction. 2015-2017. Prof.dr. M. Schmidt. Post-doc: Dr. B. Han

Pender Foundation for Pulmonary Fibrosis: Exchange of fresh human lung tissue of patients transplanted for pulmonary fibrosis between RUG/UMCG (Groningen) and Erasmus MC (Rotterdam). 2014-2018. Dr. B.N. Melgert, Dr. B. van den Blink

Phadia; In vitro Diagnostiek en Eerstelijns Allergie Leidraad (IDEAL) 2009-2017. Prof.dr. A.E.J. Dubois, Prof.dr. T. van der Molen, Dr. B.M.J. Flokstra-de Blok.


Roche (Basel, Switzerland): Pirfenidone in Crohn’s disease and other fibrotic disorders. 2016-2017. Prof.dr. B.N. Melgert, Prof. dr. G. Dijkstra


STW Improvement of Diagnostic mMethods for ALlery assessment. Cashew allergy in children as a showcase (IDEAL/ORCA study). 2012-2016. Prof.dr. A.E.J. Dubois, Dr. B.M.J. Flokstra-de Blok. MD/PhD-student: C.D. van Ginkel. technician: A. Oomkes-Pilon

STW Open Technology Programme: Design, synthesis and validation of potent and isozyme selective arginase inhibitors for therapeutic use in asthma. 2015-2020. Prof. dr. A.S.S. Dömling, Prof. dr. H. Meurs, Prof. dr. P.H. Elsinga. PhD student: M.P.M. van den Berg

TEVA the Netherlands: Center for Translational Pediatric Pulmonology. 2016 - 2020 Prof.dr. G.H. Koppelman, Prof.dr.D.S. Postma, Dr. M.N. Nawijn, Dr. B.W.M. Willemse, Dr. E. Kersten.


University of Groningen. Application of eHealth to improve care for asthma and COPD patients in primary care: from focus groups to data mining. 2012-2016. Prof.dr. T. van der Molen, Prof.dr. R. Sanderman. PhD student: E.I. Metting
University Medical Center Groningen: Work absence, productivity loss and indirect costs in patients with asthma, COPD and ACOS. 2016-2017. Dr. J.W.H. Kocks, Dr. B.M.J. Flokstra-de Blok, Dr. J.F.M. van Boven, Prof.dr. T van der Molen, M. Román-Rodríguez, Prof.dr. J.B. Soriano. PhD Student: B.J.H. Dierick


University Medical Center Groningen (Doelmatigheidsonderzoek) & Stichting Vrienden van het Beatrixkinderziekenhuis (Grantnumber 671437): GERAS-project NeoLifes (prof dr AF Bos)/Neolifes-lungs. Dr. E.J.L.E. Vrijlandt, W. Stalman, M. van Smaalen


ZonMW. Citrienfonds: Doen of laten? Terugdringen van onnodige zorg. Afbouwen onnodig gebruik van inhalatie corticosteroïden bij COPD. 2016-2018. Dr. J.W.H. Kocks, Dr. T Schermer, Dr. C. de Jong, Dr. J. van Boven, Prof.dr. T. van der Molen, Dr. R. Riemersma, E. Brill, Dr. M. van den Berge.

Also a substantial contribution for several projects has been obtained from the Stichting Astma Bestrijding (SAB) and the Northern CARA Foundation (NCS).

Research projects of the GRIAC spin-off company Aquilo:

Aquilo: Evaluation of two novel compounds in a guinea pig model of acute asthma. 2015-2016. Prof.dr. R. Gosens, Dr. L.E.M. Kistemaker.

Aquilo: Evaluation of two novel compounds on airway remodeling in guinea pig lung slices. 2015-2016. Prof.dr. R. Gosens, Dr. L.E.M. Kistemaker.

Aquilo: Evaluation of two novel compounds in an animal model of chronic asthma. 2015-2016. Prof.dr. R. Gosens, Dr. L.E.M. Kistemaker.
Publications 2016

Dissertations

R.F. Hoffmann
Cigarette smoke-induced oxidative stress in COPD. Effects on mitochondrial function, the lipidome and glucocorticoid responsiveness in airway epithelium
29-02-2016
Promotores: Prof. Dr. H.I. Heijink, Prof. Dr. A.J.M. van Oosterhout
Co-promotor: Dr. N.H.T. ten Hacken

D. van Hemelen
Characterization of allergen-specific T cell subsets in allergy
29-02-2016
Promotor: Prof. Dr. A.J.M. van Oosterhout
Co-promotores: Dr. M.C. Nawijn, Dr. J.N.G. Oude Elberink

H. Klooster
Bronchoscopic lung volume reduction. A new treatment modality for patients with severe emphysema
25-04-2016
Promotor: Prof. Dr. H.A.M. Kerstjens
Co-promotores: Dr. D.J. Slebos, Dr. N.H.T. ten Hacken, Dr. J.E. Hartman

C. Draijer
Macrophages in asthma. 3 different types, 2 bad choices, 1 solution
29-04-2016
Promotores: Prof. Dr. B.N. Melgert, Prof. Dr. K. Poelstra
Co-promotor: Dr. M.N. Hylkema

J. Song
Lung epithelial cell differentiation in human and mouse: environment, epigenetics and epigenetic editing
30-05-2016
Promotor: Prof. Dr. M.G. Rots
Co-promotor: Dr. M.N. Hylkema

J. Cao
Early life exposure to toxic environments: effects on lung and immune cell development in mice and men
30-05-2016
Promotor: Prof. Dr. W. Timens
Co-promotor: Dr. M.N. Hylkema

X. Zeng
Genetic and environmental determinants of respiratory health
12-10-2016
Promotor: Prof. Dr. H.M. Boezen
Co-promotor: Dr. J.M. Vonk

S.R. Jansen
Second messengers in cancer. Cyclic AMP meets beta-catenin in tumor progression
24-10-2016
Promotores: Prof. Dr. M. Schmidt, Prof. Dr. R. Gosens
R. van Altena
Multi-drug resistant tuberculosis in the Netherlands. Personalized treatment and outcome
15-11-2016
Promotores: Prof. Dr. T.S. van der Werf, Prof. Dr. H.A.M. Kerstjens
Co-promotor: Dr. J.W.C. Alffenaar

A.I.R. Spanjer
The WNT receptor Frizzled-8 in pulmonary remodelling and inflammation
25-11-2016
Promotores: Prof. Dr. R. Gosens, Prof. Dr. H.I. Heijink, Prof. Dr. H. Meurs, Prof. Dr. D.S. Postma

C.E. Boorsma
Macrophages: the overlooked target for pulmonary fibrosis and COPD
02-12-2016
Promotores: Prof. Dr. B.N. Melgert, Prof. Dr. W. Timens, Prof. Dr. K. Poelstra

W.J. Poppinga
Compartmentalized signaling in the lung: A-kinase anchoring proteins as novel drug targets for chronic obstructive pulmonary disease
02-12-2016
Promotores: Prof. Dr. M. Schmidt, Prof. Dr. H. Meurs, Prof. Dr. H. Maarsingh, Prof. Dr. H.I. Heijink

J. Saleh-Langenberg
Epinephrine auto-injector for anaphylaxis in food allergic patients
12-12-2016
Promotor: Prof. Dr. A.E.J. Dubois
Co-promotor: Dr. B.M.J. Flokstra-de Blok

B. Han
Novel strategies in the treatment of COPD: Focus on oxidative stress and A-kinase anchoring proteins
12-12-2016
Promotores: Prof. Dr. M. Schmidt, Prof. Dr. H. Meurs, Prof. Dr. H. Maarsingh

Publications SCI journals


Publications in Dutch


Contributions to other research institutes

Dissertations

N.C. Petrus
Studies on cow’s milk allergy
18-03-2016 University of Amsterdam
Promotor: Prof. Dr. W.M.C. van Aalderen
Co-promotor: Dr. A.B. Sprikkelman

L.I.Z. Kunz
Effects of Inhaled corticosteroids on Clinical and Pathological Outcomes in COPD. Insight from the GLUCOLD study
30-11-2016 University of Leiden
Promotores: Prof. Dr. P. Hiemstra, Prof. Dr. P. Sterk, Prof. Dr. D.S. Postma

Publications SCI journals


