Proposal writing

Focus on Excellence and Impact

MED research advisors

Research strategies

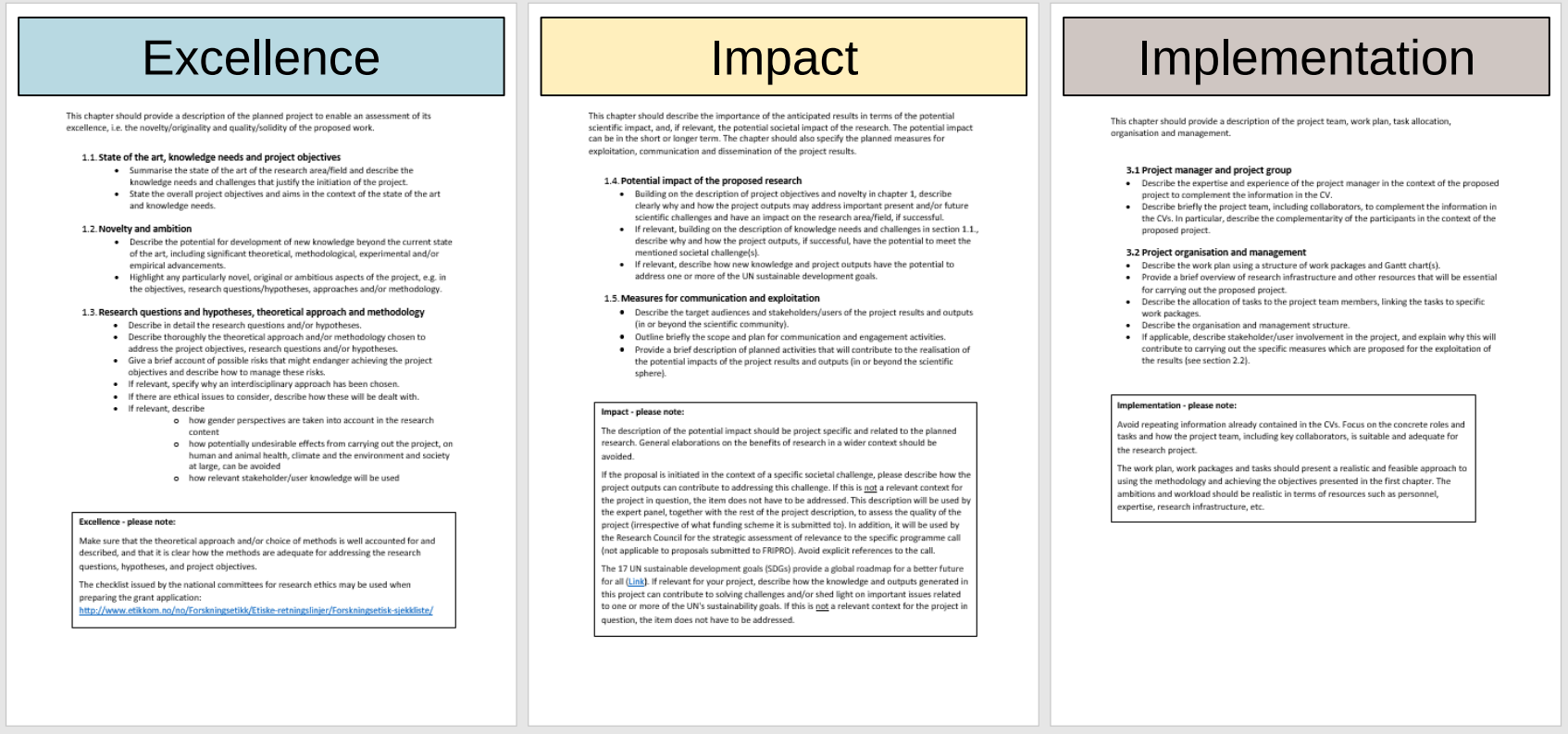
Writing style

Academic writing	⇔	Grant writing
Past oriented *Work that has been done*		Future oriented *Work that should be done*
Expository rhetoric *Explaining to the reader*		Persuasive rhetoric *«Selling» to the reader*
Impersonal tone *Objective, dispassionate*		Personal tone *Convey excitement*
Specialized terminology *«Insider jargon»*		Specialized terminology *Easily understood*

- Should be general enough that a non-specialist can understand
- Be logical/consistent throughout your text (e.g. content, terminology)
- Use simple structures and active tense
- Use short(er) sentences → can be read easily and quickly

Proposal structure

NFR - Project description template 2019 (10 pages)



Excellence

This chapter should provide a description of the planned project to enable an assessment of its excellence, i.e. the novelty/originality and quality/solidity of the proposed work.

1.1. **State of the art, knowledge needs and project objectives**
- Summarise the state of the art of the research area/field and describe the knowledge needs and challenges that justify the initiation of the project.
- State the overall project objectives and aims in the context of the state of the art and knowledge needs.

1.2. **Novelty and ambition**
- Describe the potential for development of new knowledge beyond the current state of the art, including significant theoretical, methodological, experimental and/or empirical advancements.
- Highlight any particularly novel, original or ambitious aspects of the project, e.g. in the objectives, research questions/hypotheses, approaches and/or methodology.

1.3. **Research questions and hypotheses, theoretical approach and methodology**
- Describe in detail the research questions and/or hypotheses.
- Describe thoroughly the theoretical approach and/or methodology chosen to address the project objectives, research questions and/or hypotheses.
- Give a brief account of possible risks that might endanger achieving the project objectives and describe how to manage these risks.
- If relevant, specify why an interdisciplinary approach has been chosen.
- If there are ethical issues to consider, describe how these will be dealt with.
- If relevant, describe
  - how gender perspectives are taken into account in the research content
  - how potentially undesirable effects from carrying out the project, on human and animal health, climate and the environment and society at large, can be avoided
  - how relevant stakeholder/user knowledge will be used

Excellence - please note:

Make sure that the theoretical approach and/or choice of methods is well accounted for and described, and that it is clear how the methods are adequate for addressing the research questions, hypotheses, and project objectives.

The checklist issued by the national committees for research ethics may be used when preparing the grant application:
http://www.etikkom.no/no/Forskningsetikk/Etiske-retningslinjer/Forskningsetisk-sjekkliste/

Impact

This chapter should describe the importance of the anticipated results in terms of the potential scientific impact, and, if relevant, the potential societal impact of the research. The potential impact can be in the short or longer term. The chapter should also specify the planned measures for exploitation, communication and dissemination of the project results.

1.4. **Potential impact of the proposed research**
- Building on the description of project objectives and novelty in chapter 1, describe clearly why and how the project outputs may address important present and/or future scientific challenges and have an impact on the research area/field, if successful.
- If relevant, building on the description of knowledge needs and challenges in section 1.1., describe why and how the project outputs, if successful, have the potential to meet the mentioned societal challenge(s).
- If relevant, describe how new knowledge and project outputs have the potential to address one or more of the UN sustainable development goals.

1.5. **Measures for communication and exploitation**
- Describe the target audiences and stakeholders/users of the project results and outputs (in or beyond the scientific community).
- Outline briefly the scope and plan for communication and engagement activities.
- Provide a brief description of planned activities that will contribute to the realisation of the potential impacts of the project results and outputs (in or beyond the scientific sphere).

Impact - please note:

The description of the potential impact should be project specific and related to the planned research. General elaborations on the benefits of research in a wider context should be avoided.

If the proposal is initiated in the context of a specific societal challenge, please describe how the project outputs can contribute to addressing this challenge. If this is not a relevant context for the project in question, the item does not have to be addressed. This description will be used by the expert panel, together with the rest of the project description, to assess the quality of the project (irrespective of what funding scheme it is submitted to). In addition, it will be used by the Research Council for the strategic assessment of relevance to the specific programme call (not applicable to proposals submitted to FRIPRO). Avoid explicit references to the call.

The 17 UN sustainable development goals (SDGs) provide a global roadmap for a better future for all (Link). If relevant for your project, describe how the knowledge and outputs generated in this project can contribute to solving challenges and/or shed light on important issues related to one or more of the UN's sustainability goals. If this is not a relevant context for the project in question, the item does not have to be addressed.

Implementation

This chapter should provide a description of the project team, work plan, task allocation, organisation and management.

3.1 Project manager and project group
- Describe the expertise and experience of the project manager in the context of the proposed project to complement the information in the CV.
- Describe briefly the project team, including collaborators, to complement the information in the CVs. In particular, describe the complementarity of the participants in the context of the proposed project.

3.2 Project organisation and management
- Describe the work plan using a structure of work packages and Gantt chart(s).
- Provide a brief overview of research infrastructure and other resources that will be essential for carrying out the proposed project.
- Describe the allocation of tasks to the project team members, linking the tasks to specific work packages.
- Describe the organisation and management structure.
- If applicable, describe stakeholder/user involvement in the project, and explain why this will contribute to carrying out the specific measures which are proposed for the exploitation of the results (see section 2.2).

Implementation - please note:

Avoid repeating information already contained in the CVs. Focus on the concrete roles and tasks and how the project team, including key collaborators, is suitable and adequate for the research project.

The work plan, work packages and tasks should present a realistic and feasible approach to using the methodology and achieving the objectives presented in the first chapter. The ambitions and workload should be realistic in terms of resources such as personnel, expertise, research infrastructure, etc.

- Always read the template thoroughly and completely!
- Follow the template and guidelines and provide <u>all</u> the information requested (if applicable)

Proposal structure

Excellence

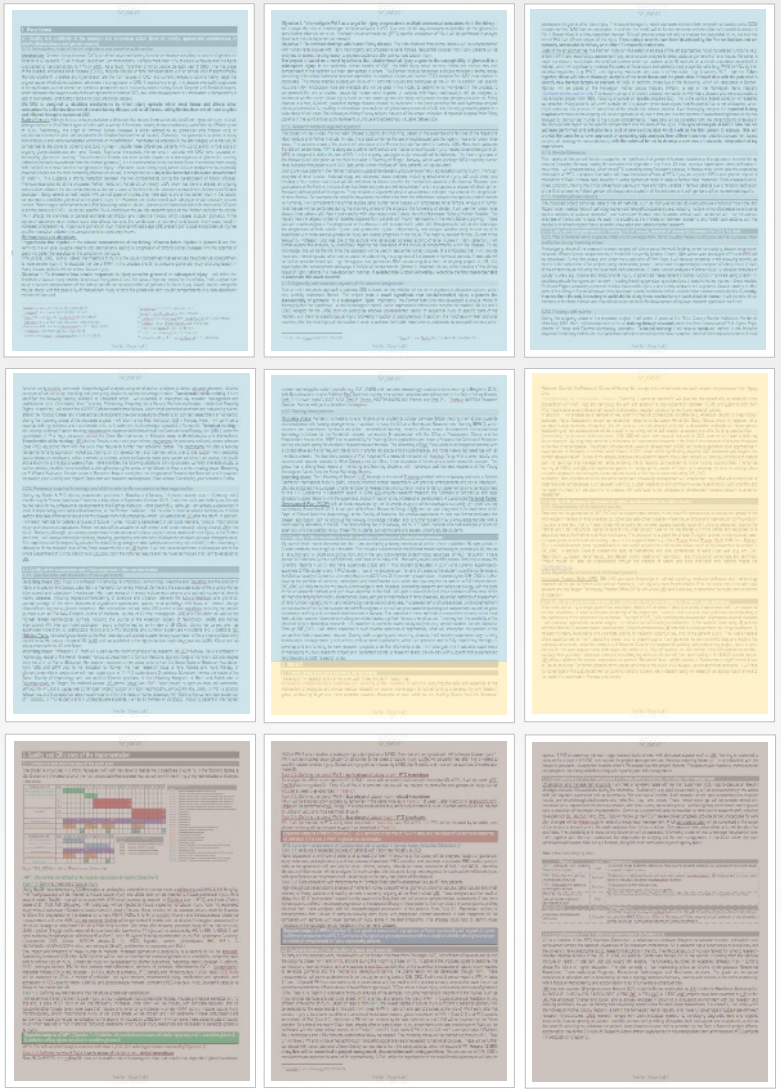
4-5 pages

Impact

1-2 pages

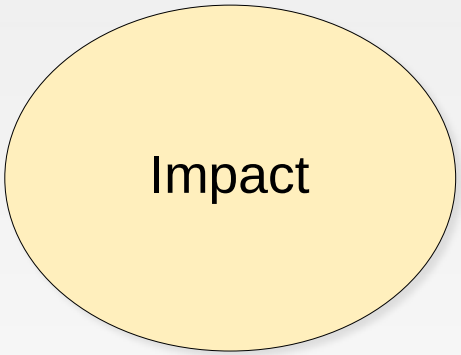
Implementation

3 pages

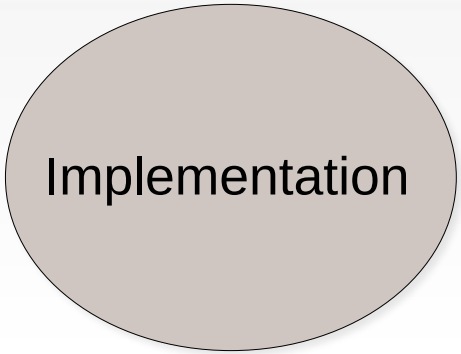


Proposal structure

- State of the art and knowledge needs
- Research questions and hypotheses
- Project objectives
- (Novelty and ambition)
- Concept/Theoretical approach and methodology



- Expected/Potential impact of the proposed research
  scientific, societal, economic
- Measures to maximise impact
  dissemination, exploitation and communication



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- Research questions and hypotheses
- Project objectives
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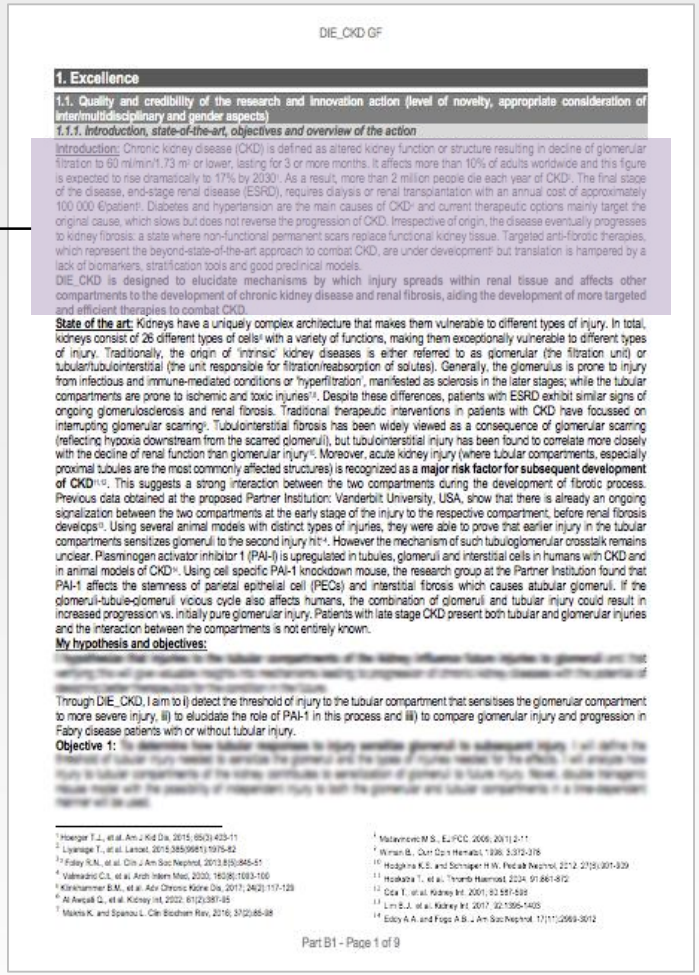
- Concept/Theoretical approach and methodology

Impact

Implementation

Introduction

- “Big picture”
- Outline problem
- Need statement
- How project fits



DIE_CKD GF

1. Excellence

1.1. Quality and credibility of the research and innovation action (level of novelty, appropriate consideration of inter/multidisciplinary and gender aspects)

1.1.1. Introduction, state-of-the-art, objectives and overview of the action

Introduction: Chronic kidney disease (CKD) is defined as altered kidney function or structure resulting in decline of glomerular filtration to 60 ml/min/1.73 m² or lower, lasting for 3 or more months. It affects more than 10% of adults worldwide and this figure is expected to rise dramatically to 17% by 2030[1]. As a result, more than 2 million people die each year of CKD[2]. The final stage of the disease, end-stage renal disease (ESRD), requires dialysis or renal transplantation with an annual cost of approximately 100 000 €/patient[3]. Diabetes and hypertension are the main causes of CKD[4] and current therapeutic options mainly target the original cause, which slows but does not reverse the progression of CKD. Irrespective of origin, the disease eventually progresses to kidney fibrosis: a state where non-functional permanent scars replace functional kidney tissue. Targeted anti-fibrotic therapies, which represent the beyond-state-of-the-art approach to combat CKD, are under development[5] but translation is hampered by a lack of biomarkers, stratification tools and good preclinical models.

DIE_CKD is designed to elucidate mechanisms by which injury spreads within renal tissue and affects other compartments to the development of chronic kidney disease and renal fibrosis, aiding the development of more targeted and efficient therapies to combat CKD.

State of the art: Kidneys have a uniquely complex architecture that makes them vulnerable to different types of injury. In total, kidneys consist of 26 different types of cells[6] with a variety of functions, making them exceptionally vulnerable to different types of injury. Traditionally, the origin of ‘intrinsic’ kidney diseases is either referred to as glomerular (the filtration unit) or tubular/tubulointerstitial (the unit responsible for filtration/reabsorption of solutes). Generally, the glomerulus is prone to injury from infectious and immune-mediated conditions or ‘hyperfiltration’, manifested as sclerosis in the later stages; while the tubular compartments are prone to ischemic and toxic injuries[7,8]. Despite these differences, patients with ESRD exhibit similar signs of ongoing glomerulosclerosis and renal fibrosis. Traditional therapeutic interventions in patients with CKD have focussed on interrupting glomerular scarring[9]. Tubulointerstitial fibrosis has been widely viewed as a consequence of glomerular scarring (reflecting hypoxia downstream from the scarred glomeruli), but tubulointerstitial injury has been found to correlate more closely with the decline of renal function than glomerular injury[10]. Moreover, acute kidney injury (where tubular compartments, especially proximal tubules are the most commonly affected structures) is recognized as a **major risk factor for subsequent development of CKD**[11,12]. This suggests a strong interaction between the two compartments during the development of fibrotic process. Previous data obtained at the proposed Partner Institution: Vanderbilt University, USA, show that there is already an ongoing signalization between the two compartments at the early stage of the injury to the respective compartment, before renal fibrosis develops[13]. Using several animal models with distinct types of injuries, they were able to prove that earlier injury in the tubular compartments sensitizes glomeruli to the second injury hit[14]. However the mechanism of such tubuloglomerular crosstalk remains unclear. Plasminogen activator inhibitor 1 (PAI-I) is upregulated in tubules, glomeruli and interstitial cells in humans with CKD and in animal models of CKD[15]. Using cell specific PAI-1 knockdown mouse, the research group at the Partner Institution found that PAI-1 affects the stemness of parietal epithelial cell (PECs) and interstitial fibrosis which causes atubular glomeruli. If the glomeruli-tubule-glomeruli vicious cycle also affects humans, the combination of glomeruli and tubular injury could result in increased progression vs. initially pure glomerular injury. Patients with late stage CKD present both tubular and glomerular injuries and the interaction between the compartments is not entirely known.

My hypothesis and objectives:

[redacted]

Through DIE_CKD, I aim to i) detect the threshold of injury to the tubular compartment that sensitises the glomerular compartment to more severe injury, ii) to elucidate the role of PAI-1 in this process and iii) to compare glomerular injury and progression in Fabry disease patients with or without tubular injury.

Objective 1: [redacted]

[1] Hoerger T.J., et al. Am J Kid Dis. 2015; 65(3):423-11
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[6] Al Awqati Q., et al. Kidney Int. 2002; 61(2):387-95
[7] Maiese K. and Spanou L. Clin Biochem Rev. 2016; 37(2):85-98
[8] Malvinovic M.S., Eur PCC. 2005; 20(1):2-11
[9] Wilson B., Curr Opin Hematol. 1996; 3:372-378
[10] Hodgkins K.S. and Schnaper H.W. Pediatr Nephrol. 2012; 27(8):1301-309
[11] Hoekstra T., et al., Thromb Haemost. 2004; 91:861-872
[12] Ota T., et al. Kidney Int. 2001; 60:597-606
[13] Lim B.J., et al. Kidney Int. 2017; 92:1395-1403
[14] Eddy A.A. and Fogo A.B., J Am Soc Nephrol. 17(11):2999-3012

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DIE_CKD GF

Objective 2: [redacted]

Objective 3: [redacted]

In the traditional animal models of CKD, the initial injury could be very limited and involve only one compartment of the nephron but then later spread to others. The Partner institute developed a double transgenic animal model consisting of inducible diphtheria receptor expression in proximal tubules and human CD25 receptor for LMB2 immunotoxin in podocytes. This model enables subsequent injury of 1st proximal tubules and podocytes as the 2nd hit. In addition, cell specific inducible PAI-1 knockdown mice are available and will be used in this model, to determine its involvement in the process.To complement the animal studies, sequential human renal biopsies of patients with Fabry nephropathy, will be analyzed to determine whether early tubular injury leads to more severe glomerular injury and greater disease progression later on. Fabry disease is a rare, X-linked, lysosomal storage disease caused by mutations in the gene encoding the acid hydrolase enzyme alpha-galactosidase A, resulting in intracellular accumulation of globotriaosylceramide (Gb3) and related glycosphingolipids in a wide range of cell types The Norwegian Kidney Biopsy registry has one of the largest collection of repeated biopsies from Fabry patients in the world and as such represents a unique and exceedingly valuable dataset (25).

1.1.2. Research Methodology and Approach

The project will be divided into two main phases: outgoing and incoming, based on the expertise and facilities of the respective Host Institute and Partner institute. In total, the project combines the use of double/quadruple transgenic mice and human renal tissue. The outgoing phase of the project will take place at the Partner institute, Vanderbilt University, USA. Here, work packages 1 and 2 will be delivered. WP1 is designed to define the threshold and mechanisms of tubular injury, needed to sensitize glomeruli. WP2, is designed to define the role of PAI-1 in the ongoing tubuloglomerular crosstalk will be delivered. The incoming phase of the fellowship will take place at the Host Institution, University of Bergen, Norway, where work package WP3 analysing human renal biopsies from patients with CKD (sequential kidney biopsies of Fabry patients) will be delivered.

Strong previous data from the Partner Institution suggest the deleterious tubule-to-glomeruli signalization during injury[16]. Thorough analyses of renal function, histopathology and advanced tissue analyses, including mitochondrial injury, cell cycle arrest and hypoxia of the murine renal tissue will be performed to closely observe the mechanistic aspects of the injuries. Research and publications of the Partner institute show that these analyses are well established[16] and the proposed analyses will shed light on the quantitative aspects of the injuries. These detailed analyses will provide valuable data and open new views on the progression of renal fibrosis. To overcome the possible drawbacks that often arise from the differences between the species (rodent models vs humans), I will complement the animal studies using human renal tissues with progressed renal fibrosis. Analysis of human renal tissues will be performed during the incoming phase of the project at the University of Bergen. I will use the human renal tissues from patients with Fabry nephropathy with processed renal fibrosis from the Norwegian National Kidney Registry. The registry has the largest number of repeated biopsies from patients with Fabry nephropathy in the world (25 and growing). These data will enable analysis of the progression of the disease in a time-dependent matter. With this approach, I will be able to analyse the progression of both tubular injuries and glomerular injuries independently and analyse whether early tubular injury is associated with more serious glomerular injury and overall prognosis in the future. The major supervisor for the US part of the fellowship, Professor Fogo was one of the authors who developed consized scoring of renal injuries in Fabry patients[18]. I will further expand the analysis, by specifically targeting the time-lapse of the individual compartments within the disease. To my knowledge, this will be the first time this approach will be used in sequential kidney biopsies. It is anticipated that it will provide novel and interesting data, which can be useful for determining the prognosis of the disease in individual patients. These data will be further complemented with high-throughput next-generation RNA sequencing data from an ongoing project at UiB, that investigates the transcriptomic pathways in individual compartments (glomeruli, proximal tubules, distal tubules) of the kidney tissue of Fabry patients in a time-dependent manner. **If awarded this Global Fellowship, I would be the first researcher able to undertake this novel research.**

1.1.3 Originality and innovative aspects of the research programme

The current therapeutic approach to address CKD is based on the inhibition of the renin-angiotensin-aldosteron system, which only partially addresses fibrosis. [redacted] Importantly, the Partner Institution has developed a unique model to thoroughly test the hypothesis – a double transgenic model - which expresses diphteria toxin receptor on proximal tubules and a CD25 receptor for the LMB2 toxin on podocytes enables unprecedented testing of sequential injury of specific parts of the nephron, with the initial specific tubular injury followed by induction of podocyte injury. In addition, the hypothesis will test functional recovery after the initial injury of the tubules in order to address the hidden mechanisms undetected by standard methods which

[16] Lim B.J., et al. Kidney Int. 2017; 91:1395-1403
[18] Fogo A.B., et al. Nephrol Dial Transplant. 2012; 25:2768-2777

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Introduction

Example

According to the Global Asthma Report 2014 it is estimated that asthma affects as many as 334 million people of all ages in all parts of the world [1]. Both childhood asthma and long-term asthma are risk factors for chronic obstructive pulmonary disease (COPD) [2],.... It is a cause of substantial burden to people, often causing a reduced quality of life, not only due to the physical effect, but also the psychological and social effects.
Asthma is caused by a complex interaction of genetics and environmental factors. … the 'hygiene hypothesis'. It states that due to increased hygiene and consequently lack of exposure to microorganisms early in life, the immune system becomes inefficient in fighting off certain diseases and makes the individuals more susceptible to autoimmune diseases [4, 5]. Despite years of research, there is still no cure for asthma and COPD, nor are there any effective strategies in place to combat their development. In recent years, periodontal disease has been associated with many systemic conditions such as diabetes, cardiovascular, and perhaps more surprisingly, pulmonary diseases [6, 7]. However, the directionality (cause or effect) and the mechanisms explaining this link are not yet understood. Inflammatory conditions in the oral cavity such as periodontitis are characterized by a high burden of gram-negative bacteria. I hypothesize that oral microbiota dominated by gram-negative bacteria with the capacity to induce a particularly strong inflammatory response in the host may lead to reduced lung function, asthma and COPD. In contrast to asthma and COPD, inflammatory conditions in the oral cavity such as periodontitis can be prevented as well as easily diagnosed and successfully treated. If I can provide evidence for a causal relationship between oral health and lung health, these results will provide a rational for an oral hygiene program to improve respiratory health. Because poor oral health increases with age and is associated with low social economic status, there is a huge potential to improve quality of life in older age and also to reduce social inequalities in health.

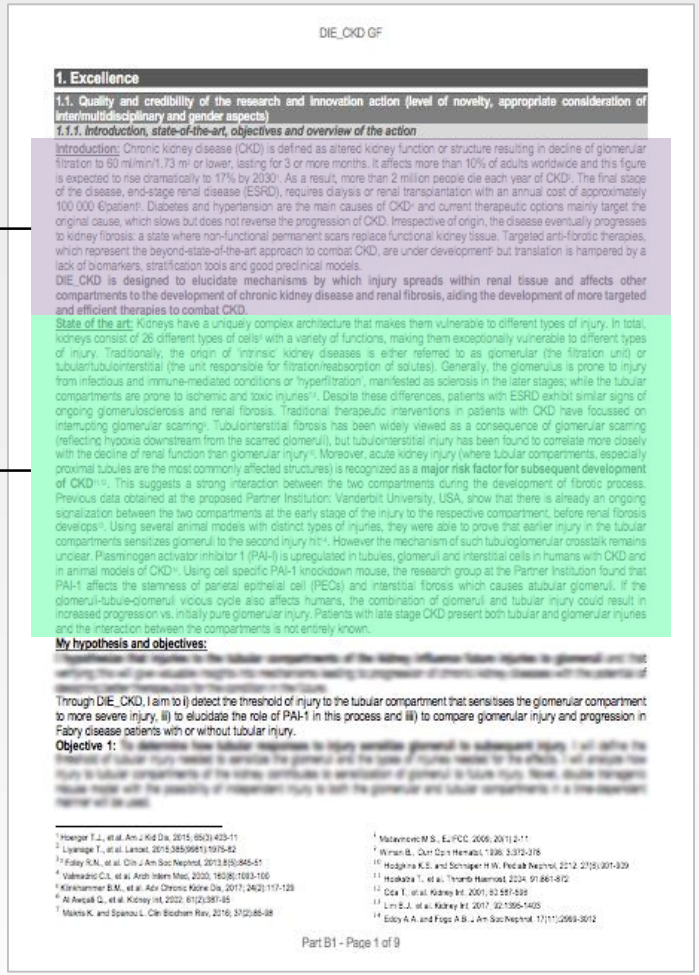
Bertelsen, ERC Starting Grant 2018

Introduction

- “Big picture”
- Outline problem
- Need statement
- How project fits

State of the art

- Current body of knowledge (context)
- Knowledge gap/ scientific challenge
- Solution



DIE_CKD GF

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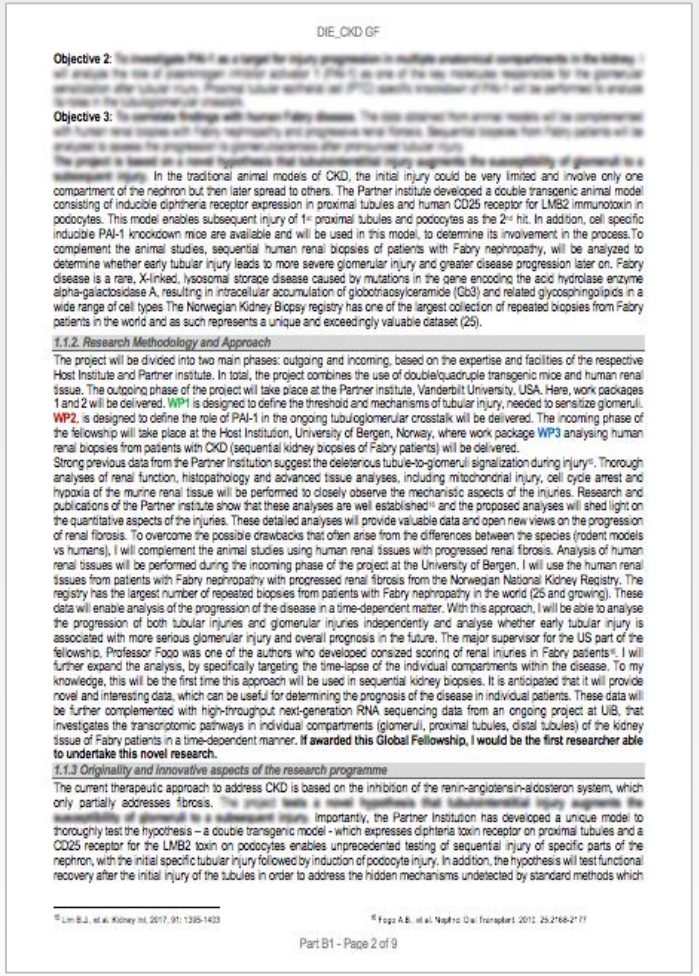

DIE_CKD GF

Objective 2: [redacted]

Objective 3: [redacted]

The project is based on several hypotheses that both potentially explain the susceptibility of glomeruli to a subsequent injury. In the traditional animal models of CKD, the initial injury could be very limited and involve only one compartment of the nephron but then later spread to others. The Partner institute developed a double transgenic animal model consisting of inducible diphtheria receptor expression in proximal tubules and human CD25 receptor for LMB2 immunotoxin in podocytes. This model enables subsequent injury of 1st proximal tubules and podocytes as the 2nd hit. In addition, cell specific inducible PAI-1 knockdown mice are available and will be used in this model, to determine its involvement in the process.To complement the animal studies, sequential human renal biopsies of patients with Fabry nephropathy, will be analyzed to determine whether early tubular injury leads to more severe glomerular injury and greater disease progression later on. Fabry disease is a rare, X-linked, lysosomal storage disease caused by mutations in the gene encoding the acid hydrolase enzyme alpha-galactosidase A, resulting in intracellular accumulation of globotriaosylceramide (Gb3) and related glycosphingolipids in a wide range of cell types The Norwegian Kidney Biopsy registry has one of the largest collection of repeated biopsies from Fabry patients in the world and as such represents a unique and exceedingly valuable dataset (25).

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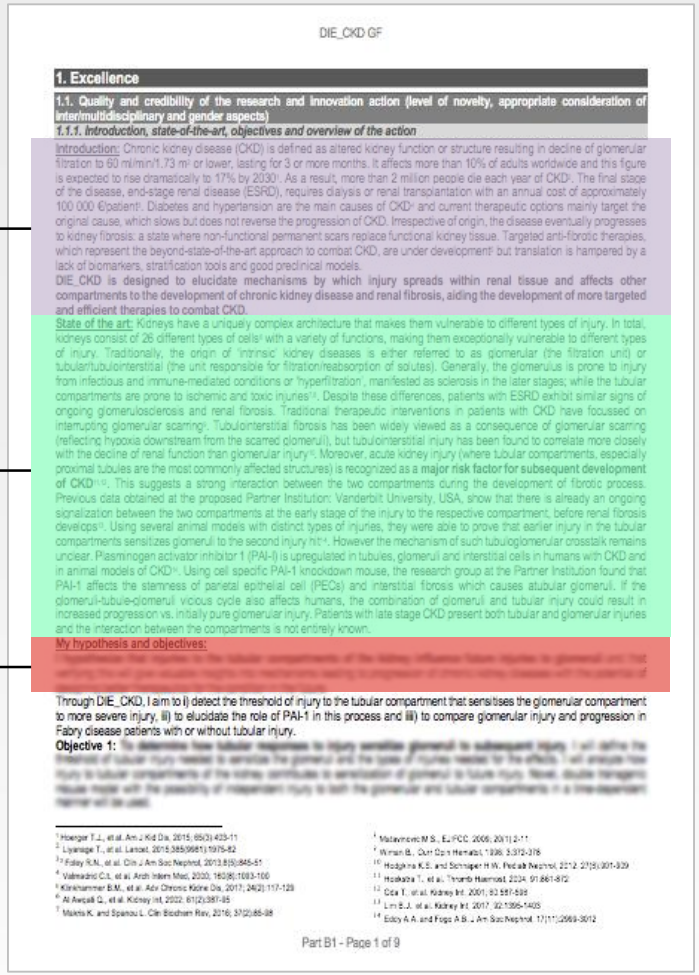
Hypothesis



DIE_CKD GF

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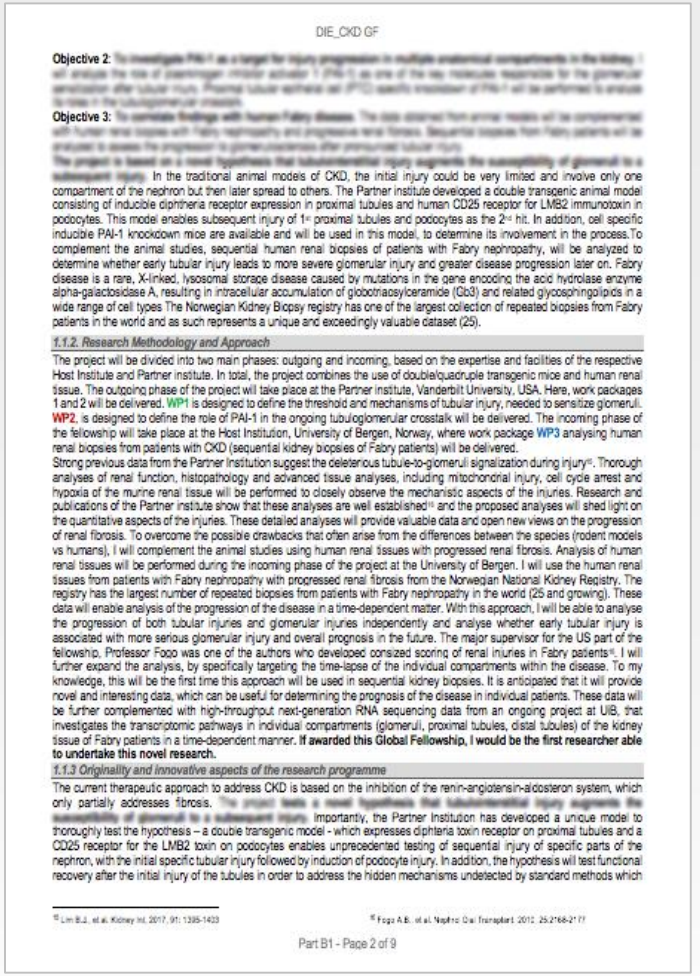

DIE_CKD GF

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Babickova, MSCA-IF-GF 2018

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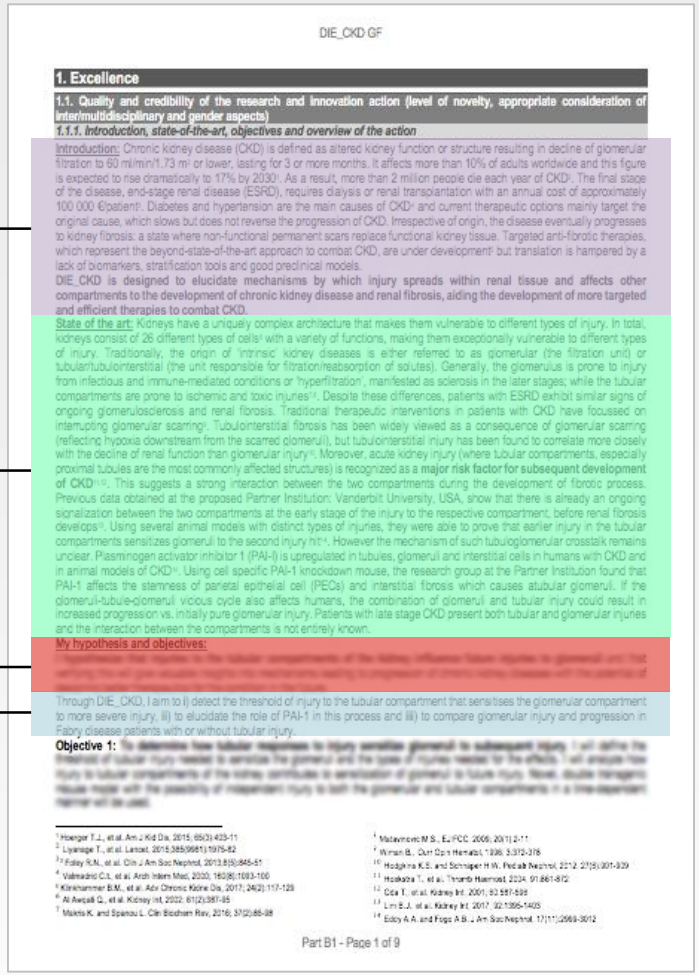
Hypothesis Aims

What you hope to achieve



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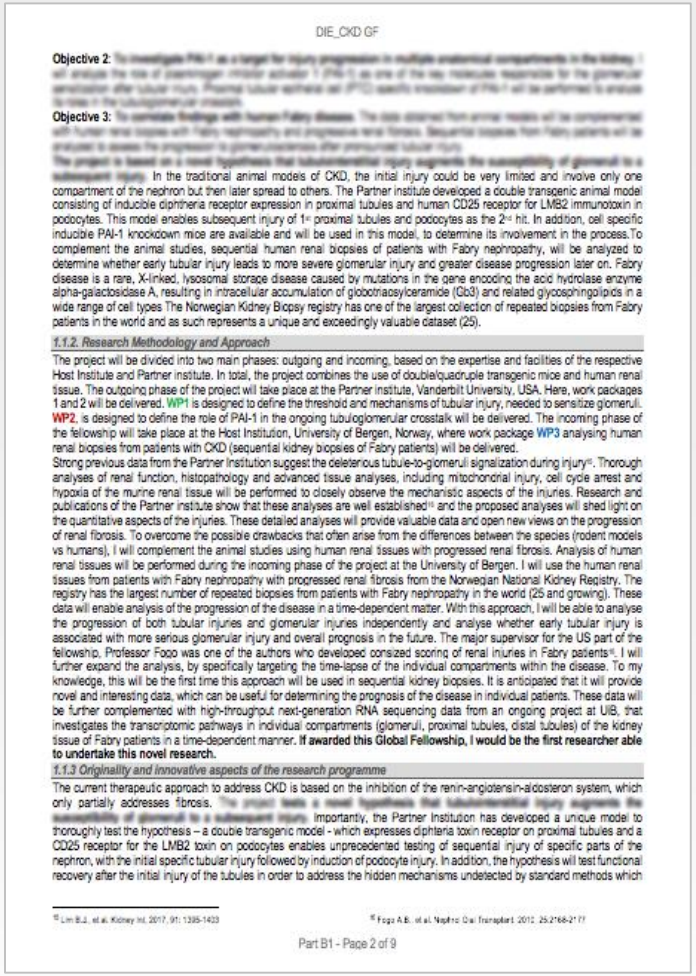

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Aims

Objectives
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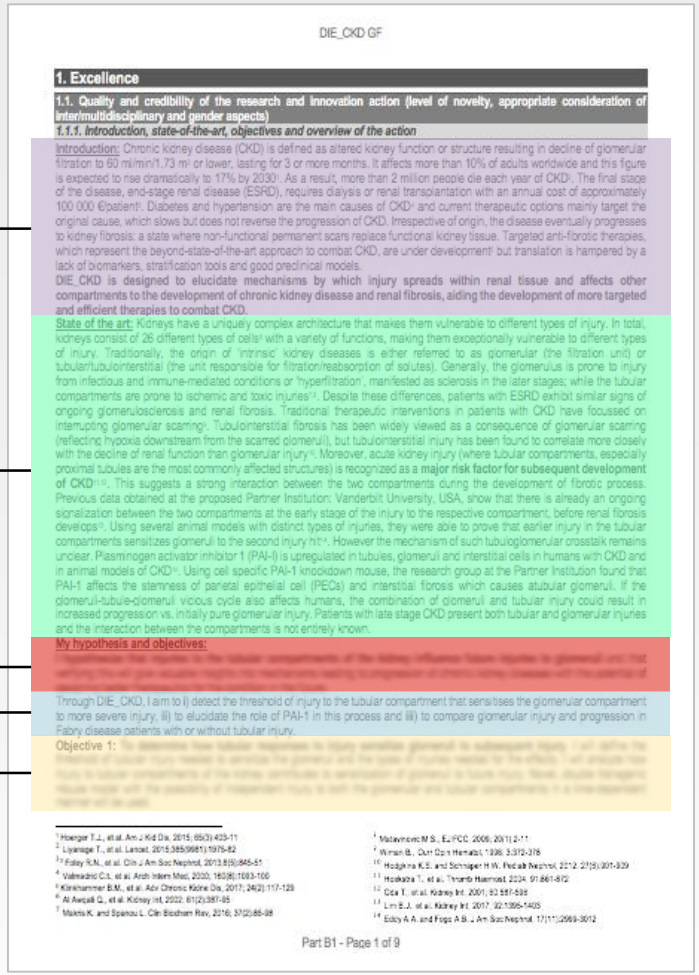
***What** are the action(s) you plan to take in order to achieve your aim(s)*



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[12] Oda T., et al. Kidney Int. 2001; 60:597-696
[13] Lim B.J., et al. Kidney Int. 2017; 92:1395-1403
[14] Eddy A.A. and Fogo A.B., J Am Soc Nephrol. 17(11):2999-3012

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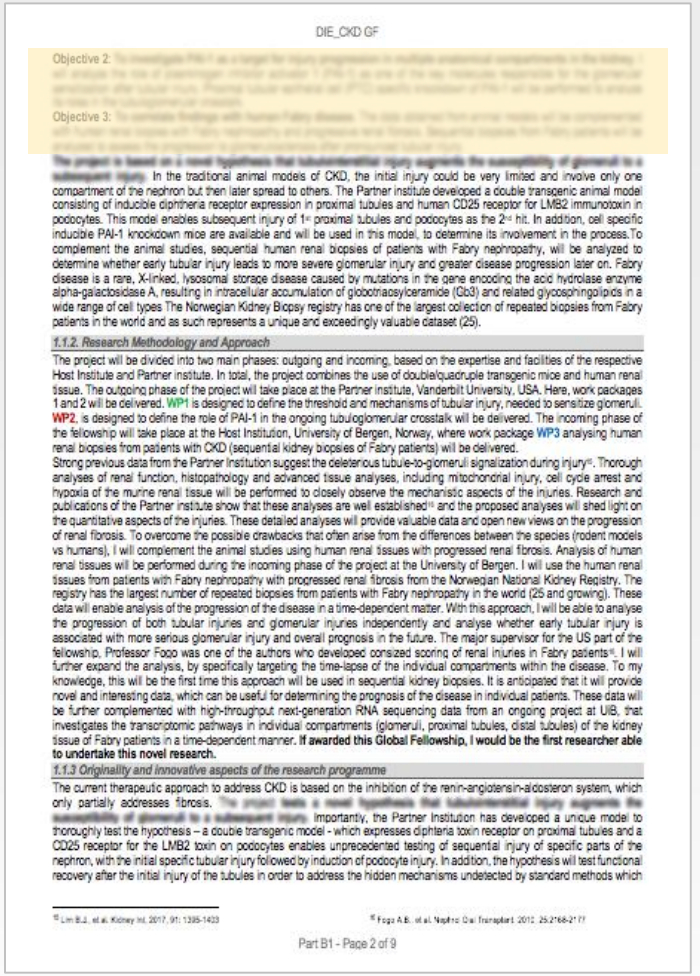

DIE_CKD GF

Objective 2:

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1.1.3 Originality and innovative aspects of the research programme

The current therapeutic approach to address CKD is based on the inhibition of the renin-angiotensin-aldosteron system, which only partially addresses fibrosis. The project tests a novel hypothesis that tubulointerstitial injury augments the susceptibility of glomeruli to a subsequent injury. Importantly, the Partner Institution has developed a unique model to thoroughly test the hypothesis – a double transgenic model - which expresses diphteria toxin receptor on proximal tubules and a CD25 receptor for the LMB2 toxin on podocytes enables unprecedented testing of sequential injury of specific parts of the nephron, with the initial specific tubular injury followed by induction of podocyte injury. In addition, the hypothesis will test functional recovery after the initial injury of the tubules in order to address the hidden mechanisms undetected by standard methods which

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Objectives

Example 1

The *primary objective* is to understand at a molecular level the malignant cellular phenotypes that characterize cancer cells selected for by an obese environment and how these promote cancer progression in obese patients.

Specific objectives

1. Clonal dynamics analysis of tumor progression in obese hosts via DNA barcoding.
2. Characterization of aggressive cancer cell populations by in vivo selection in obese and non-obese mice.
3. Define the molecular role of PPARA in obesity-induced hormone receptor negative breast cancer.
4. Mutational enrichment analysis in obese and non-obese human hormone receptor negative breast cancer samples.

Halberg, NFR FRIPRO Young Research Talents 2017

Objectives

Example 2

The *primary objective* is to study how bacterial composition dominated by potent pro-inflammatory LPS producing bacteria in oral and environmental samples affect lung function and respiratory disease over time, and to verify the association and identify mechanisms using experimental models.

Work Package 3 – Casual associations between LPS-producing bacteria and lung health

Objective:

To verify and identify mechanisms for the association between different LPS-forms and bacteria producing different LPS-forms identified in WP2 and asthma (with mice models of asthma and in vitro models of human lung epithelia)

Research questions for WP3:

1. Does exposure to the Lipid A moieties that represents hexa- or penta-acylated LPS have different effects on asthma development?
2. Does exposure to hexa-acylated LPS producing bacteria (as identified in WP II) have different effects on asthma development than penta-acylated LPS producing bacteria?
3. Does co-culturing of human lung epithelia with Lipid A moieties and with the hexa- and penta-acyltated LPS producing bacteria support the associations observed in the epidemiological studies?

Bertelsen, NFR Bedrehelse 2017

DIE_CKD GF

1. Excellence

1.1. Quality and credibility of the research and innovation action (level of novelty, appropriate consideration of inter/multidisciplinary and gender aspects)

1.1.1. Introduction, state-of-the-art, objectives and overview of the action

Introduction: Chronic kidney disease (CKD) is defined as altered kidney function or structure resulting in decline of glomerular filtration to 60 ml/min/1.73 m² or lower, lasting for 3 or more months. It affects more than 10% of adults worldwide and this figure is expected to rise dramatically to 17% by 2030[1]. As a result, more than 2 million people die each year of CKD[2]. The final stage of the disease, end-stage renal disease (ESRD), requires dialysis or renal transplantation with an annual cost of approximately 100 000 €/patient[3]. Diabetes and hypertension are the main causes of CKD[4] and current therapeutic options mainly target the original cause, which slows but does not reverse the progression of CKD. Irrespective of origin, the disease eventually progresses to kidney fibrosis: a state where non-functional permanent scars replace functional kidney tissue. Targeted anti-fibrotic therapies, which represent the beyond-state-of-the-art approach to combat CKD, are under development[5] but translation is hampered by a lack of biomarkers, stratification tools and good preclinical models.

DIE_CKD is designed to elucidate mechanisms by which injury spreads within renal tissue and affects other compartments to the development of chronic kidney disease and renal fibrosis, aiding the development of more targeted and efficient therapies to combat CKD.

State of the art: Kidneys have a uniquely complex architecture that makes them vulnerable to different types of injury. In total, kidneys consist of 26 different types of cells[6] with a variety of functions, making them exceptionally vulnerable to different types of injury. Traditionally, the origin of 'intrinsic' kidney diseases is either referred to as glomerular (the filtration unit) or tubular/tubulointerstitial (the unit responsible for filtration/reabsorption of solutes). Generally, the glomerulus is prone to injury from infectious and immune-mediated conditions or 'hyperfiltration', manifested as sclerosis in the later stages; while the tubular compartments are prone to ischemic and toxic injuries[7,8]. Despite these differences, patients with ESRD exhibit similar signs of ongoing glomerulosclerosis and renal fibrosis. Traditional therapeutic interventions in patients with CKD have focussed on interrupting glomerular scarring[9]. Tubulointerstitial fibrosis has been widely viewed as a consequence of glomerular scarring (reflecting hypoxia downstream from the scarred glomeruli), but tubulointerstitial injury has been found to correlate more closely with the decline of renal function than glomerular injury[10]. Moreover, acute kidney injury (where tubular compartments, especially proximal tubules are the most commonly affected structures) is recognized as a **major risk factor for subsequent development of CKD**[11,12]. This suggests a strong interaction between the two compartments during the development of fibrotic process. Previous data obtained at the proposed Partner Institution: Vanderbilt University, USA, show that there is already an ongoing signalization between the two compartments at the early stage of the injury to the respective compartment, before renal fibrosis develops[13]. Using several animal models with distinct types of injuries, they were able to prove that earlier injury in the tubular compartments sensitizes glomeruli to the second injury hit[14]. However the mechanism of such tubuloglomerular crosstalk remains unclear. Plasminogen activator inhibitor 1 (PAI-I) is upregulated in tubules, glomeruli and interstitial cells in humans with CKD and in animal models of CKD[15]. Using cell specific PAI-1 knockdown mouse, the research group at the Partner Institution found that PAI-1 affects the stemness of parietal epithelial cell (PECs) and interstitial fibrosis which causes atubular glomeruli. If the glomeruli-tubule-glomeruli vicious cycle also affects humans, the combination of glomeruli and tubular injury could result in increased progression vs. initially pure glomerular injury. Patients with late stage CKD present both tubular and glomerular injuries and the interaction between the compartments is not entirely known.

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[4] Vallianou C.I., et al. Arch Inter Med. 2020; 160(8):1083-100
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[8] Malyszko M.S., Ex FCC. 2006; 20(1):2-11
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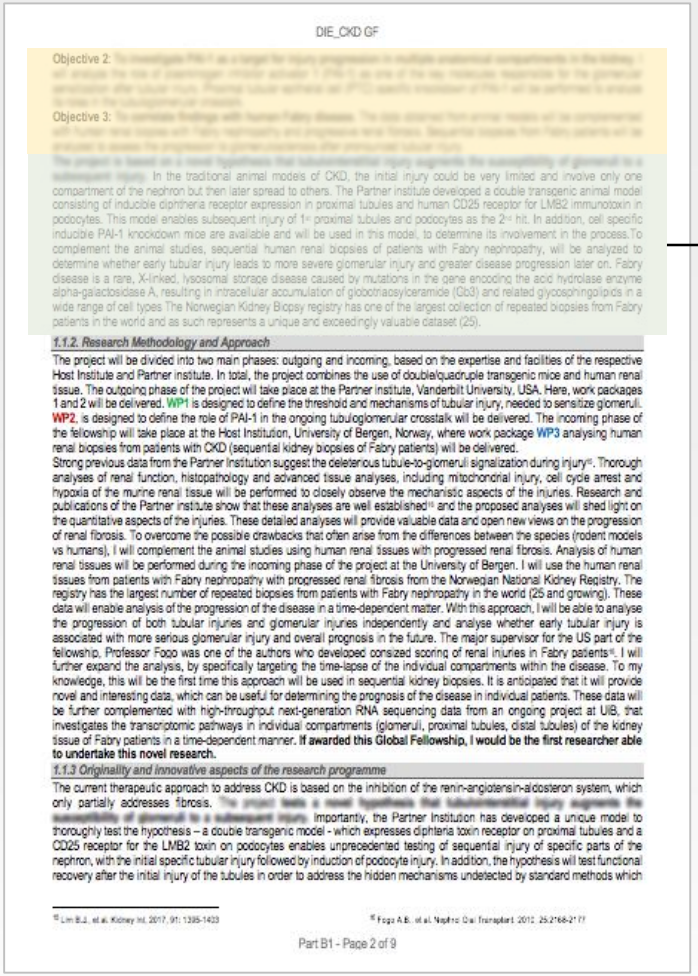

DIE_CKD GF

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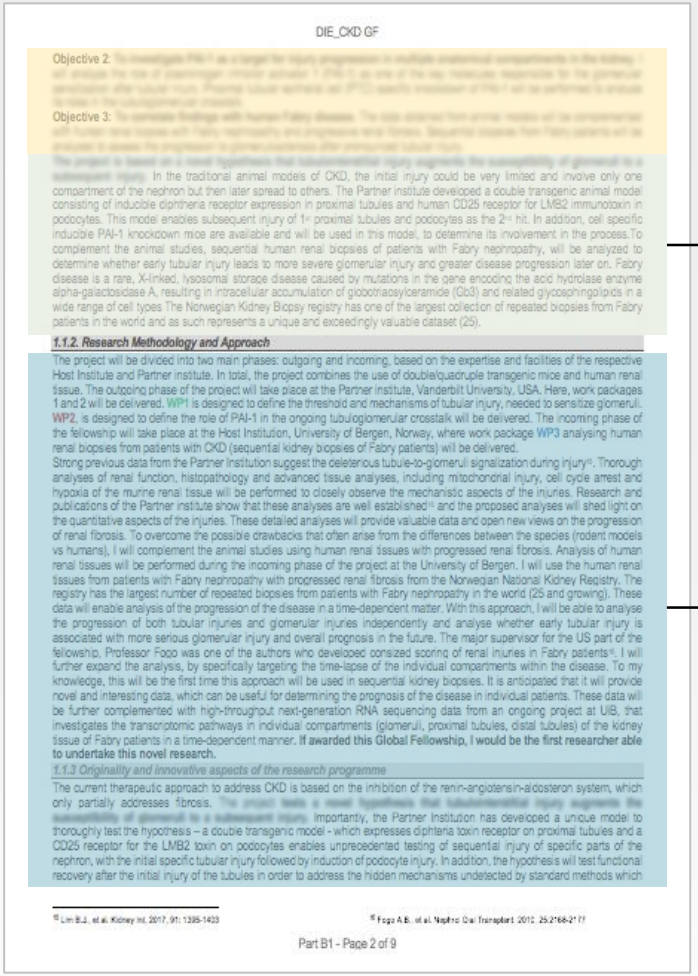

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Novelty

- Novel hypothesis
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Theoretical approach and Methodology

***How** are you going To reach your goals?*

Theoretical approach and Methodology

- General/solid research design
- Based on your skills and ambitions
- Methods carefully and thoroughly justified
- Data collection instruments and procedures
- Planned data analysis

- Ethical issues
- Gender perspectives
- Risk assessment and mitigation measures

Theoretical approach and Methodology

seek to profoundly characterize the changes in clonal cellular dynamics enforced by the selection pressure provoked by an obese environment using high-complexity DNA barcoding (***specific aim #1***). To enable further downstream studies of the fittest subpopulation of tumors in obese mice, we further aim to characterize and analyze the transcriptome of *in vivo* selected cancer cells with higher metastatic potential in obese compared to non-obese mice (***specific aim#2***). Next, established BioBanks will be scrutinized in an unbiased manner using systemic search algorithms of obesity-related changes in the gene expression profile of aggressive cancers in patients (described in detail in section *2.4 Experimental Motivation for the Proposal, specific aim #3*) as well as for the enrichments/depletion of genetic mutations in obese compared to non-obese cancer patients (***specific aim #4***).

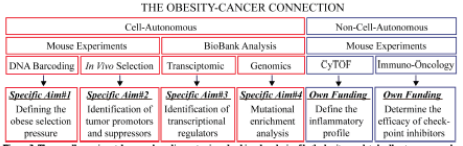


Figure 3. The overall experimental approach applies systemic and unbiased analysis of both obesity-regulated cell-autonomous and non-cell-autonomous processes of the obesity-cancer connection.

2.3 Clinical Perspectives

The ultimate goal of translational research is to develop new therapeutic possibilities. The proposed studies are designed to answer the question: are obese cancer patients in need of a different treatment regimen than non-obese patients? Thus far, obese cancer patients are standardly receiving the same treatment as non-obese patients, although we do not have strong evidence underlying this treatment strategy[31]. Given the altered selection pressure on the heterogeneous tumor population in the obese microenvironment, it is likely that the evolutionary fittest tumor cell in obese patients is phenotypically distinct from that seen in the non-obese cancer patients. Combined with the strong epidemiological connection between obesity and cancer mortality, it is therefore very plausible that obese cancer patients could benefit from more precise and targeted treatment regimens by combining currently applied and new drugs. It is our hope that the mechanistic insight gained in this proposal will pave the way for such development of therapeutic approaches to inhibit tumor progression in obese patients.

2.4 Experimental motivation for the proposal and preliminary results

To establish a strong clinical foundation for our molecular studies of the obesity-cancer connection we first sought to confirm previous epidemiological studies on the relation between obesity and breast cancer[3,4,6,26,27,29,35]. To that end, the Mohn Cancer Research Laboratory, University of Bergen (Dr. Stian Knappskog and Dr. Per Eystein Lønning), has developed a comprehensive breast cancer BioBank that contains information on patient BMI, age, hormone receptor status and tumor transcriptome (Illumina beadchip) of 223 patients at the time of diagnosis as well as disease specific survival (~15 years follow up). After diagnosis all patients were treated with chemotherapy. Using this extensive cohort, we first found that overweight and obesity (defined by the world health organization as BMI>25) did not have any overall effect on disease specific survival (**Figure 4A**). Next, we stratified the patients according to clinical variables as age and hormone receptor status. Interestingly, we demonstrate that only in PM patients, high BMI was associated with significantly

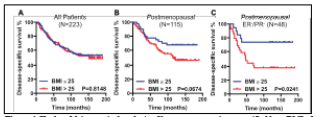


Figure 4. Kaplar-Meier survival analysis of breast cancer patients stratified by a BMI of 25 kg/m^2 (A) Survival curve of all patients included in the study (N=223) (B) Survival curve of postmenopausal patients, defined by age>50 years old (N=115) (C) Survival curve of postmenopausal patients with ER- PR-breast cancer (N=48). *Xiaosheng, Unpublished data.*

shorter disease-specific survival (**Figure 4B**). And further, this relation was even more pronounced and significant (LogRank test) in patients with ER and PR negative tumors (**Figure 4C**). ***Importantly, at the time of diagnosis there were no differences between the low and high BMI groups in either tumor size (48.1 cm^2 vs. 53.7cm^2, p=0.81) or tumor stage (all enrolled patients were stage III), strongly suggesting that in the PM/ER-/PR- breast cancer subgroup, the shorter disease-specific survival rates is caused by an affect on tumor aggressiveness including potential resistance to therapy and metastatic colonization.*** No connection between BMI and survival was observed in premenopausal ER$^+$/PR$^+$, ER$^+$/PR$^-$ or PM/ER$^-$/PR$^+$ patients despite similar BMI distributions.

The close association between obesity and cancer mortality in hormone receptor negative breast cancer patient groups suggest that obesity creates a metabolic environment that facilitates a selection of a more aggressive cancer cell subpopulation. We reasoned that this cellular adaption is reflected by gene expression changes and therefore extracted genes whose expression was deregulated in the PM/ER-/PR- breast cancer patients. Deregulated genes were defined by a fold change of 2 and a false discovery rate <0.05 (determined by Rank Product analysis) between the high (BMI>25) and low (BMI<25) BMI groups. The results are displayed as a volcano plot in **Figure 5A** and reveal a total of 56 down- and 45 up-regulated genes. To identify potential upstream e.g. transcriptional and post-transcriptional regulators that potentially regulates a network of these downstream genes and thus might form the foundation for a more efficient pharmaceutical targeting strategy, we next applied a de novo cis-regulatory motif discovery tool (FIRE). This algorithm utilizes mutual information theory to systemically and in an unbiased manner identify enriched/depleted 5' and 3' UTR motifs in a list of deregulated genes[33]. We and others, have previously used this algorithm to identify regulators of miRNA processing[34] adipogenesis[35] and cancer initistion[36]. The FIRE analysis revealed a single 5' [TATGACC] motif that was significantly enriched among down-regulated genes in the overweight and obese group (z-score 13.8; p-value: 2x10^{-6}; **Figure 5B**). Interestingly, this motif matches the canonical DNA binding site of the transcription factor PPARA (motif alignment p-value 0.0025).

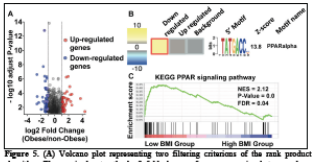


Figure 5. (A) Volcano plot representing two filtering criterions of the rank product algorithm. The x-axis denotes the log2 fold change of gene expression between obese (BMI>27) and non-obese (BMI<25) patients and the y-axis represents the significance levels of the expression differences calculated as the False Discovery Rate. Red highlights significant up-regulated genes in obese patients. Blue highlights significant down-regulated genes in obese patients. Yellow highlights selected down regulated genes that contain the 5' FIRE motif [TATGACC]. (B) Unbiased 5' and 3' motif discovery using the FIRE algorithm among deregulated genes as compared to background genes. (C) GSEA was performed using the microarray data to compare gene expression profiles between overweight (BMI>25) and non-overweight (BMI<25) patients. Enrichment plots of expression signatures gene set of KEGG PPAR signaling pathway. The barcode plot indicates the position of the genes in query gene set; red and blue colors represent positive and negative correlation with patients' BMI. (D)Pathways enrichment results showed that the PPAR signaling pathway was up-regulated in non-obese patients compared with obese patients. These gene-expression signatures were obtained from the KEGG database. *Xiaosheng Liu, Unpublished data.*

PPARA is a member of the Nuclear Receptor Family and is a main regulator of fatty acid homeostasis[37]. Consistent with the FIRE result, pathway analysis of the down-regulated genes revealed enrichment in genes associated with PPAR signaling and fatty acid regulation (**Figure 5C**). The function of PPARA is poorly described in tumor biology, but is extensively studied in field of metabolism. One of the main functions of the transcription factor is to induce the uptake of free fatty acid (FFA) from the blood stream into liver and muscle during fasting[37]. This prompted us to further inspect the specific genes that harbor the 5' FIRE motif. Interestingly, several of these are known to be involved in lipid uptake and storage e.g. CEDIA, CD36 and PLIN1. For, yet unknown reasons, it is believed that cancer cells actively refrain from utilizing external FFA as a fatty acid source, but rather prefer to rely on de-novo made fatty acids[38-40]. Interestingly, obesity results in increased levels of circulating FFA that upon entry into non-adipose cells such as pancreatic beta cells, cardiomyocytes, hepatocytes (and possibly cancer cells) are converted to ceramides – a process known as lipotoxicity due to the pro-apoptotic effects of ceramides[41]. ***Based on our preliminary data we therefore hypothesize that cancer cells in obese environments are selected for low expression of PPARA target genes to prevent lipotoxicity through apoptosis.***

To evaluate this hypothesis, we first tested whether ER/PR negative breast cancer cells are able to take up lipids in a PPARA dependent manner. We incubated MDA-MB-231 in media containing Bodipy-labeled FFA (C:16 Palmitic acid (PA)) in the presence or absence of a highly specific PPARA activator, fenofibrate[42] (FF), and measured the FFA uptake by FACS analysis (**Figure 6A**). Interestingly, this demonstrated that FFA uptake in cancer cells can be enhanced ~3.5-fold by PPARA activation. We next tested the effects of PPARA on PA-induced lipotoxicity by measuring apoptosis in PA treated breast cancer cells in both loss- and gain-of-function experiments. Depletion of endogenous PPARA by 55% using lentivally delivered shRNA's in MDA-MB-231 cells resulted in protection from PA induced apoptosis (**Figure 6B**). Conversely, treatment with FF forced an increased sensitivity to PA induced apoptosis (**Figure 6C**).

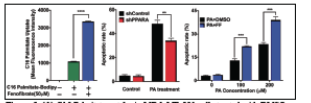


Figure 6. (A) C16 Palmitate uptake in MDA-MB-231 cells treated with DMSO or 50uM fenofibrate as determined by FACS. (B, C) Apoptosis as determined by Annexin V$^+$ FACS analysis in PPARA depleted (B) and PPARA activated (C) MDA-MB-231 cells in the presence or absence of C16 Palmitate (PA). Error bars represents SEM. **p<0.01, ***p<0.001. *Xiaosheng Liu, Unpublished data.*

Based on our data, we hypothesize that PPARA target genes are repressed in aggressive tumors in obese patients to counteract the detrimental effects of lipotoxicity. Also, and interestingly, these preliminary results raise the possibility of introducing FF as an anti-cancer therapy in the obese setting. FF is a widely used and FDA approved drug for the treatment of hypercholesterolemia and hyperlipidemia. In preliminary experiments, ER-/PR- EO771[43] cells were xenografted into high fat fed mice (10 weeks) and treated with a daily oral dose of 100mg/kg FF or vehicle. FF treatment significantly reduced tumor growth (**Figure 7**). These exciting initial experiments lend further support for the use of FF as a therapeutic possibility in obese breast cancer patients.

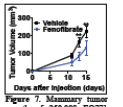


Figure 7. Mammary tumor growth of 250.000 EO771 cells grown in high fat diet fed C57BL6 mice. Mice was treated with either vehicle or 100mg/kg fanofibrate given daily by oral gavage. n=12/group. *Line Pedersen, Unpublished data*

Taken together, these data provides proof-of-concept that cancer cells exploit the altered metabolic landscape of obese cancer patients through selection of a more aggressive subpopulation and suggests a novel and therapeutically interesting PPARA-linked mechanism for the obesity-cancer connection in hormone receptor negative breast cancer.

3. Research Plan

The proposed research plan aims to create an interdisciplinary, innovative and mechanistic framework to explore the biology of tumor progression in obese breast cancer patients. As such, the project comprises four specific objectives that address the central hypothesis:

Specific aim #1: Clonal dynamics analysis of tumor progression in obese hosts via DNA barcoding.
Specific aim #2: Characterization of aggressive cancer cell populations by in vivo selection in obese and non-obese mice.
Specific aim #3: Define the molecular role of PPARA in obesity-induced hormone receptor negative breast cancer.
Specific aim #4: Mutational enrichment analysis in obese and non-obese human hormone receptor negative breast cancer samples.

Specific aim #1: Clonal dynamics analysis of tumor progression in obese hosts via DNA barcoding. The development of intratumoral clonal heterogeneity during tumor progression in obese and non-obese mice breast cancer cells will be tracked by DNA barcoding[44]. Compared to next-generation sequencing DNA barcoding has the advantage of higher sensitivity as well as including effects of epigenetic heterogeneity[45]. We aim to introduce single DNA barcodes with a complexity of approximately 50.000 in MDA-MB-231 and EO771 breast cancer cells using lentiviral delivery systems (Cellcracker Barcode System, Cellecta). 500.000 cells (each clone will be represented by 10 cells) will then be injected into obese and non-obese mice. Following removal of the tumor, DNA will be isolated, the barcodes amplified by PCR, sequenced by next generation sequencing and the abundance of each bar code determined. By comparing the barcode

Theoretical approach and Methodology

Example

... This concept will be tested extensively in both mouse models and in BioBank material from breast cancer patients. In mice, we seek to profoundly characterize the changes in clonal cellular dynamics enforced by the selection pressure provoked by an obese environment using high-complexity DNA barcoding (**specific aim #1**). To enable further downstream studies of the fittest subpopulation of tumors in obese mice, we further aim to characterize and analyze the transcriptome of in vivo selected cancer cells with higher metastatic potential in obese compared to non-obese mice (**specific aim#2**). Next, established BioBanks will be scrutinized in an unbiased manner using systemic search algorithms of obesity-related changes in the gene expression profile of aggressive cancers in patients (described in detail in section 2.4 Experimental Motivation for the Proposal, **specific aim #3**) ...

Halberg, NFR FRIPRO Young Research Talents 2017

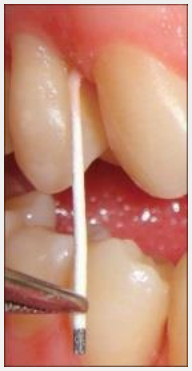
In total, the project combines the use of double/quadruple transgenic mice and human renal tissue. The outgoing phase of the project will take place at the Partner institute, Vanderbilt University, USA. Here, work packages 1 and 2 will be delivered. **WP1** is designed to define the threshold and mechanisms of tubular injury, needed to sensitize glomeruli. **WP2**, is designed to define ... The incoming phase of the fellowship will take place at the Host Institution, University of Bergen, Norway, where work package **WP3** analysing … will be delivered.

Babickova, MSCA-IF-GF 2018

Theoretical approach and Methodology

Example

Gingival fluid samples and 16S rRNA sequencing



Figur 4: Gingival fluid sampling

Gingival fluid from RHINESSA (Bergen centre) and ECRHS (Bergen and Tartu) will be analysed by high throughput sequencing. Gingival fluid, from between the teeth and gum (Figure 4), was collected with sterile paper points at 5 per-protocol predetermined sites in the lower jaw and 5 sites in the upper jaw. These were frozen directly after collection, in separate vials for the upper and lower jaw samples.

...

The analyses were performed at the UNC Microbiome Core Facility at the University of NorthCarolina, USA. The ECRHS III and IV gingival fluid samples will be analyzed in Norway (subcontractor) by the same methodology. In short, bacterial DNA from the 16S rRNA gene is isolated from the gingival fluid and the V3-V4 region of the 16S rRNA is amplified and sequenced by Illumina® MiSeq platform.

...

After laboratory analyses, me and my ERC team will perform further analyses in QIIME and R and other relevant statistical softwares.

Bertelsen, ERC Starting Grant 2018

Impact

This chapter should describe the importance of the anticipated results in terms of the potential ***scientific impact***, and, if relevant, the potential ***societal impact*** of the research. The potential impact can be in the ***short or longer te***rm.

The chapter should also specify the planned measures for ***exploitation, communication and dissemination*** of the project results.

Proposal structure

Excellence

Impact

Implementation

- Expected/Potential impact of the proposed research
  Scientific, Societal, Economic
- Measures to maximise impact
  Dissemination, Exploitation and Communication

Impact, impact and impact!

Make sure that the reader cannot forget **your** proposal

Objectives	*Why do we want to achieve*
Results	*What do we want to achieve*
Impact	*What are these results going to bring to society* Wherever possible use quantified indicators and targets

The Framework
Three Impact dimensions

Scientific impact
Create and diffuse high-quality new knowledge, skills, technologies and solutions to glabal challenges

Societal impact
Strengthen the impact of research and innovation in developing, supporting and implementing EU policies, and support the uptake of innovative solutions in industry and society to address global challenges

Economic impact
Foster all forms of innovation, including breakthrough innovation and strengthening market deployment of innovative solutions

The Framework
Key impact pathways

Scientific impact
1. Creating high-quality new knowledge
2. Strengthening human capital in R&I
3. Fostering diffusion of knowledge and Open Science

Societal impact
4. Addressing EU policy priorities through R&I
5. Delivering benefits & impact via R&I missions
6. Strengthening the uptake of innovation in society

Economic impact
7. Generating innovation-based growth
8. Creating more and better jobs
9. Leveraging investments in R&I

…then tailor to your proposal

Scientific impact

Create and diffuse high-quality new knowledge, skills, technologies and solutions to glabal challenges

…taken together, these will **ensure** thorough **analysis** of the renal tissue and the **production of novel data** with the potential to identify **new therapy targets** or markers of CKD…**These data will be correlated with the transcriptomic analyses** of the biopsies with regard to the specific compartment and the state of the injury… This type of analysis of NKBR data **has not yet been performed** and will provide a **pool of new exciting data** which I will be **the first person to analyse**. This will provide the basis for **a novel approach** of combining data analyses from different sources (detailed compartment based analysis of histology vs transcriptomics), with the potential for me to develop a **new area of research**, independent of my supervisors.

Babickova, MSCA-IF-GF 2018

…then tailor to your proposal

Societal impact

Strengthen the impact of research and innovation in developing, supporting and implementing EU policies, and support the uptake of innovative solutions in industry and society to address global challenges

…**WHO** states that the prevalence of **asthma and COPD will increase in the coming years** [1, 3]. With **rising life expectancy and ageing populations** in many countries [54], and **reduced quality of life** which follows with these diseases, this will lead to a higher burden of poor life quality **for a large part of the population worldwide** - unless we can find ways to prevent the development of chronic respiratory diseases… Worldwide, **the 2010 Global Burden of Disease Study** estimated that oral conditions affected 3.9 billion people [55] and that the estimation of untreated caries of permanent teeth was 2.4. billion [56]… **A study on elderly people in Norway and Sweden** found that **inequality in oral health** was associated with **social conditions** (e.g. educational level, foreign country of birth, marital status and social network) [57]. If I can provide evidence for a causal relationship between oral microbiome/oral health and lung health, **these results will provide a rationale** for an oral hygiene program to improve respiratory health. **Because poor oral health is associated with low social economic status**, the implementation of the results of this project has **huge potential to reduce social inequalities in health…**

Bertelsen, ERC Starting Grant 2018

…then tailor to your proposal

…then tailor to your proposal

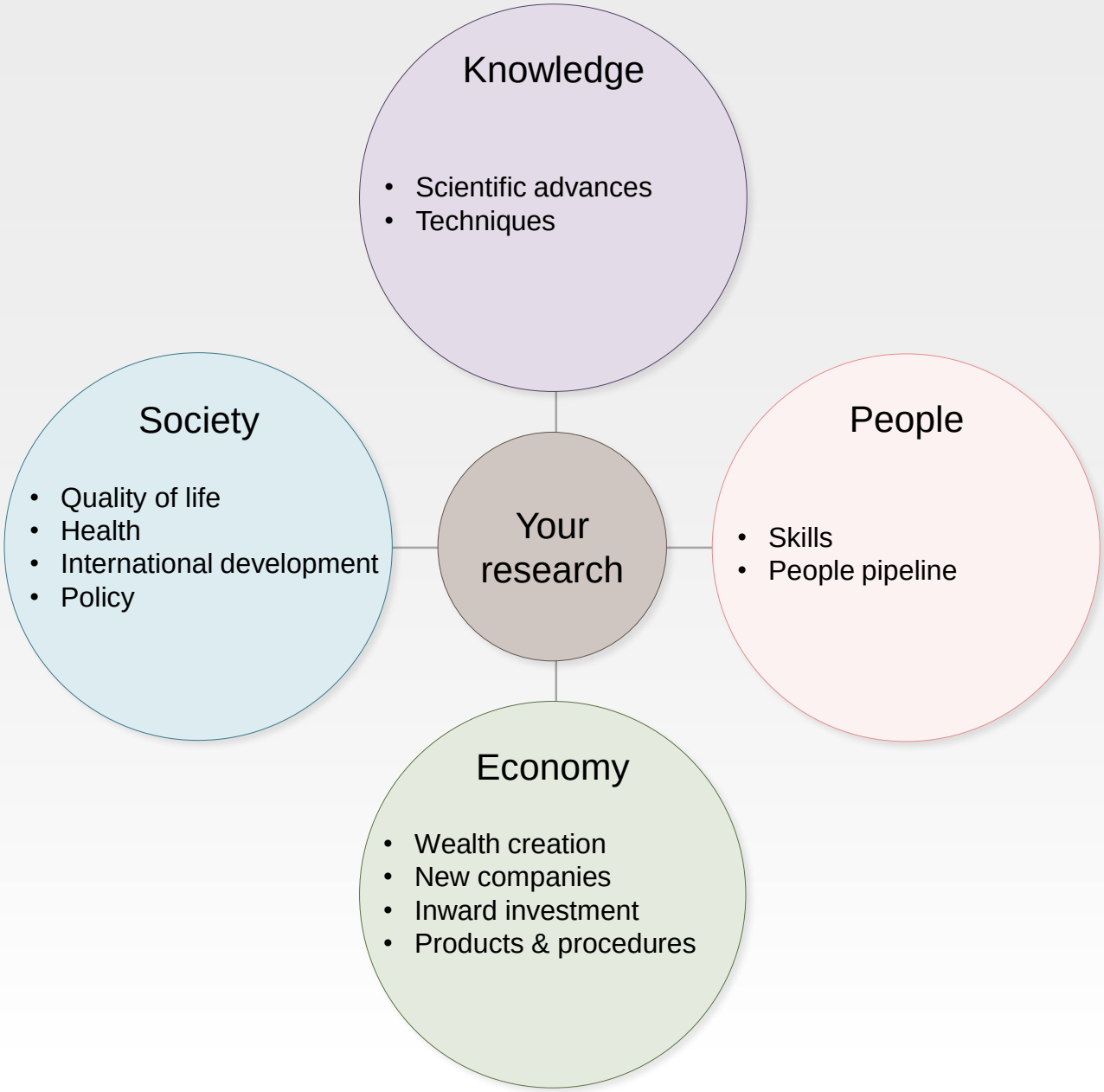
Economic impact

Foster all forms of innovation, including breakthrough innovation and strengthening market deployment of innovative solutions

…The whole set of actions designed in MY-GATEWAY focuses on **start-ups** in the Czech Republic, Romania and Slovenia as the ultimate end-users. Thanks to our efforts, they will be **better connected to the local, regional and European ecosystems**, they will have **more chances to meet key players** such as start-up support organisations, accelerators, investors. They will have **better access to qualified employees** and will be better positioned to successfully **apply for** commercial procurement, public and private **funding.** In a longer term perspective, we expect the involved start-ups to have a **competitive advantage to their growth strategy** compared to those that did not participate in activities.

Increasing the connectivity of the targeted ecosystems and facilitating their access to funding opportunities **has indirect, but relevant, impact on their possibility to employ new staff**. Furthermore, at the ecosystem level, this brings **crucial advantages**, as **young people may be encouraged to launch their own business**, while earlier they would have preferred a corporate job…

Europa Media, 2018


Knowledge
• Scientific advances
• Techniques
Society
• Quality of life
• Health
• International development
• Policy
Your research
People
• Skills
• People pipeline
Economy
• Wealth creation
• New companies
• Inward investment
• Products & procedures

Proposal structure

Excellence

Impact

Implementation

- Expected/Potential impact of the proposed research
  Scientific, Societal, Economic
- Measures to maximise impact
  Dissemination, Exploitation and Communication

Dissemination means sharing research results with potential users - peers in the research field, industry, other commercial players and policymakers. By sharing your research results with the rest of the scientific community, you are contributing to the progress of science in general.

Whereas **exploitation** is the use of results in public policymaking (providing a service, or in standardization activities) or for commercial purposes (creating and marketing a product or process).

Communication	≠	**Dissemination**
About the **project** and **results**		About **results only**
Multiple audiences *Beyond the project´s own community (include the media and the public)*		**Audiences that may use the results** in their own work *e.g. peers (scientific or the project´s own community), industry/other commercial actors, professional organisations, policy-makers*
Inform and **reach out** to society, show the benefiy of research		**Enable** use and **uptake** of **results**

Dissemination

Example

... Data and results generated by DIE_CKD will be disseminated broadly to the **scientific communities** to secure the spread of the knowledge **in the field of** renal diseases, but **potentially also** other diseases where tissue fibrosis and inter-cellular communication may play a role (e.g. liver cirrhosis). Data will be published via **open access journals**, optionally utilizing dedicated funds at the Partner and Host Institutions. **Sensitive data** falling under privacy rules will not be shared with third parties and deposited on a secure serves at the Partner and Host Institutions. The project aims to generate at least 3 original articles in **international, peer-reviewed journals** with forefront leading impact in the targeted fields (**e.g. Am J Physiol Renal Physiol, PloS ONE, Am J Pathol**). This is **a realistic target** given my proficiency in manuscript preparation and the innovative nature of the research to be carried in DIE_CKD. In addition, I aim to present the data, at **international and local conferences**, at least 3 per year (**e.g. Am. Soc. Nephrology, European Renal Assoc., and Bergen Spring meeting of nephrology**), and Institutional workshops and seminars…

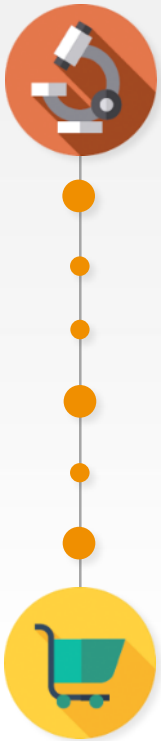
Babickova, MSCA-IF-GF 2018

Exploitation

Example

…**Intellectual Property Rights (IPR**): DIE_CKD generates knowledge on cell-cell signalling, molecular pathways and methodology protocols which can be further used without restrictions. **I will regularly scan** for protectable IP in the project and liaise with legal advisors and the **Bergen Technology Transfer Office (BTO)** with whom UiB have close ties, to determine **the routes and conditions** of protection…

Exploitation route



Advancement of knowledge (case studies, guidelines, best practices,...)

Contribution to standards

Initiation of new projects

Contribution to standards (recommendations, conclusions, reports for policy-makers)

Setting of a new business

Education, training

Licensing

Sales of new products

Communication

Example

Information pertaining to ongoing activities and project results will be disseminated to a variety of audiences**, both from academic and non-academic**, in order **to increase awareness of the project and it's results** and to ensure a full and broad understanding of the implications of the project and it's outcomes. The topic of DIE_CKD: decoding the development of progressive renal diseases – with potential applications to other targets – is relevant to the **following stakeholders: 1)** the scientific community, **2)** patients and their families **3**) relevant patient associations, **3)** health professionals, **4)** potential business partners incl. drug developers, **5)** research funders, **6)** students and scientists looking for research opportunities, and **7)** the general public. The Host's **website** offers opportunities to inform about the project and its breakthroughs. I will generate my own **scientific blog** and **explore the professional network** media like LinkedIn and ResearchGate for the purpose of updating audiences on my project. I plan to write articles for the **local popular press** both paper and online (e.g. **Atlas of science**, as used before: https://atlasofscience.org/the-capillary-web-gets-lost-in-diseased-kidneys/) describing my work and the benefit from participating in the MSCA-funded project. **UiB offers a platform** for science communication (annual **"Research Days"**, which includes a "Researcher's Night") which I plan to use as an outlet. For communication of my project activities to the public, I will always use **non-technical language**. I will take full advantage of the **UiB Department of Communications** to assist me in disseminating my research via appropriate channels to non-scientific audiences in Norway and beyond.

Communication

Example

I have experience with communication of results from previous research in **interviews on radio, TV and on podcasts**. The ECRHS and RHINESSA studies have websites with information for **participants, researcher, and for the general public**. For the RHINESSA study we **have a webpage in Norwegian** with information aimed at the Norwegian study participants. All the other study centres also have **webpages in their local languages**. On our **English webpage**, we provide information intended for **both researchers** as well as for the **public in general**. We also produce **newsletters** for all the RHINESSA and ECRHS participants in the Bergen study centre with information about the most recent findings. These are mailed to all participants and published on the RHINESSA website. Press publicity and popular summary disseminations of all our publications are made available on the website. Furthermore, my intention is that the **results from BRuSH will contribute to oral health awareness** campaigns that will target the general public. I believe there is a huge benefit to the society to provide dental care at reduced cost, in particular to people with low income and low social status. **We will inform policy makers, professional health care providers and user organizations about the results** from BRuSH, and discuss the usefulness of different intervention strategies (e.g. dental care at lower cost or awareness campaigns). **My goal is to reach a European and Worldwide audience**, e.g through the **WHO information webpages** and other relevant information channels that can reach a broad audience.

Upcoming calls

Prices and Awards

Upcoming calls relevant for IGS

Nordforsk

Call for proposals for interdisciplinary research projects

The program is specifically aimed towards genuinely interdisciplinary projects that combine disciplines which are far removed from one another and rarely collaborate, or that pursue an original research question requiring the exact combination of competencies from different disciplines proposed in the application.

- At least two of the three areas of science:
  Life science; Physical Sciences & Engineering; Social Sciences and Humanities
- 10 - 15 mill NOK, up to 4 years
- Partners from at least three Nordic countries
- **Deadline (pre-proposal):** 13 November 2019, 13.00 CET

Upcoming calls relevant for IGS

Nordforsk

Nordic Research Infrastructure Hubs

To strengthen Nordic cooperation on a specific, large-scale research infrastructure project with the aim of building and expanding Nordic competence within its area.

- Workshops, training, seminars and conferences; mobility including guest researchers; other expenses that promote the cooperative framework and are necessary for implementation of the hub.
- 3 mill NOK for the period 2020-2022.
- **Deadline**: 22 October 2019

Upcoming calls relevant for IGS

European and Developing Countries Clinical Trials Partnership (EDCTP)

10 calls for proposals

To support clinical research and related activities on poverty-related diseases:

- **Paediatric drugs formulations for poverty-related diseases (RIA)** - 10 October 2019
- **Strategic actions on product-related implementation research (RIA)** - 10 October 2019
- **Strategic actions supporting large-scale clinical trials (RIA)** - 7 November 2019
- **New drugs and vaccines for priority pathogens in antimicrobial resistance (RIA)** - 7 November 2019
- **Ethics and regulatory capacities (CSA)** - 21 November 2019
- **Career development fellowships (TMA)** - 27 November 2019
- **EDCTP-AREF Preparatory fellowships (TMA)** - 27 November 2019
- **Senior fellowships Plus (TMA) -** 1 February 2020
- **Clinical research & product development fellowships (TMA)** - 28 February 2020
- **Vaccines against Lassa virus - joint call with CEPI (RIA)** - 7 April 2020

Relevant upcoming calls
Horizon 2020

Marie Skłodowska-Curie actions (MSCA)

To help develop training networks, promote staff exchanges and fund mobility programmes between countries, optionally to the non-academic sector.

- Innovative Training Networks (ITN) - MSCA-ITN-2020 - Aim to train a new generation of creative, entrepreneurial and innovative early-stage researchers, able to face current and future challenges and to convert knowledge and ideas into products and services for economic and social benefit.

  Deadline: 14 January 2020

European Research Council (ERC)

Supports the best of the best across all fields of science.

- ERC Consolidator Grant - For researchers of any nationality with ***7-12 years of experience since completion of PhD***, a scientific track record showing great promise and an excellent research proposal who have established a research team and want to strengthen the team and their career in Europe. Up to €2 Million for 5 years.
  Deadline: 4 February 2020

Relevant upcomin… Horizon 202…

WEBINAR: on 2020 Calls for Infectious Diseases and Improving Global Health – 18 October

Societal Challenge 1

- Scaling up innovation for active and healthy ageing - ID: SC1-HCC-08-2020; **Deadline:** 22 April 2020

  The Action is expected to develop and apply user-centered strategies for implementation of transformative solutions, in particular in the field of active and healthy aging, smart age-friendly homes and chronic disease management

- Supporting deployment of eHealth in low and lower middle income countries in Africa for better health outcomes - ID: SC1-HCC-09-2020; **Deadline:** 22 April 2020

  Projects should reach a higher level of international cooperation and networking in eHealth programs and policies between European countries or regions and low and middle income African countries, focusing on areas that are beneficial to the target countries / regions and their citizens in eHealth.

- New approaches for clinical management and prevention of resistant bacterial infections in high prevalence settings - ID: SC1-BHC-34-2020; **Deadline:** 7 April 2020

  Proposals should focus on the identification of best practices, and the development and validation of interventions, infection prevention and clinical management plans for dealing with resistant bacterial infections in high prevalence settings.

Relevant upcoming calls
Research Council of Norway

FRIPRO (Researcher Project, Young Research Talents, Mobility Grant)

BEHANDLING, BEDREHELSE, HELSEVEL

Deadline: 6 May 2020

Milestone Project – Research Commercialisation Project

A short-term Commercialisation Project undertaken to complete the next, most critical milestone phase in order to move along the long-term commercialisation pathway

- 200 000 – 500 000 NOK, project length up to a year

Fellesløftet 2020

Deadline: 6 May 2020

- Transdisciplinary
- Groundbreaking and novel research
- Generation of new research fields, new methodology, theories and perspectives
- Collaboration between two of these three research areas:
  - Social science and Humanities
  - Life science
  - Natural sciences and Technology

Prices and Awards

The Meltzer Foundation

Research Funds. **Deadline:** 1 December 2019
To promote the academic activities of the University of Bergen (and others) and to support especially gifted students.

- Project Grants for students and PhD
- Travel grants

Awards. **Deadline:** usually 1 December
- Award for Young Researchers
- Award for Excellence in the Dissemination of Research
- Honorary Award for Excellence in Research

Prices and Awards

Research Council of Norway – Awards

- Award for Excellence in Dissemination
- Young Outstanding Researcher
- Innovation Award

Olav Thon Foundation - Awards. **Deadline:** 15 September

- Award for Excellent Education
- International Research Award for Mathematics/Natural Sciences and Medicine

Søren Falch awards. **Deadline:** 1 March

- Organized by the faculty of Medicine
- Junior Award
- Senior Award

Useful information

- Department newsletter
- Externel funding webpage
- Events at Research Council of Norway
- Project Establishment Support (PES) – To be used before a specific deadline: consultancy, travel, meeting or workshops, «frikjøp», etc.
- Positioning Funding (POS) – Not connected to a specific call, competence building, networking, etc. towards a future Horizon2020 application

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