Evaluation of Medicine and Health (EVALMEDHELSE) 2023-2024

Self-assessment for research groups

Date of dispatch: **15. September 2023**
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Institution (name and short name): Stavanger University Hospital (SUH)
Administrative unit (name and short name): Stavanger University Hospital (SUH)
Research group (name and short name): Breast Cancer Research group (FFB)
Date: 31.01.24
Contact person: Håvard Søiland / Kristin Jonsdottir
Contact details (email): hsoiland@gmail.com / kristin.jonsdottir@sus.no

Content

Innhold

1. Organisation and strategy

1.1 Research group´s organisation

Describe the establishment and the development of the research group, including its leadership (e.g. centralised or distributed etc.), researcher roles (e.g. technical staff, PhD, post docs, junior positions, senior positions or other researcher positions), the group's role in researcher training, mobility and how research is organised (e.g. core funding organisation versus project based organisation etc.).

The Research Group for Breast Cancer (FFB) was established in 2014 and focuses on the entire treatment course for breast cancer patients. FFB is a collaboration group comprised of several partners, but mainly consist of researchers from the three departments i.) Department of Surgery (research group for endocrine and breast surgery) ii.) Department of Pathology (research group of quantitative Pathology) and iii.) Department of Hematology and Oncology (research group for Cancer and Medical Physics). The group is led by Professor Håvard Søiland at the Department of Surgery in strong collaboration with Professor Emiel Janssen at the department of Pathology and Senior consultant in oncology Bjørnar Gilje, MD, PhD at Department of Hematology and Oncology.

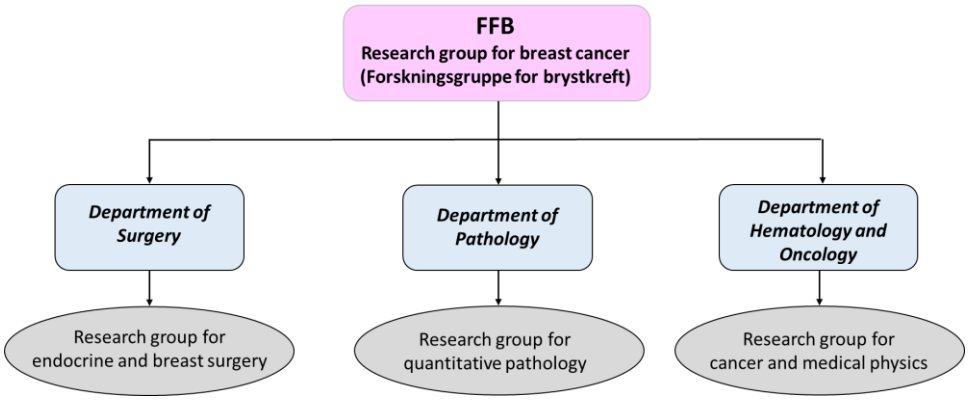

Figure illustrating the organization of the breast cancer research group (FFB)

Håvard Søiland is a breast cancer surgeon and holds a professorship of surgery at the University of Bergen since 2011. He has been involved in, and initiated, several breast cancer project at the hospital since he was finished with his PhD in 2008.

FFB is a research group with broad expertise. Among the 33 members included in FFB are molecular biologists, pathologists, radiologists, medical physicists, oncologists, biostatisticians, breast and endocrine surgeons, plastic surgeons, nursing researchers, nurses, research coordinators and user representatives. Four of the members are professors, two are PhD students and one is a post doc. Most of the members have clinical or administrative work at the hospital as their main activity, but four members works full-time (100%) with research or biobanking. Therefore, most of the research carried out in the research group is externally funded through various projects, highlighted in table 4.

As FFB is a collaboration group the members are mostly associated with other research groups, either at the hospital or at the university. Therefore, FFB organizes four meetings a year where members present results and provide updates on all ongoing breast cancer projects, for the exchange of ideas and interdisciplinary collaboration.

Table 1. List of number of personnel by categories
Instructions: *Please provide number of your personnel by categories.*
For institutions in the higher education sector, please use the categories used in DBH, https://dbh.hkdir.no/datainnhold/kodeverk/stillingskoder. Please add new lines or delete lines which are not in use.

	Position by category	No. of researcher per category	Share of women per category (%)	No. of researchers who are part of multiple (other) research groups at the admin unit	No. of temporary positions
No. of Personnel by position	Department chief physician	2	0%	1	
	Head of department	3	66%	1	
	User participation	1	100%		
	Chief adviser	1	100%	1	
	Professional development nurse	1	100%		
	Associate professor	1	100%		
	MD in specialization	1	100%		
	Senior physicians	4	25%	3	
	PhD-candidates	2	100%	1	2
	Section leaders	3	100%	2	
	Chief Medical Office	4	50%	3	
	Senior Advisor	1	0%		
	Medical physicist	3	33%	3	
	Radiation therapist	2	50%	2	
	Chief engineers	2	50%	2	
	Special Engineers	1	100%	1	
	Special consultant	1	100%		
Of these, no. of personnel has dual positions					
	Professors	4	25%	2	
	PhD- students 50%	2	100%	2	2
	Post Docs 50%	1	100%	1	1

1.2 Research group´s strategy

a) Describe the research group's main goals, objectives and strategies to obtain these (e.g. funding, plans for recruitment, internationalization etc.) within the period 2012-2022.

The research group's main goal is to improve the diagnostics and treatment of breast cancer patients. More specifically, this includes the following objectives i.) improving diagnostics through precision medicine, and new biomarker discoveries, ii) improving treatment through participation in clinical studies, iii.) improving follow-up through early detection of disease progression, based on biomarker analyses and iv.) improving patients 'quality of life.

To achieve this goal, the group has had the following strategies in the period 2012-2022.

1.Building infrastructure for biobanking. Increased research activities have resulted in increased number of breast cancer projects and therefore a need of build infrastructure of biobanking.

Breast cancer is special in that late relapse and deaths may occur 5-30 years after the primary tumour was removed. This has led to the foundation of a large regional **p**rospective **b**reast **c**ancer **b**iobank (**PBCB**) where the aim is to follow all included patients for 10 years. Since 2012, PBCB has collected liquid biopsies in the form of blood- and urine, and tissue samples together with clinical information and patient-reported data (questionnaires = PROM data) of almost 1200 patients who have undergone breast cancer treatment at Haukeland University Hospital (HUS) or Stavanger University Hospital (SUH). Additionally, we have biobank related to the EU project **REBECCA**. These Biobanks have contributed to new and better biobank infrastructure for biobanking at SUH during the period 2012-2022. Furthermore, these collections enables several important types of studies on breast cancer in our region, and has formed the basis for research collaboration nationally and internationally.

2.Building state-of-the-art laboratory facilities and biomarker research. The group has contributed significantly to the hospital's provision of facilities for next generation sequencing, digital pathology, mammography, and expanded radiology for personalised medicine. The biobanking and the lab facilities have given the research group opportunities for extensive research on biomarkers, both for improvement of diagnostics and early detection of disease progression. There have been many publications on these topics throughout the years.

3. Participate in clinical studies: Members at the Department of Hematology and Oncology have a long history of conducting high-quality clinical studies. In recent years, SUH has also received external funding for establishing a general infrastructure for running of clinical trials at the hospital. This has resulted in further increased participation in clinical studies to the benefit of the patients.

4. Multidisciplinary team. Through a cooperation agreement the three departments work together in The Research group for Breast cancer, and together we contribute to cross disciplinary research that increases opportunities for external research funding. This collaboration is continued in the EU project REBECCA.

5. International collaboration Through our multidisciplinary team and research the group has become an attractive partner for national and international breast cancer partners, as well as for recruitment of new researchers.

6. **Funding:** Members of the group apply for external funding, both nationally and internationally, to carry out high-quality research in order to improve the diagnostics and treatment of breast cancer patients.

*b) Please describe the **benchmark** of the research group. The benchmark for the research group should be written by the administrative unit in collaboration with the research group. The benchmark can be a reference to an academic level of performance (national or international) or to the group's contributions to other institutional or sectoral purposes*.

The administrative unit at SUH expects the research group to conduct international recognised research on breast cancer and related disorders. Key benchmarks for success in the period 2012-2022 are:

Research Group and Resources

1. Educate PhDs and postdocs in order to increase the breast cancer research activity at the hospital.
2. Strengthen existing collaborations, and establish new ones, to utilize the data/results and resources as much as possible to obtain a broader research activity.
3. Increase resources from external funding.

Scientific

1. Increase the number of publications in highly recognized international journals (level 2 journals).
2. Increase international collaboration and international co-authorship.
3. Increase the number of projects and clinical trials managed by members in the group.
4. Increase the number of professor-competent employees.
5. Participate in EU projects and thus contribute to research-based innovation.

Dissemination

1. Create awareness of our breast cancer research through dissemination of the results in popular form on the web, in social media, through presentations, at www.brystkreftforskning.no, SUH's website, local newspapers, radio and television.

Economic

1. Increase overall research funding from national and international sources.
2. Increase our participation in research project funded by the Norwegian Research Council (NFR), the Norwegian Cancer Society and the EU, which have the largest calls for tenders.

User involvement

Facilitate active collaboration with user representatives, defined as patients and/or their relatives, in all projects that originate from the research group. User representatives must be involved in all stages of the research projects, and meetings must be held continuously throughout the project period.

c) Describe the research group`s contribution to education (master´s degree and/or PhD).

Several of the members of the research group contributes to teaching both internally at the hospital, at the international high School in the region, at the University of Stavanger, and the University of Bergen. The lectures have been for medical students, biological chemistry students and high school students attending the research education program at the international school of Stavanger. Professor Emiel Janssen has been responsible for a bachelor course in Basic pathology and Professor Oddmund Nordgård for a bachelor course in molecular genetics and bioinformatics (BIO230) at the University of Stavanger. Professor Kirsten Lode hosts a qualitative research forum four times annually, serving as a platform for in-depth discussions on qualitative research methodology. In addition to this, members of the FFB research group also contribute to education through dissemination of research results through presentations at national and international conferences/meetings.

Moreover, the research group has supervised in total 26 PhD students, 44 master- and 26 bachelor students.

d) Describe the support the host institution provides to the research group (i.e., research infrastructure, access to databases, administrative support etc.).

The administrative unit supports all research groups at the hospital with research administration related to external funding, and in particular funding and project management related to EU-financing. The hospital gives external and internal approval of research projects, and they provide expertise with contracts/agreements. Under the administrative unit, there is also a section for biostatistics, a biobanking unit and a clinical research unit that supports the groups with statistics and data management as well as collection of samples in clinical studies.

The breast cancer research group have received help from the administrative unit regarding biobanking, structuring and the establishment of structured databases. In connection with the EU projects and other international project, the administrative unit has supported the project management and assisted with contracts/agreements.

1.3 Relevance to the institutions

Describe the role of the research group within the administrative unit. Consider the research group's contribution towards the institutional strategies and objectives, and relate the research group`s benchmark to these.

The breast cancer research group have contributed to several goals in the institutional strategies such as:

- collection of biological material for research purpose, stored in established biobanks, which is both an institutional and national strategy.
- being involved in two big EU projects (CLARIFY and REBECCA), which has increased the chare of external funding to the hospital.
- extensive external and international funding to their breast cancer research from different sources
- more international collaboration
- more publications in higher ranked journals
- a strong collaboration with the users through Stavanger breast cancer society and involvement of the user representatives with regular meetings throughout the entire project period.

1.4 Research group´s resources

Describe the funding portfolio of the research group for the last five years (2018-2022).

The breast cancer research group has received funding for several projects using the PBCB material: Personalized Monitoring in Breast Cancer (PhD and post doc scholarship) and Long-term molecular monitoring of operable breast cancer patients. These fundings come from the Western Region of Health in Norway, from The Folke Hermansen foundation and the SR bank foundation (both local

funds). In recent years, the projects have received 10 million NOK from SR bank foundation for a period of a 5 years (2023-2027).

In addition to this, the group also have received funding from Western Norway Regional Health Trust to "Implementation of artificial intelligence as support tools for pathology in Helse Vest" as well as EU funding for the two projects i) REsearch on BrEast Cancer induced chronic conditions supported by Causal Analysis of multi-source data (REBECCA) and ii) CLoud ARtificial Intelligence For pathologY (CLARIFY).

Table 2. Describe the sources of R&D funding for the research group in the period 2018-2022.

	2018 (NOK)	2019 (NOK)	2020 (NOK)	2021 (NOK)	2022 (NOK)
Basic funding					
Funding from industry and other private sector sources			2 000 000	1 500 000	1 500 000
Commissioned research for public sector					
Research Council of Norway					
Grant funding from other national Sources		1 977 000	5 977 000	6 937 000	8 845 335
International funding e.g. NIH, NSF, EU framework programmes		1 200 000	9 700 000	1 000 000	
Other	60 000	2 155 000	949 000	2 772 000	

1.5 Research group´s infrastructures

Research infrastructures are facilities that provide resources and services for the research communities to conduct research and foster innovation in their fields. These include major equipment or sets of instruments, knowledge-related facilities such as collections, archives or scientific data infrastructures, computing systems communication networks. Include both internal and external infrastructures.

a) Describe which national infrastructures the research group manages or co-manages.

Members of the research group for breast cancer are involved in several national boards and networks. These include:
Biobank Norway, Norwegian national research infrastructure body (NorCRIN), National network for breast cancer research, Regional prospective breast cancer biobank (PBCB), National research center for clinical cancer treatment (MATRIX), IMPRESS-Norway - clinical trial for cancer patients, National infrastructure for precision diagnostics in cancer treatment (InPreD), Norwegian Cancer Precision Medicine Implementation Consortium (CONNECT), National competence network for personalised medicine (NorPreM), Member of the steering committee of the Norwegian registry on radiotherapy. Member of the steering committee of the Norwegian Breast Cancer Society, responsible for guidelines for the treatment of early and advanced breast cancer patients in Norway.
Leader of the national committee responsible for the education of oncologists in Norway from 2014 until 2019.

b) Describe the most important research infrastructures used by the research group.

The research group is using the following national research infrastructures services:

- MR Core Facility, Trondheim, Norway
- The Norwegian Consortium for Sequencing and Personalized Medicine (Oslo University Hospital) https://www.norseq.org/
- Service for sensitive data (TSD, University of Oslo) Services for sensitive data (TSD) - University of Oslo (uio.no)
- RedCap (established at RHF west).

1.6 Research group´s cooperations

Table 3. *Reflect on the current interactions of the research group with other disciplines, non-academic stakeholders and the potential importance of these for the research (e.g. informing research questions, access to competence, data and infrastructure, broadening the perspectives, short/long-term relations).*

Interdisciplinary (within and beyond the group)	The group is composed across departmental boundaries and along the patient's pathway axis. FFB consists of molecular biologists, pathologists, radiologists, oncologists, physicists, radiation therapists, breast and endocrine surgeons, bioinformatician, statistics, plastic surgeons, nursing researchers, nurses, research coordinators, user representatives and representatives from the medical humanities field (cultural scientist).
Collaboration with other research sectors e.g. higher education, research institutes, health trusts and industry.	The research group has several members associated with the university of Stavanger and University of Bergen. Additionally, there are strong collaborations with the University of Oslo and Norwegian University of Science and Technology, Georgia State university (USA), Griffith University (Australia), Aarhus University Hospital (Denmark) and several other national and international health trusts (most important: Haukeland University hospital, Oslo University hospital)
Transdisciplinary (including non academic stakeholders) *Transdisciplinary research involves the integration of knowledge from different science disciplines and (non-academic) stakeholder communities with the aim to help address complex societal challenges.*	The Group has strong collaboration with researchers and personnel within AI, computer science, and digital patoholgy Moreover, our commitment extends beyond academia, as evidenced by our strong affiliations with local breast cancer and cancer societies. Through the EU project REBECCA and through interdisciplinary seminars arranged at UiS/HelseCampus there has been a number of interactions with patient associations, non-academic stakeholders. In these meetings/events, information about the research projects has been provided. A stakeholder workshop has also been arranged within the REBECCA project where representatives of the Norwegian Cancer Society, Norwegian Smart care cluster and Helse Vest participated.

2. Research quality

2.1 Research group's scientific quality

Describe the research profile of the research group and the activities that contribute to the research group´s scientific quality. Consider how the research group's work contributes to the wider research within the research group's field nationally and internationally.

Profile: The research group is a dynamic and interdisciplinary team with broad expertise in research into breast cancer and its side effects. FFB's approach to research, education and collaboration actively contributes to obtaining new scientific knowledge for the benefit of patients.

Below is a list of activities that contribute to the research group's quality:

1. **Interdisciplinary Composition**: Through the establishment of the FFB, the interdisciplinary collaboration linked to breast cancer research at SUH was significantly strengthened. The group comprises of highly skilled personnel from a number of disciplines ranging "from bench to bedside".
2. **State of the art biomarker research:** Over the years, we have acquired extensive research experience, and have established state-of-the-art laboratory facilities for biomarker research at SUH.
3. **Biobanks:** The Prospective Breast Cancer Biobank is a unique biobank in a European perspective, which contains liquid biopsy samples taken every 6 months from 1,200 breast cancer patients through 10 years of follow-up.
4. **Strong Collaborations**: The members of FFB have extensive national and international collaboration. This network has resulted in partnerships in two EU projects on breast cancer, where group members are involved as work package leaders. In addition, the members participate in several international boards and networks such as: the Skagen Group (a group of European experts of radiation therapy of early stage breast cancer, collaborating in the planning and conducting of multicenter- multinational clinical trials), the ESTRO-ACROP Focus group BREAST (developing international guidelines for radiation therapy of breast cancer patients) the UEMS Section of Radiation Oncology (establishing a common core curriculum for the specialty with acceptance throughout Europe), European Liquid Biopsy Society.
5. **Clinical Studies**: Members at the Department of Hematology and Oncology have a long history of conducting high-quality clinical studies, and at any given time have a dozen of ongoing clinical trials.
6. **Patient Organisation Engagement**: The research group have close collaboration with the Norwegian Cancer Society, and the user representatives actively contribute to meetings by giving input and feedback to our research. The patient organizations also contribute by marketing our projects to users and the public by disseminating results and invite members of the group to present our research at member meetings.

Please add a link to the research group`s website:

Prospective Breast Cancer Biobank - Helse Stavanger HF (helse-stavanger.no)

Pathology Research Group - Helse Stavanger HF (helse-stavanger.no)

Cancer and Medical Physics - Helse Stavanger HF (helse-stavanger.no)

Table 4. List of projects

Instructions: *Please select 5-10 projects you consider to be representative/the best of the work in the period 1 January 2012 – 31 December 2022. The list may include projects lead by other institutions nationally or internationally. Please delete tables that are not used.*

Project 1: ***PerMoBreCan - Personalized Monitoring in Breast Cancer*** ***(2015 -2045)***	**Project owner(s)** (project leaders organisation)	Emiel Janssen, Håvard Søiland, Kjersti Tjensvoll, Oddmund Nordgård, Bjørnar Gilje,
	Total budget and share allocated to research group	The project is funded from additional sources and in total NOK 19, 2 mill. A gift is awarded the project for the period 2023-2027 with NOK 2 million per project year, total 10 mill NOK
	Objectives and outcomes (planned or actual) **and link to website**	PerMoBreCan is working to establish robust circulating biomarkers (e.g.: circulating tumor cells, cell-free tumor DNA, exosomes, and cytokines from blood) for earlier detection of systemic recurrence with a view to providing the possibility of early secondary adjuvant therapy. Website: Personalized Monitoring in Breast Cancer - Helse Stavanger HF (helse-stavanger.no)
Project 2: ***REBECCA- REsearch on BrEast Cancer induced chronic conditions supported by Causal Analysis of multi-source data*** ***(2021-2038)***	**Project owner(s)** (project leaders organisation)	Local PI: Kjersti Tjensvoll, co- PIs: Emiel Janssen, Bjørnar Gilje, Tone Holen Lende, Kristin Jonsdottir. Koordinators: Marius Stensland, Håvard Søiland, Ingrid Holsvik, Karina Bru, Vibeke Blåfjelldal, Marie Ausdal,
	Total budget and share allocated to research group	Total budget: 5,28 mill EUR To SUH: 0,75 mill EUR Additional funding from national and other sources: NOK 1,3 mill
	Objectives and outcomes (planned or actual) **and link to website**	The EU-funded project REBECCA taps into the potential of Real-World Data to support clinical research and to improve existing clinical workflows. It will combine clinical data with data obtained from multiple wearables, online behaviour and registry data to study the complex array of chronic comorbidities developed during breast cancer recovery. The data will be deployed within 7 clinical studies in 3 countries, involving over 650 individuals, and it will help shape future guidelines and practices for post-cancer treatment. Webiste: Home - REBECCA (rebeccaproject.eu)

Project 3: ***PEtreMAC*- PErsonalized TREatment of high-risk MAmmary Cancer** *(2015-2030)*	**Project owner(s)** (project leaders organisation)	Stian Knappskog (Bergen University Hospital), Local PIs Bjørnar Gilje for recruitment of patient and Emiel Janssen is responsible for analysing all the samples for Ki67 status, as well as hormone receptor and HER2.
	Total budget and share allocated to research group	Total budget: unknown To SUH: Cost for reagents was covered
	Objectives and outcomes (planned or actual) **and link to website**	Despite advances in recent years, there is still clear room for improvement in pharmacological treatment of locally advanced breast cancer. With this study, we wish to prospectively test whether personalised cancer treatment, based on both new and more traditional, predefined biomarkers, will improve treatment response/survival in patients with locally advanced breast cancer. Patients are stratified into the treatment group based on TP53 mutation status and Ki67 status, as well as hormone receptor and HER2 analysis prior to initiation of treatment. We will implement the most promising targeted therapeutics, palbociclib, pertuzumab and the PARP inhibitor olaparib for patients with selected genetic subtypes of breast cancer. Objective: To identify new predictive markers of treatment efficacy, as well as achieve improved treatment response and survival in patients with locally advanced breast cancer through modern, personalised cancer treatment. Website: PETREMAC – NBCG
Project 4: ***CLARIFY*** ***(EU project)*** *(2020 - 2024)*	**Project owner(s)** (project leaders organisation)	Local PI: Emiel Janssen
	Total budget and share allocated to research group	Total Budget: 3,2 mill EUR TO SUH: 285 000 EUR
	Objectives and outcomes (planned or actual) **and link to website**	CLARIFY's main goal is to develop a robust automated digital diagnostic environment based on artificial intelligence and cloud-oriented data algorithms that facilitates whole-slide-image (WSI) interpretation and diagnosis everywhere with the aim of maximising the benefits of digital pathology and aiding pathologists in their daily work. Outcomes: network and education of pathologists are the most valuable outcome of this project. Website: Clarify | Clarify Project site (clarify-project.eu)
Project 5:	**Project owner(s)** (project leaders organisation)	Helse Stavanger HF – Stavanger University Hospital. (Project leaders: Reino Heikkila, Oddmund Nordgård).

Molecular detection of minimal residual disease (MRD) in breast cancer *1998-2019*	**Total budget and share allocated to research group**	Total budget within the period (2012-2019): 3 million NOK
	Objectives and outcomes (planned or actual) **and link to website**	Objective: Investigate the clinical relevance of minimal residual disease (primarily bone marrow micrometastases) in operable breast cancer. Outcomes: Disseminated tumor cells in bone marrow samples obtained before and after surgery were shown to have prognostic value, both within a short (< 5 years) and long timeframe. Website: Project web site in Cristin.no.
Project 6: ***Prognostic and predictive Biomarkers in breast cancer*** *(2012 – 2025)*	**Project owner(s)** (project leaders organisation)	PI Emiel Janssen
	Total budget and share allocated to research group	Total budget: NOK 12 mill
	Objectives and outcomes (planned or actual) **and link to website**	The objective is to reduce over- and under-treatment of breast cancer patients by finding new biomarkers and validate establish biomarkers. Main outcome is: • Evaluation of Ki67 as biomarker for high risk of recurrence in breast cancer patiens, have resulted in innovation project for Implementation of artificial intelligence as support tools for pathology in Helse Vest • International Consortium for Advancing Research on TNBC = Triple negative breast cancer (ICART); The goal is to find new biomarkers that can identify patients who need more or less treatment compared to current treatment. Collaborative project with Georgia State University, Atlanta, USA and University of Nottingham, UK • Evaluation of different microRNA as new biomarkers for breast cancer, a project that has led to cooperation with Oslo University Hospital, Akershus University Hospital and Vestre Viken Most of the projects are described here: Pathology Research Group - Helse Stavanger HF (helse-stavanger.no)
Project 7:	**Project owner(s)** (project leaders organisation)	Håvard Søiland and Gunnar Mellgren (Haukeland University Hospital), and Emiel Janssen

Endocrine factors in breast cancer *(2013 – 2027)*	**Total budget and share allocated to research group**	Total budget: NOK 9 mill
	Objectives and outcomes (planned or actual) **and link to website**	Luminal patients comprise about 75 % of all breast cancer patients. As these patients have a hormone-receptor positive tumor, it is crucial to study endocrine factors to improve the endocrine treatment for these patients. Outcome:1. In premenopausal patients with Luminal tumors (estrogen and/or progesterone receptor positive) have seen a worse long-term survival if the active tamoxifen metabolites are low. PMID: 33252186 2.We have found that Adherence to tamoxifen and aromatase inhibitors is 36% over a 5-year period. This will have negative impact on survival. PMID: 30641300 3. We have developed ultrasensitive LCMSMS method for direct measurement of biological active estrogen, progesterone, and androgens. We may differentiate which patient that have high levels of direct these tumor stimulating hormones in postmenopausal patients, and if higher levels affect patient's outcome. 4. We have also developed methods that may determine all three aromatase inhibitors. Personalised tamoxifen treatment - Helse Stavanger HF (helse-stavanger.no) Adherence to antiestrogen therapy - Helse Stavanger HF (helse-stavanger.no)
Project 8: ***Radiation therapy*** *(2009 – 2025)*	**Project owner(s)** (project leaders organisation)	Department of Hematology and Oncology, section for radiotherapy and physics Chief Medical Office Ingvil Mjaaland and Chief engineer Mari Hjelstuen
	Total budget and share allocated to research group	4.7 mill NOK to one of the sub-projects ("Sykehuset i våre Hender", The Norwegian cancer foundation)
	Objectives and outcomes (planned or actual) **and link to website**	1. Development of a method for respiratory guided radiotherapy in order to reduce the dose to the heart and the ipsilateral lung, leading to the implementation of deep inspiration breath hold techniques for patients with left sided breast cancer in all Norwegian and most Danish radiotherapy centers. 2. A large international randomized multicenter trial on hypofractionated breast radiation therapy in patients with early breast cancer after breast conserving surgery, practice changing. 3. A large international randomized multicenter trial on hypofractionated locoregional radiation therapy in patients with early breast cancer.

		4. A large international randomized multicenter trial investigating the omission of radiotherapy in low risk breast cancer patients after breast conserving surgery. 5. Follow up of patients who received ultrahypofractionated breast radiotherapy after breast conserving surgery during the first phase of the Covid-19 pandemic.
Project 9: ***Digital pathology in Health West*** ***(2020 – 2024)***	**Project owner(s)** (project leaders organisation)	Local PI Emiel Janssen, cco
	Total budget and share allocated to research group	Total budget: 15 mill.
	Objectives and outcomes (planned or actual) **and link to website**	Digital pathology in Western Norway Regional Health Authority; We will develop, validate and implement new digital tools to measure proliferation in tissue from breast cancer patients. Collaborative project with Helse Bergen. Outcome: National digital patology PiV - We create tomorrow's pathology services - Helse Bergen HF (helse-bergen.no)
Project 10: ***The Effects of Insulin and Insulin-related Characteristics, and Short-Term Low-glycemic and High-glycemic Carbohydrate Intervention on Breast Cancer Proliferation*** *(2009 – 2027)*	**Project owner(s)** (project leaders organisation)	PI Håvard Søiland, coworkers Tone Holen Lende, Emiel Janssen and Marie Austdal
	Total budget and share allocated to research group	Total Budget: 6 mill. NOK
	Objectives and outcomes (planned or actual) **and link to website**	The Effects of Insulin and Insulin-related Characteristics, and Short-Term Low-glycemic and High-glycemic Carbohydrate intervention on Breast Cancer Proliferation; Tumors from patients who have been given a high dose of carbohydrates before surgery are biologically altered and show higher proliferation. Outcome: We have investigated which proteins are altered (glycosylation) in blood and tissues to understand more about the interaction between diet and tumor development. This has led to a collaborative project with Griffith University, , Australia, Georgia State University, US and the Norwegian group of Cancer Imaging and Mulit-Omics Research at Norwegian University of Science and Technology (NTNU) Prosjekt #529380 - The Effects of Insulin and Insulin-related Characteristics, and Short-Term Low-glycemic and High-glycemic Carbohydrate Intervention on Breast Cancer Proliferation - Cristin

Table 5. Research group's contribution to publications

Instructions: *Please select 5-15 publications from the last 5 years (2018-2022) with emphasis on recent publications where group members have a significant role.* ***If the publication is not openly available, it should be submitted as a pdf file attached to the self-assessment.*** *We invite you to refer to the Contributor Roles Taxonomy in your description: https://credit.niso.org/.*

Cf. Table 1. List of personell by categories: Research groups up to 15 group members: 5 publications. Research groups up to 30 group members: 10 publications. Research groups above 30 group members: 15 publications.

Please delete tables that are not used.

Publication 1: Title: Liquid biopsies and PROM-data for integrative monitoring of early-stage breast cancer patients— A study protocol of the Prospective Breast Cancer Biobanking (PBCB) project in Western Norway Journal: BMJ Open. Year: 2022 DOI: 10.1136/bmjopen-2021-054404 URL: https://bmjopen.bmj.com/content/12/4/e054404	**Authors** (Please highlight group members)	**Håvard Søiland, Emiel AM Janssen, Thomas Helland, Magnus Hagland , Oddmund Nordgård, Siri Lunde, Tone Hoel Lende, Kjersti Tjensvoll, Bjørnar Gilje, Kristin Jonsdottir, Einar Gudlaugsson, Kirsten Lode,** Kari Britt Hagen, Birgitta Haga Gripsrud, Ragna Lind, Anette Heie, Turid Aas, **Marie Austdal, Nina Gran Egeland**, Linn Skartveit, Ann Cathrine Kroksveen, **Satu Oltedal, Jan Terje Kvaløy**, Ernst A Lien, Linda Sleire and Gunnar Mellgren on behalf of the the PBCB-study group
	Short description	A study protocol of the Prospective Breast Cancer Biobanking (PBCB) project in Western Norway.
	Research group's contribution	Many members of FFB have contributed to this work
Publication 2: Title: Detection of disseminated tumor cells in bone marrow predict late recurrences in operable breast cancer patients Journal: BMC Cancer Year: 2019 DOI: 10.1186/s12885-019-6268-y	**Authors** (Please highlight group members)	**Tjensvoll K, Nordgård O, Skjæveland M, Oltedal S, Janssen EAM, Gilje B**
	Short description	Pre-operative DTC detection, but not MAI status, predicts late recurrences in operable breast cancer.
	Research group's contribution	Members of the group did all of the work.

URL: https://bmccancer.biomedcentral.com/articles/10.1186/s12885-019-6268-y		
Publication 3: Title: Metabolic consequences of perioperative oral carbohydrates in breast cancer patients - an explorative study. Journal: BMC Cancer Year: 2019 DOI: 10.1186/s12885-019-6393-7 URL: https://bmccancer.biomedcentral.com/articles/10.1186/s12885-019-6393-7	**Authors** (Please highlight group members)	**Lende TH, Austdal M,** Bathen TF, **Varhaugvik AE, Skaland I, Gudlaugsson E, Egeland NG, Lunde S,** Akslen LA, **Jonsdottir K, Janssen EAM, Søiland H, Baak JPA**
	Short description	Preoperative carbohydrate load increases systemic levels of lactate and pyruvate and tumor levels of glutathione and glutamate in ER-positive patients. These biological changes may contribute to the inferior clinical outcomes observed in luminal T2 breast cancer patients.
	Research group's contribution	The group did most of the work
Publication 4: Title: Low Z-4OHtam concentrations are associated with adverse clinical outcome among early stage premenopausal breast cancer patients treated with adjuvant tamoxifen Journal: Mol Oncol. Year: 2021 DOI: 10.1002/1878-0261.12865 URL: https://febs.onlinelibrary.wiley.com/doi/10.1002/1878-0261.12865	**Authors** (Please highlight group members)	Helland T, Naume B, Hustad S, Bifulco E, **Kvaløy JT**, Saetersdal AB, Synnestvedt M, **Lende TH, Gilje B, Mjaaland I,** Weyde K, Blix ES, Wiedswang G, Borgen E, Hertz DL, **Janssen EAM, Mellgren G, Søiland H**
	Short description	This is the first study to confirm the association between a published active tamoxifen metabolite threshold and BC outcome in an independent patient cohort. Premenopausal patients receiving 5-year of tamoxifen alone may benefit from therapeutic drug monitoring to ensure tamoxifen effectiveness.
	Research group's contribution	Håvard Søiland and Emiel Janssen were supervisors for the PhD student T. Helland and contributed to all the stages of the research and writing
Publication 5: Title: Olaparib Monotherapy as Primary Treatment in Unselected Triple Negative Breast Cancer Journal: Ann Oncol	**Authors** (Please highlight group members)	Hans P. Eikesdal, Synnøve Yndestad, Asmaa Elzawahry, Alba Llop-Guevara, **Bjørnar Gilje,** Egil S. Blix, Helge Espelid, Steinar Lundgren, Jürgen Geisler, Geirfinn Vagstad, Laura Minsaas, Beryl Leirvaag, **Einar G. Gudlaugsson**, Hildegunn S. Aase, Turid Aas, Judith Balmaña, Violetta Serra, **Emiel A.M. Janssen**, Stian Knappskog, Per E. Lønning.

Year: 2021 DOI: 10.1016/j.annonc.2020.11.009 URL: https://www.annalsofoncology.org/article/S0923-7534(20)43164-3/fulltext	**Short description**	Olaparib yielded a high clinical response rate in treatment-naïve TNBCs revealing HR deficiency, beyond germline HR mutations.
	Research group's contribution	The department of pathology at SUH acted as the national center for all the pathology analysis. They performed all the immunohistochemistry and the analysis of all the IHC stainings. We also counted the Mitotic Activity Index and estimated the percentages of Tumor Infiltrating Lymfocytes.
Publication 6: Title: Drug monitoring of tamoxifen metabolites predicts vaginal dryness and verifies a low discontinuation rate from the Norwegian Prescription Database. Journal: Breast cancer research and treatment Year: 2019 DOI: 10.1007/s10549-019-05294-w URL: https://link.springer.com/article/10.1007/s10549-019-05294-w	**Authors** (Please highlight group members)	Thomas Helland, Kari Britt Hagen, Martha Eimstad Haugstøyl, **Jan Terje Kvaløy, Siri Lunde**, **Kirsten Lode,** Ragna A Lind, **Birgitta Haga Gripsrud, Kristin Jonsdottir,** Jennifer Gjerde, Ersilia Bifulco, Steinar Simon Hustad, Janne Jonassen, Turid Aas, **Tone Hoel Lende**, Ernst Asbjørn Lien, **Emiel AM Janssen, Håvard Søiland**, Gunnar Mellgren
	Short description	This real-world data study suggests that measurements of tamoxifen metabolite concentrations may be predictive of vaginal dryness in breast cancer patients and verifies NorPD as a reliable source of adherence data
	Research group's contribution	Håvard Søiland and Emiel Janssen were supervisors for the PhD student T. Helland and contributed to all the stages of the research and writing
Publication 7: Title: MiR-18a and miR-18b are expressed in the stroma of oestrogen receptor alpha negative breast cancers. Journal: BMC Cancer Year: 2020 DOI: 10.1186/s12885-020-06857-7 URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7201801/	**Authors (Please highlight group members)**	**Gran Egeland N, Jonsdottir K,** Ragle Aure M, Kristine Sahlberg, Vessela Kristensen, Deirdre Cronin-Fenton, **Skaland I, Gudlaugsson E, Baak JPA and Janssen EAM.**
	Short description	The study demonstrates that miR-18a and miR-18b expression is associated with ER- breast tumours that display a high degree of inflammation. This expression is potentially associated specifically with macrophages. These results suggest that miR-18a and miR-18b may play a role in the systemic immunological response in ER- tumours.
	Research group's contribution	The members of the research group did most of the work

Publication 8: Title: Ki67 digital image analysis on TMAs and recurrence risk in tamoxifen-treated breast cancer patients Journal: Clin Epidemio. Year: 2020 DOI: 10.2147/CLEP.S248167 URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7383278/	**Authors (Please highlight group members)**	**Nina Gran Egeland, Kristin Jonsdottir,** Kristina Lystlund Lauridsen, **Ivar Skaland**, Cathrine F. Hjorth, **Einar Gudlaugsson,** Stephen Hamilton-Dutoit, Timothy L Lash, Deirdre Cronin-Fenton, **Emiel AM Janssen**
	Short description	The findings suggest that Ki-67 digital image analysis in TMAs is not associated with increased risk of recurrence among tamoxifen-treated ER-positive breast cancer or ER-negative breast cancer patients. Overall, the findings do not support an increased risk of recurrence associated with Ki-67 expression.
	Research group's contribution	Members of the group did most of the work
Publication 9: Title: miRNA normalization enables joint analysis of several datasets to increase sensitivity and to reveal novel miRNAs differentially expressed in breast cancer Journal: PLoS Comput Biol. Year: 2021 DOI: 10.1371/journal.pcbi.1008608 URL: https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1008608	**Authors** (Please highlight group members)	Shay Ben-Elazar, Miriam Ragle Aure, **Kristin Jonsdottir**, Suvi-Katri Leivonen, Vessela N.Kristensen, **Emiel A.M. Janssen,** Kristine Kleivi Sahlberg, Ole Christian Lingjærde and Zohar Yakhini.
	Short description	The study present and examine a method based on quantile normalization, Adjusted Quantile Normalization (AQuN), to combine miRNA expression data from multiple studies in breast cancer into a single joint dataset for integrative analysis. Analyses identified new potential biomarkers and therapeutic targets for both clinical groups. As a specific example, using the AQuN-derived datasetdetect hsa-miR-193b-5p to have a statistically significant over-expression in the ER positive group, a phenomenon that was not previously reported.
	Research group's contribution	Members of the group contributed with samples and involved in analysing, discussion, and writhing
Publication 10:	**Authors** (Please highlight group members)	Karuna Mittal, Jaspreet Kaur, Meghan Jaczko, Guanhao Wei, Michael. S. Toss, Emad A. Rakha, **Emiel A. M. Janssen, Håvard Søiland,** Michelle D. Reid, Omer Kucuk, Meenakshi V. Gupta, Ritu Aneja.

Title: Centrosome amplification: A quantifiable cancer cell trait with prognostic value in solid malignancies Journal: Cancer Metastasis Rev. Year: 2021 DOI: 10.1007/s10555-020-09937-z URL: https://link.springer.com/article/10.1007/s10555-020-09937-z/	**Short description**	In this review, we discuss the prevalence, extent, and severity of CA in various solid cancer types, the utility of quantifying amplified centrosomes as an independent prognostic marker. We also highlight the clinical feasibility of a CA-based risk score for predicting recurrence, metastasis, and overall prognosis in patients with solid cancers.
	Research group's contribution	Members of the group contributed to the draft, knowledge and writing.
Publication 11: Title: Postmastectomy Radiation Therapy Planning After Immediate Implant-based Reconstruction Using the European Society for Radiotherapy and Oncology-Advisory Committee in Radiation Oncology Practice Consensus Guidelines for Target Volume Delineation Journal: Clinical Oncology Year: 2021 DOI: 10.1016/j.clon.2020.09.004 URL: https://www.sciencedirect.com/science/article/pii/S0936655520303654?via%3Dihub	**Authors** (Please highlight group members)	Kaidar-Person, O; Yates, ES; Andersen, K; Boersma, LJ; Boye, K; Canter, R, Costa, E; Daniel, S; Hol, S; Jensen, I; Lorenzen, EL; **Mjaaland, I;** Nielsen, MEK; Poortmans, P; **Vikstrøm, J;** Webb, J; Offersen BV.
	Short description	Postmastectomy Radiation Therapy Planning After Immediate Implant-based Reconstruction Using the European Society for Radiotherapy and Oncology-Advisory Committee in Radiation Oncology Practice Consensus Guidelines for Target Volume Delineation.
	Research group's contribution	Target volume delineation, dose planning, writing of manuscript
Publication 12: Title: A comparison of conventional and dynamic radiotherapy planning techniques for early-stage breast cancer utilizing deep inspiration breath-hold Journal: Acta Oncol Year: 2018 DOI: 10.1080/0284186X.2018.1497294	**Authors** (Please highlight group members)	**Vikström J, Hjelstuen MH, Wasbø E, Mjaaland I, Dybvik KI**
	Short description	A comparison of conventional and dynamic radiotherapy planning techniques for early-stage breast cancer utilizing deep inspiration breath-hold
	Research group's contribution	Alone contributor

URL: https://www.tandfonline.com/doi/full/10.1080/0284186X.2018.1497294		
Publication 13: Title: Hypofractionated Versus Standard Fractionated Radiotherapy in Patients With Early Breast Cancer or Ductal Carcinoma In Situ in a Randomized Phase III Trial: The DBCG HYPO Trial Journal: J Clin Oncol. Year: 2020 DOI: 10.1200/JCO.20.01363 URL: https://ascopubs.org/doi/10.1200/JCO.20.01363?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed	**Authors** (Please highlight group members)	Offersen BV, Alsner J, Nielsen HM, Jakobsen EH, Nielsen MH, Krause M, Stenbygaard L, **Mjaaland I,** Schreiber A, Kasti UM, Overgaard J; Danish Breast Cancer Group Radiation Therapy Committee.
	Short description	Hypofractionated Versus Standard Fractionated Radiotherapy in Patients With Early Breast Cancer or Ductal Carcinoma In Situ in a Randomized Phase III Trial
	Research group's contribution	Inclusion of patients, data collection in Norway, writing of manuscript
Publication 14: Title: Dose constraints for whole breast radiation therapy based on the quality assessment of treatment plans in the randomised Danish breast cancer group (DBCG) HYPO trial. Journal: Clin Transl Radiat Oncol. Year: 2021 DOI: 10.1016/j.ctro.2021.03.009 URL: https://www.ctro.science/article/S2405-6308(21)00032-X/fulltext	**Authors** (Please highlight group members)	Thomsen MS, Berg M, Zimmermann S, Lutz CM, Makocki S, Jensen I, **Hjelstuen MHB**, Pensold S, Hasler MP, Jensen MB, Offersen BV.
	Short description	Dose constraints for whole breast radiation therapy based on the quality assessment of treatment plans in the randomised Danish breast cancer group (DBCG) HYPO trial
	Research group's contribution	Conceptualisation and writing of manuscript

Table 6. Please add a list with the research group´s monographs/scientific books.
Please delete lines which are not used.

	Title - Authors (Please highlight group members)- link to webpage (if possible)
1	Pedersen, A., Reinertsen, I., **Janssen, E.A.M.**, Valla, M. (2022). Artificial Intelligence in Studies of Malignant Tumours. In: Akslen, L.A., Watnick, R.S. (eds) Biomarkers of the Tumor Microenvironment. Springer, Cham
2	The role of liquid biopsy. I: A primer in pancreas. Stockholm: Karolinska Universitetssjukehuset 2023 ISBN 978-91-527-5468-9. s. 191-196

2.2 Research group´s societal contribution

Describe the societal impact of the research group's research. Consider contribution to education, economic, societal and cultural development in Norway and internationally.

Education: FFB contributes to the education of researchers and other health personnel both at national and international level. At national level, members of the research group teach science at both the University of Stavanger and Bergen (see section 1.2c). In addition, the group contributes to education of researchers at an international level by presenting the research group's projects and results at international, and national, meetings and conferences. Through patient brochures, presentations at meetings in patient organizations such as the Cancer Society and the breast cancer school, the group also contributes to educating patients and their relatives. Training of the public is carried out through dissemination of results online (see section 1.2), and through interviews/presentations in the media (TV and radio). An example of presentations in the media include Professor Håvard Søiland in-depth interview of the groups research at "Dagsrevyen", NRK1 (Norwegian national broadcasting). Members of the group give presentation for breast cancer patients in the region and prof. Emiel Janssen gives a yearly lecture on breast cancer at the International School of Stavanger.

Economic: Over- and under-treatment of cancer patients is costly for the society, and there is therefore a need for more precise treatment and diagnostics. Our research aims to improve breast cancer diagnosis and treatment. This is expected to result in improved prognosis, early detection of disease progression and improved quality of life for breast cancer patients. An expected consequence of this is reduced societal costs associated with the cancer treatment. In addition, our research contributes to innovation (e.g. the EU projects REBECCA and CLARIFY), which in the future not only may save costs but also stimulate to economic growth by using new and innovative methods/technologies in the diagnosis and treatment of breast cancer.

Societal: The societal impact of our research includes changes in the way breast cancer patients are diagnosed, treated and followed after surgery. More precise diagnostics and treatment are expected to result in earlier detection of the cancer, fewer side effects and better rehabilitation, which will save the society for enormous costs. The patients will also have improved chances of survival. Hence, through our research, and the establishment of biobanks and registries, the research group contributes to new discoveries and developments that are highly relevant to both the patients and the society in general.

Cultural: Members of the group contribute to social impact and cultural development by presenting their research work in a populist manner at various events such as the "research days" (Forskningsdagene), the Cancer Society's member meetings, public events organized by the Folke Hermansen's foundation, the Pint of Science festival etc.

Table 7. The research group's societal contribution, including user-oriented publications, products (including patents, software or process innovations

Not applicable.

3. Challenges and opportunities

Information about the strengths and weaknesses of the research group is obtained through the questions above. In this chapter, please reflect on what might be the challenges and opportunities for developing and strengthening the research and the position of the research group.

For the research group for breast cancer (FFB), at SUH, we experience the following challenges and opportunities.

Weaknesses

One of the primary challenges we face is the scarcity of resources, both in terms of human resources and equipment. This scarcity can hinder the pace and breadth of our research initiatives. Several of the medical doctors and medical physicists in the group have part-time positions linked to clinical operations, leaving them with limited availability for research activities. Balancing clinical responsibilities with research commitments poses a significant challenge. The necessity for our researchers to engage in clinical practice is essential when planning and conducting clinical trials. However, this often results in time constraints, making it challenging to allocate sufficient time to the research endeavours.

The physical expansion of our laboratory is constrained by various factors, limiting our capacity to accommodate new projects, new equipment and employ new researchers. This constraint can impede the growth and diversification of our research initiatives. Unfortunately, our research group currently lacks adequate support from the University of Stavanger. The absence of institutional support can hinder our ability to access necessary resources, collaborate with other departments, and establish a more prominent presence in the academic community.
Additionally, our vulnerability associated with key competencies, both with regard to research and clinical skills, is a concern. It is essential to address this vulnerability to ensure the overall robustness of our research endeavours.

Opportunities

Since we are not one of the biggest hospitals in Norway, the collaborations between the departments are efficient and the members have a strong and close collaboration. This close connection allows us to seamlessly exchange ideas, experiences, and resources, which helps accelerate our scientific work. In addition, we are an interdisciplinary group with shared laboratory facilities, which streamlines our work and gives us access to advanced equipment that is essential for our research projects.

Our research objectives are clear, and the group has divided the fields of interest between them so that the different research groups work on different issues related to our purpose. The patient's needs and well-being are in the centre of our work. This is also reflected in our goals to improve diagnostics, treatments and the follow-up of breast cancer patients to ensure even better healthcare services for patients. Additionally, we are committed to increasing the number of clinical trials to improve our understanding of diseases and to find innovative approaches to treatment. This lays the foundation for evidence-based practice and better patient outcomes.

The research group for breast cancer has a strong national and international network, which means access to other resources, expertise and give us opportunities for collaboration. The group has achieved this because the members of the group are characterized by an extreme motivation and passion for their work. This drive is a critical factor behind our success and ability to overcome the challenges.