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Evaluation of Medicine and Health (EVALMEDHELSE) 2023-2024

Self-assessment for research groups

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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): Clinical Immunology Research Group (Clinical Immunology) Date: 31.01.2024 Contact person: Roald Omdal Contact details (email): roald.omdal@sus.no

Content

1. Organisation and strategy	. 3
1.1 Research group's organisation	. 3
1.2 Research group's strategy	. 4
1.3 Relevance to the institutions	. 5
1.4 Research group's resources	. 6
1.5 Research group's infrastructures	. 6
1.6 Research group's cooperations	. 8
2. Research quality	. 8
2.1 Research group's scientific quality	. 8
2.2 Research group's societal contribution	18
3. Challenges and opportunities	20

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 Clinical Immunology Research Group at Stavanger University Hospital was established in 2002 and has been led by Professor Roald Omdal. He is a specialist in internal medicine and rheumatology, working in clinical immunology, and has had a long-time research interest in the neurological manifestations of immunological diseases. By 2022 he has published 170 peer-reviewed scientific papers and successfully supervised 11 PhD candidates while four are ongoing, and two are postdocs in the group.

The research activities are largely focused on the neurological aspects of chronic inflammatory autoimmune diseases, and especially on biological mechanisms for chronic fatigue. This group was the first to describe small fibre neuropathy in systemic lupus erythematosus (SLE) and primary Sjögren's syndrome (pSS), and to publish reference data in a normal healthy population. Also, the group was the first to demonstrate the presence of antibodies against the NR2 subunit of the NMDA receptor in brain neuronal cells of patients with SLE and pSS, and to show that these antibodies were associated with cognitive impairment.

The main focus is now on the genetic and biological aspects of chronic fatigue, and the group works with these issues across several diseases, such as SLE, pSS, rheumatoid arthritis, inflammatory bowel diseases, psoriasis, neurodegenerative diseases, and recently also in cancer. The aim is to uncover how specific genes regulate fatigue and identify signalling molecules and pathways. Through analysis of cerebrospinal fluid by state-of-the-art spectrometry and other techniques, several highly relevant molecules involved in fatigue signalling have been identified. Genetic networks and candidate genes for fatigue has been investigated by DNA-methylation and large international GWAS studies. Currently studies on the possible association between fatigue and the bacterial and eukaryotic microbiome is ongoing in inflammatory bowel diseases.

The group has a long-time experience in running large-scale clinical investigations, has a wellequipped research laboratory, and has highly skilled laboratory personnel. Strong regional collaborators are Broegelmanns Research Laboratory (professor Roland Jonsson) and the Proteomics Unit at the University of Bergen (professor Frode Berven) at the University of Bergen, and Institute of Clinical Medicine (professor Knut Lundin) and Institute of Health and Society (professor Anne Marit Mengshoel) at the University of Oslo.

The group is a member of several international research networks with several highly skilled partners: Uppsala University (professor Lars Rönnblom), Gothenburg (professor Henrik Zetterberg), Oklahoma Medical Research Foundation (dr. Chris Lessard), Kitasato University School of Medicine, Tokyo (professor Shunsei Hirohata), The Feinstein Institute, NY (professor Kevin Tracey), Albert Einstein College of Medicine, New York (professor Chaim Putterman), Denver University, Colorado (professor Charles Dinarello), Newcastle University UK (professor Wan-Fai Ng), Université Paris-Sud (INSERM), (professor Xavier Mariette), Stanford University (professor Emmanuel Mignot), and Erasmus MC University Medical Center in Rotterdam (professor Marjan Versnel).

Currently the group participates in three EU-studies and two other large international studies.

Funding is mainly obtained from regional and EU-sources.

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, <u>https://dbh.hkdir.no/datainnhold/kodeverk/stillingskoder</u>. <u>Please add new lines or delete lines which</u> <u>are not in use.</u>

	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	Senior physician	5	20	0	0
Personnel by	Physician				
position	Psychologist	2	0	1	0
	Researchers and postdoc	4	50	0	4
	PhD-students	4	75	0	4
	Chief bioengineer	4	25	1	1
	Professor	4	0	3	0
	Assoc. professor	3	33	0	3
	Study nurse	1	100	0	0

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 main research focus is to investigate how chronic fatigue is generated and regulated in different disease entities (inflammatory, degenerative, cancer) and to find out if there are generic fatigue mechanisms, and/or mechanisms that are specific for disease categories. This includes to investigate how specific genes regulate fatigue and identify signaling molecules and pathways. Cerebrospinal fluid, serum/plasma and blood cells are substrates for investigations.

A large IBD prospective study (>700 pts) with 9 sub studies are ongoing and led at the hospital. In addition, a national IBD study (BIOSTOP) and a study on the possible association between fatigue and the bacterial and eukaryotic microbiome is ongoing in inflammatory bowel disease.

Funding is obtained through local resources (SUSI study), regional funding (Western Norway Regional Health Authority), national funding (NRC - BIOSTOP), funding by EU- projects (IDEA-FAST, NECESSITY). Other international funding is accomplished by participating in several international multi-collaborative studies as well as bilateral international projects. (FOREUM, SGENE, DISSECT, Blastocystis in Inflammatory Bowel Disease).

Most new researcher are recruited locally from the university or the hospital.

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.

- Continue to be <u>a leading actor nationally and internationally</u> on biological mechanisms related to chronic fatigue.
- Continue with fatigue research related to inflammatory autoimmune diseases (psoriasis and primary Sjøgrens syndrome), inflammatory bowel diseases including celiac disease, in cancer, and in neurodegenerative diseases (Parkinsons disease).
- Continue to investigate and explore new biomarkers for fatigue and elements related to the sickness behavior response.
- Continue with high quality research in molecular and therapeutic aspects of inflammatory bowel and celiac diseases.
- Continue to have a high and "predictable" funding from the Western Norway Regional Health Trust, and increase the ratio of international funding.
- At least 50% of publications in level 2 journals.
- Om average have 2 PhDs annually.
- Expand international collaboration.

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

Supervised 11 PhD candidates and 17 master students, while four PhD-students are ongoing, and two are postdocs in the group. In addition, several of the group members participate actively in specialist education of doctors (registrars) and supervision of medical student.

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 the Clinical Immunology Research Group at the hospital with research administration related to external funding and project management related to EU-financing and other international funding. The hospital gives external and internal approval of research projects, and they provide help with contracts/agreements. There is a section for biostatistics that supports the groups with statistics and data management, a biobanking unit and a clinical research unit. The research group has a general research biobank at the hospital.

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 research group is administratively organised under Department of Internal Medicine, while research coordination is supervised through the Research Department. The group contributes to the overall institutional research objectives through the establishment of a strong research collaboration, strengthening clinical research and practice, securing additional funding to support infrastructure and functions for research, and increased international research collaboration. This is especially exemplified by how the EU-projects involve and stimulate clinical and laboratory personnel.

In addition, in most research topics the group has successfully integrated it's research into several departments and sections of the hospital and across disciplines, contributing to cross sectional collaboration and knowledge transfer. Finally, the research group actively engages user groups in the development of proposals, research implementation and education and dissemination of findings.

A user group from The Norwegian Rheumatism Association has provided assistance through several years. This also applies to some selected users with autoimmune diseases.

1.4 Research group's resources

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

Funding portfolio of the research group is:

- National: Western Norway Regional Health Authority, Norwegian Research Council (NRC), Foundation DAM/Norwegian Brain Council (Hjernerådet).
- EU-financing: IDEA-FAST, NECESSITY, REBECCA.
- Other international funding: FOREUM, DISSECT, SGENE.
- Medical industry: AbbVie, Ferring, Tillots, Pfizer, Roche

Additionally, many of the cooperation with other institutions has resulted in in kind analyses of biological samples.

	2018 (NOK)	2019 (NOK)	2020 (NOK)	2021 (NOK)	2022 (NOK)
Basic funding	146000	50000	0	95000	0
Funding from industry and other					
private sector sources	30000	0	0	0	0
Commissioned research for public					
sector	0	0	0	0	0
Research Council of Norway	44000	75000	99000	85000	347000
Grant funding from other national					
sources	4333000	3031000	3480000	3959000	3298000
International funding e.g. NIH, NSF,					
EU framework programmes	0	174000	0	376000	655000
Other	0	0	260000	0	0

Table 2. Describe the sources of R&D funding for the research group in the period 2018-202
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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. <u>These</u> 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.

NorTrials Centre for Clinical Immunology is situated at Stavanger University Hospital (NorTrials_Inflammation@sus.no). NorTrials is a partnership between the regional health authorities and the organisations for the pharmaceutical and medical device industries, established on assignment from the Ministry of Health and Care Services in 2021.

Clinical immunology is a cross-disciplinary field that includes chronic inflammatory and autoimmune conditions. These conditions are caused or characterized by the patients' own immune system and exist within several different disciplines. Disease mechanisms and the genetic basis for some of these diseases have certain common features, and new immunomodulating drugs, both biological and synthetic, are therefore often used across disciplines. The Clinical Immunology Research Group at the hospital has collaborated multidisciplinary for several years. Together with the well-established clinical research unit at SUS, we coordinate and facilitate increased participation in clinical trials within autoimmune diseases and inflammation in Norway.

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

The research laboratory serves as a working area for many projects at the hospital, and the work can vary widely with respect to the types of materials, processes, and equipment involved. Sample preparation is a major task, and equipment necessary for correct handling and storage includes fume hood, ovens, centrifuges, refrigerators, freezers, and ultra-freezer. A variety of proteins is analysed in many projects by immunological methods and can be quantitated by Mesoscale Discovery, SIMOA technology, and two advanced microplate readers, capable of measuring absorbance, fluorescence, and luminescence. There are two advanced chromatographic systems in the research laboratory; A high performance liquid chromatography instrument with UV-detector and fraction collector and a gas chromatography instrument connected to a mass spectrometry detector.

For global proteomics, metabolomics and toxicology screening, as well as for general method development, we can perform analyses with ultra-performance liquid chromatography (UPLC, Waters) coupled to a high resolution mass spectrometry instrument (timsTOF, Bruker). For targeted analysis of proteins, peptides and metabolites, UPLC coupled with various tandem mass spectrometers of the triple-quadrupole (QqQ) type: Quattro Micro, Xevo TQ-S, and Xevo TQ-S Micro (all from Waters). Pipetting robots (Tecan and Hamilton) and HPLC-UV with fraction collector (Waters) for automatic sample preparation.

The Proteomics Unit at the University of Bergen (PROBE), is a member of the National Network of Advanced Proteomics Infrastructure (NAPI). NAPI is funded by the Research Council of Norway (INFRASTRUKTUR-program project number 295910).

Genomics:

SNP&SEQ Technology Platform at Uppsala University, Sweden (www.genotyping.se). The facility is part of the National Genomics Infrastructure supported by the Swedish Research Council (VR-RFI), Science for Life Laboratory and the Knut and Alice Wallenberg Foundation

Clinical Genomics Core of the OMRF (Oklahoma Medical Research Foundation) in Oklahoma, USA.

NORCE (Norwegian Research Centre), Stavanger – service by Orbitrap analyses.

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).

	Most of the research carried out in the research group is highly interdisciplinary based, and covers members from different sectors of clinical medicine, neurophysiology, psychology, radiology, pathology, biochemistry, immunology, molecular biology, and genetics.	
Interdisciplinary (within and beyond	In addition, a qualitative research approach to a wider	
the group)	understanding of the fatigue phenomenon is ongoing.	
	These interactions are regarded as extremely helpful and important to obtain a wider and deeper understanding of complex cerebral phenomena such as fatigue/sickness behavior and cognition.	
	The group cooperates with strong research groups at several national and internationally based universities (see 1.1 above).	
Collaboration with other research sectors e.g. higher education, research institutes, health trusts and industry.	 Research institutes: NORCE (Norwegian Research Centre), Oklahoma Medical Research Foundation, USA. Higher education: University of Bergen and Stavanger. Medical industry: AbbVie, Ferring, Tillots, Pfizer, Roche. 	
Transdisciplinary (including non		
academic stakeholders)	Members of the group give talks/information to patient organizations and write popular scientific articles in relevant	
Transdisciplinary research involves	patient journals, and give interviews to media (newspapers and	
the integration of knowledge from	television).	
different science disciplines and (non-	- The purpose of this is to achieve a more realistic understanding of	
academic) stakeholder communities	fatigue as a biologically based phenomenon, and minimalize	
with the aim to help address complex	confusion and misunderstandings in the public domain of this	
societal challenges.	common and troublesome condition.	

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.

The most important scientific contribution from the Clinical Immunology Research Group is in the field of understanding the biological mechanism that generate chronic fatigue in somatic diseases. This is exemplified by revealing a network of biomolecules that interact and through activation of cerebral neurons induce the "sickness behavior" phenomenon, in which fatigue is a dominant component. In addition to proinflammatory cytokines (IL-1 β , etc) downregulatory biomolecules of inflammation and cellular stress (heatshock proteins, etc), and neuropeptides (hypocretin) could participate in fatigue regulation whatever the primary inflammatory/autoimmune disease entity. This understanding is important because there is a considerable knowledge gap in the understanding of fatigue. For the individual and for society it implies considerable costs to the economy with medical expenses, sick leave, and lost productivity as the main expenses. A more consistent and scientific based understanding is called for by many patients, their families, physicians, and health authorities. In addition, potential therapeutic options may become available through the results of our findings.

In addition, the research group contributes significantly to an understanding of the genetic background and biomolecular mechanisms of chronic inflammatory and autoimmune diseases. This is accomplished through different international collaborations.

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

Clinical Immunology - 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. <u>Please delete tables that are not used.</u>

Project 1:	Project owner(s) (project leaders organisation)	Oklahoma Medical Research Foundation (OMRF)
SGENE - Discovery and	Total budget and share	Total budget unknown
Characterization of Genetic	allocated to research group	Our group: In kind work
Risk Loci in Sjogren's	Objectives and outcomes	The Sjögren's Genetics Network (SGENE) is an international collaboration focused on
Syndrome.	(planned or actual) and link	identifying and understanding the genetic variations that influence Sjögren's pathology.
2013 - ongoing	to website	Collectively, SGENE collaborators from 26 different sites (5 in the United States; 21 in
		foreign countries) have recruited a large cohort of geographically diverse participants
		of European ancestry.
		Website: <u>dbGaP Study (nih.gov)</u>
Project 2:	Project owner(s) (project	The DISSECT consortium, Uppsala University (prof Lars Rønnblom)
	leaders organisation)	(AstraZeneca-SciLifeLab joint research programme: DISSECT)
The DISSECT consortium.	Total budget and share	Total budget unknown
2013 - 2022	allocated to research group	Our group: In kind work
	Objectives and outcomes	To "dissect" disease mechanisms in three systemic inflammatory autoimmune diseases
	(planned or actual) and link	Website: Rheumatology - Department of Medical Sciences - Uppsala University,
	to website	<u>Sweden (uu.se)</u>
Project 3:	Project owner(s) (project	Peter Gergely (Novartis)
	leaders organisation)	Xavier Mariette, INSERM (coordinator)
NECESSITY	Total budget and share	Total budget euro 15,4 mill
2019 - 2025	allocated to research group	The research group: euro 31,8 K
	Objectives and outcomes	To identify and validate new clinical end-points for primary Sjogren's syndrome with
	(planned or actual) and link	the ambition to provide tailored outcome measures for use in future clinical trials
	to website	Website: <u>NECESSITY (necessity-h2020.eu)</u>

Project 4:	Project owner(s) (project	Nikolay Manyakov, Janssen Pharmaceutica NV
	leaders organisation)	Wan-Fai Ng, University of Newcastle upon Tyne; UK
IDEA-FAST	Total budget and share	Euro 42 mill
2019 - 2025	allocated to research group	The research group: euro 123,6 k
	Objectives and outcomes	To identify digital endpoints that provide reliable, objective and sensitive evaluation of
	(planned or actual) and link	activities of daily life (ADL), disability and health related-quality of life (HRQoL) for the
	to website	following neurodegenrative diseases (NDD): Parkinson's Disease (PD), Huntington's
		Disease (HD) and the following immune-mediated inflammatory diseases (IMID):
		Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), Primary Sjögren's
		Syndrome (PSS), and Inflammatory Bowel Disease (IBD).
		Website: IDEA-FAST (idea-fast.eu)
Project 5:	Project owner(s) (project	FOREUM, Foundation for Research in Rheumatology
	leaders organisation)	Leader: Wan-Fai Ng, University of Newcastle upon Tyne; UK
Stratified Medicine in primary	Total budget and share	Total euro 600 000
Sjögrens Syndrome	allocated to research group	The research group: euro 41 k
2018 - 2023	Objectives and outcomes	Primary Sjögren's syndrome (PSS) is a chronic complex immune-mediated rheumatic
	(planned or actual) and link	disease with no effective treatment to date. PSS affects 0.05-0.1% of the adults. A key
	to website	barrier to therapeutic development is the marked heterogeneity in clinical
		manifestations and pathobiological profiles among PSS patients. We have recently
		described a strategy to stratify PSS patients into four subtypes with distinct clinical
		phenotypes and transcriptomic signatures.
		Website: <u>FOREUM – Funded Research (foreum.org)</u>
Project 6:	Project owner(s) (project	Clinical Immunology Research Group, Stavanger University Hospital
	leaders organisation)	
Biological mechanisms of	Total budget and share	18,5 mill NKR
chronic fatigue	allocated to research group	
2010 - ongoing	Objectives and outcomes	I o uncover biological mechanisms for chronic fatigue associated with inflammatory
	(planned or actual) and link	autoimmune diseases
	to website	Website: <u>Clinical Immunology - Helse Stavanger HF (helse-stavanger.no)</u>

Project 7:	Project owner(s) (project	Clinical Immunology Research Group, Stavanger University Hospital
Cognitive dysfunction in autoimmune diseases	Total budget and share allocated to research group	4 mill NKR
2009 - 2021	Objectives and outcomes (planned or actual) and link to website	To investigate mechanisms for cerebral dysfunction in primary Sjogren's syndrome and systemic lupus erythematosus Website: <u>Clinical Immunology - Helse Stavanger HF (helse-stavanger.no)</u>
Project 8:	Project owner(s) (project leaders organisation)	Clinical Immunology Research Group, Stavanger University Hospital
Inflammatory bowel disease	Total budget and share	9 mill NKR
and celiac disease	allocated to research group	
2013 - ongoing	Objectives and outcomes	To investigate biomolecules, fatigue, and treatment options in prospective studies in
	(planned or actual) and link	IBD and celiac disease.
	to website	Website: Stavanger University Hospital Inflammatory Bowel Disease Trial
		(clinicaltrials.gov)

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/.

Publication 1: Title: Anti-HMGB1 auto-Abs influence fatigue in patients with Crohn's disease.	Authors (Please highlight group members)	Kvivik I, Grimstad T, Jonsson G, Kvaløy JT, Omdal R
Journal: Innate Immun. Year: 2021	Short description	A study that shows that antibodies against the proinflammatory molecule HMGB1 ameliorates fatigue
DOI: <u>10.1177/17534259211014252</u> URL: <u>https://journals.sagepub.com/doi/10.1177/17534259211014252</u>	Research group's contribution	Conception of idea, clinical work, lab and statistical work, drafting, discussions.
Publication 2: Title: Genetic variants at the RTP4/MASP1 locus are associated with fatigue in Scandingvian patients with primary Siggrep's syndrome	Authors (Please highlight group members)	Norheim KB, Imgenberg-Kreuz J, Alexsson A, Johnsen SJA, Bårdsen K, Brun JG, Dehkordi RK, Theander E, Mandl T, Jonsson R, Ng WF, Lessard CJ, Rasmussen A, Sivilis K, Ronnblom L, Omdal R
Journal: BMJ Journals Year: 2021	Short description	First description of fatigue-related genes in pSS
DOI: <u>10.1136/rmdopen-2021-001832</u> URL: <u>https://rmdopen.bmj.com/content/7/3/e001832</u>	Research group's contribution	Conception of idea, clinical and statistical work, drafting, discussions.
Publication 3: Title: Neurofilament light is a biomarker of brain involvement in lupus and primary Sjögren's syndrome.	Authors (Please highlight group members)	Tjensvoll AB, Lauvsnes MB, Zetterberg H, Kvaløy JT, Kvivik I, Maroni SS, Greve OJ, Beyer MK, Hirohata S, Putterman C, Alves G, Harboe E, Blennow K, Gøransson LG, Omdal R.
Journal: J Neurol. Year: 2020	Short description	First study that shows that neurofilament light is a marker of autoimmune attack on the brain in SLE
DOI: <u>10.1007/s00415-020-10290-y</u> URL: <u>https://link.springer.com/article/10.1007/s00415-020-10290-y</u>	Research group's contribution	Conception of idea, clinical and statistical work, drafting, discussions.

Publication 4: Title: Genetic and clinical basis for two distinct subtypes of primary Sjögren's syndrome- Journal: Rheumatology (Oxford). Year: 2020 DOI: 10.1093/rheumatology/keaa367 URL: https://pubmed.ncbi.nlm.nih.gov/32889544/	Authors (Please highlight group members)	Thorlacius GE, Hultin-Rosenberg L, Sandling JK, Bianchi M, Imgenberg-Kreuz J, Pucholt P, Theander E, Kvarnström M, Forsblad-d'Elia H, Bucher SM, Norheim KB, Johnsen SJA , Hammenfors D, Skarstein K, Jonsson MV, Baecklund E, Aqrawi LA, Jensen JL, Palm Ø, Morris AP; DISSECT consortium; the ImmunoArray consortium, Meadows JRS, Rantapää-Dahlqvist S, Mandl T, Eriksson P, Lind L, Omdal R , Jonsson R, Lindblad-Toh K, Rönnblom L, Wahren- Herlenius M, Nordmark G
	description	First study that shows that pSS phenotype is dependent of SSA/SSB autoantibody type.
	Research group's contribution	Blood samples, clinical data, ideas, discussions, drafting.
Publication 5: Title: Considerably lower levels of hypocretin-1 in cerebrospinal fluid is	Authors (Please highlight group members)	Bårdsen K, Gjerstad MD, Partinen M, Kvivik I, Tjensvoll AB, Ruoff P, Omdal R, Brede C
revealed by a novel mass spectrometry method compared with standard radioimmunoassay.	Short description	Development of a new "non-immunoassay" method for hypocretin measures in cerebrospinal fluid.
Journal: Anal Chem. Year: 2019. DOI: <u>10.1021/acs.analchem.9b02710</u> URL: <u>https://pubs.acs.org/doi/10.1021/acs.analchem.9b02710</u>	Research group's contribution	Conception of idea, clinical work, method development, statistical work, drafting, discussions.
Publication 6: Title: Thyroidectomy Versus Medical Management for Euthyroid	Authors (Please highlight group members)	Guldvog I, Reitsma LC, Johnsen L, Lauzike A, Gibbs C, Carlsen E, Lende TH, Narvestad JK, Omdal R, Kvaløy JT , Hoff G, Bernklev T, Søiland H
PatientsWith Hashimoto Disease and Persisting Symptoms. A Randomized Trial Journal: Ann Intern Med.	Short description	Experimental treatment of fatigue in autoimmune thyroiditis by radical removal of the thyroid gland. Prospective controlled study.
Year: 2019 DOI: <u>10.7326/M18-0284</u>	Research group's contribution	Theoretical framework, discussions, drafting.

URL: https://www.acpjournals.org/doi/10.7326/M18-0284		
Publication 7:	Authors (Please highlight group members)	Grimstad T, Kvivik I, Kvaløy JT, Aabakken L, Omdal R
Crohn's disease Journal: Innate Immunity Year: 2019	Short description	A study investigating the involvement of cellular stress proteins (HSP) on fatigue
DOI: <u>10.1080/00365521.2018.1533582</u> URL: <u>https://www.tandfonline.com/doi/full/10.1080/00365521.2018.1533582</u>	Research group's contribution	Conception of idea, lab, clinical, and statistical work, drafting, discussions.
Publication 8: <i>Title: Effect of biological treatment on fatigue in psoriasis: A meta- analysis of biological drug treatment</i> Journal: Am J Clin Dermatol Am J Clin Dermatol. Year: 2019 DOI: <u>10.1007/s40257-019-00434-w</u> URL: https://link.springer.com/article/10.1007/s40257-019-00434-w	Authors (Please highlight group members)	Skoie IM, Dalen I, Omdal R
	Short description	A meta-analysis demonstrating that all biological drugs have an effect on fatigue in patients with psoriasis.
	Research group's contribution	Conception of idea, statistical work, drafting, discussions.
Publication 9: <i>Title: Interleukin-1 related activity and hypocretin-1 in cerebrospinal fluid contribute to fatigue in primary Sjögren's syndrome</i> Journal: J Neuroinflammation.	Authors (Please highlight group members)	Bårdsen K, Brede C, Kvivik I, Kvaløy JT, Jonsdottir K, Tjensvoll AB, Ruoff P, Omdal R
	Short description	A study demonstrating that network of biomolecules in cerebrospinal fluid influence fatigue in pSS
Year: 2019 DOI: <u>10.1186/s12974-019-1502-8</u>	Research group's contribution	Conception of idea, lab, clinical, and statistical work, drafting, discussions.

URL:		
https://jneuroinflammation.biomedcentral.com/articles/10.1186/s12974-		
<u>019-1502-8</u>		
Publication 10:	Authors (Please	Skoie IM, Bårdsen K, Nilsen MM, Eidem LE, Grimstad T,
	highlight group	Dalen I, Omdal R.
Title: Fatigue and expression of heat shock genes in plaque type psoriasis.	members)	
Journal: Clin Exp Dermatol.	Short	First paper on expression of "fatigue-related" HSP-genes
Year: 2022	description	in psoriasis.
DOI: <u>10.1111/ced.15068</u>		
URL: https://academic.oup.com/ced/article-	Research group's	Conception of idea, lab, clinical, and statistical work,
abstract/47/6/1068/6693163?redirectedFrom=fulltext&login=true	contribution	drafting, discussions.
	A 11 (D)	
Publication 11:	Autnors (Please	Grimstad I, Skjellerudsveen Bivi, Kvaløy JI, Skole IVI,
Title. The influence of disease activity on fatigue in patients with	nignlight group	Carisen A, Karisen LN, Aabakken L, Omdai K.
Inte: The influence of disease activity on fatigue in patients with	members)	
Journal: Scand I Gastroenterol	Short	A study showing how disease activity is not influencing
Vegr: 2021	description	fatigue severity in UC.
DOI: 10, 1080/00365521, 2021, 2007281	Research group's	Conception of idea, lab, clinical, and statistical work,
1181 ·	contribution	drafting, discussions.
https://www.tandfonline.com/doi/full/10.1080/00365521.2021.2007281		
Publication 12:	Authors (Please	Lauvsnes MB, Tjensvoll AB, Maroni SM, Kvivik I,
	highlight group	Grimstad T, Greve OJ, Harboe E, Gøransson LG,
Title: The blood-brain barrier, TWEAK, and neuropsychiatric involvement	members)	Putterman C, Omdal R.
in human systemic lupus erythematosus and primary Sjögren's syndrome.	Short	TWEAK is a multifaceted biomolecule we investigated
Journal: Sage journal, Lupus.	description	with relevance to how it influences the integrity of the
Year: 2018	-	BBB and hence cognitive functions.

DOI: <u>10.1177/0961203318804895</u>	Research group's	Conception of idea, clinical, and statistical work, drafting,
URL: <u>https://journals.sagepub.com/doi/10.1177/0961203318804895</u>	contribution	discussions.

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

1	Sjögren's Syndrome (Oxford Rheumatology Library 2016). Fatigue chapter by Omdal R and Norheim K.
2	Lærebok I immunologi (Tutorial in Immunology) (Universitetsforlaget 2019). Vikse J

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.

The research group, led by Roald Omdal, has made substantial contributions to the field, particularly in the investigation of fatigue and the effects of exercise on its manifestation. Their research, prominently featured on helse-stavanger.no, explores the nuanced relationship between fatigue and the benefits of physical conditioning. By examining the impact of exercise on fatigue, the group strives to provide valuable insights into enhancing overall well-being.

The group's commitment extends to addressing the pressing issue of long COVID, as evidenced by their involvement in a Norwegian study aimed at unraveling the root causes of this lingering condition. Their work, featured on NRK.no (The Norwegian broadcasting Corporation) and dagensmedisin.no (a Norwegian medical and healthcare news publication), signifies a dedicated effort to understand and mitigate the long-term effects of COVID-19, contributing to the global discourse on this emerging health concern.

Furthermore, the research group is actively engaged in unraveling the biological underpinnings of chronic fatigue and related conditions. Publications on forskning.no* delve into the reasons behind the prevalence of chronic fatigue, while their exploration of fatigue in celiac disease, as highlighted on helse-stavanger.no, showcases the breadth of their research portfolio.

The dedication of this research group is underscored by their recognition in prestigious awards, as seen in the coverage on helse-stavanger.no, where they emerged as winners of the year's research prizes. Such accolades speak to the significance and impact of their contributions in advancing our understanding of various health conditions, ultimately benefiting society as a whole.

Every year, Professor Roald Omdal, along with several other research members, engages in a series of highly sought-after talks and scientific lectures tailored for patients and the general public.

Websites for the performances mentioned above, unfortunately only in Norwegian:

- Roald Omdal: Fatigue og effekten av kondisjonstrening (helse-stavanger.no)
- <u>Norsk studie skal finne årsaken til long covid (NRK.no)</u>
- Leter etter biologisk årsak til long covid (dagensmedisin.no)
- Her er vinnerne av årets forskningspriser (helse-stavanger.no)
- Hvorfor har så mange kronisk utmattelse? (forskning.no)
- Fatigue ved cøliaki en ofte oversett plage (helse-stavanger.no)
- <u>Slik beviste de at fatigue ikke er latskap (helse-stavanger.no)</u>

* Forskning.no is a Norwegian online science news platform that aims to communicate scientific findings to a broader audience, making complex research more accessible to the general public.

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

 Instructions: Please select 5–10 of your most important user-oriented publications or other products from the last 5–10 years with emphasis on recent

 publications/products. For each item, please use the following formatting. <u>Please delete lines which are not used.</u>

No.	Name of publication/product	Date of publication/product	Link to the document
1	Fatigue gets better when you exert yourself!	2018	Fatigue blir bedre når du anstrenger deg! - Spafo Norge
			[website in Norwegian]
2	Chronic fatigue – a challenge in clinical practice	2018	Kronisk fatigue – ei utfordring i klinisk praksis (helsetilsynet.no)
			[website in Norwegian]
3	Exercise against fatigue	2021	Fatigue: Trening mot tretthet (viover60.no) [website in
			Norwegian]

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.

Challenges

In the forthcoming years, the research group faces the crucial task of ensuring the well-being of its members, particularly those who have recently earned their PhDs. The primary objectives involve securing permanent research positions and attracting new post-doctoral candidates.

Maintaining the integrity of research endeavors and fostering collaboration on primary research tasks pose potential challenges. Striking a balance between preserving the group's cohesiveness and allowing for individual contributions remains a key consideration.

Economic security emerges as a critical concern, demanding strategic planning and resource allocation to sustain the group's initiatives effectively.

Opportunities

Notably, the research group has positioned itself at the forefront by concentrating on a specific niche chronic fatigue. This condition is increasingly recognized as a significant issue in numerous chronic diseases affecting the population. The group stands as pioneers in delving into the intricate biological mechanisms underlying this phenomenon, marking a milestone in the pursuit of knowledge in this field.