

Søker:	Victor Greiff (IMMI), Geir Kjetil Sandve (IFI)
Name of hub	immunoHUB : a common resource and ecosystem for immune receptor sequence data storage and analysis
Vertsinstitutt (hub):	Department of Immunology (IMMI, Faculty of Medicine)
Samarbeidsparter (noder):	Institute of Clinical Medicine, Institute of Informatics, Department of Pharmacology, Department of Mathematics, Department of Linguistics, Oslo Cancer Cluster, Oslo University Hospital, Akershus Hospital, ELIXIR
Søknadsbeløp:	2.420.000 NOK
Søknadsperiode:	3 years: 2019–2022 [effectively: 2020–2023, since most of 2019 will be over] (if possible: 3+2yrs)

1: Formål og gevinster

1.1: Hva er formålet?

The aim of immunoHUB is to improve the UiO life science and medical researchers' access to an end-to-end software service and tool ecosystem for immune receptor sequence storage and analysis of immune receptor sequence data (immunomics). Briefly, immune receptors are key molecules of the immune system because they are sensors of disease (bacteria, virus, cancer, autoimmunity). The entirety of all immune receptors is called “immunome”. Immune receptors have been shown to be an invaluable tool for disease diagnostics and immunotherapy as recently comprehensively reviewed by us (Brown et al., 2019, *Molecular Systems Design and Engineering*). To illustrate the importance of immune receptors for public health and the economy: many current blockbuster drugs targeting cancer and autoimmunity rely on the exquisite disease-specificity of immune receptors with a current market value of >120 Billion USD (yearly growth: >20 Billion USD). **UiO is one of the world-leading research hubs in immune receptor research with globally leading scientists in this area** (e.g., Geir Kjetil Sandve and Victor Greiff [bioinformatics, software standardization, machine learning focus], Ludvig M. Sollid [autoimmunity focus, (former) Leader of SFF, Jebsen Center, ERCadvG], Bjarne Bogen (vaccine focus, Jebsen Center), Johanna Olweus [cancer focus, Jebsen Center], Jan Terje Andersen and Inger Sandlie [drug developability focus, many patents on custom antibody immune receptor sequences]). In addition to these thought leaders in immune receptor research, there exist numerous UiO and University Hospital (OUS) research groups that have been or are currently gearing up to analyze immune receptors in a plethora of human disease settings (see list of research groups in Section 2.4). In fact, virtually any UiO/OUS clinical or academic research group working in immunology currently has or will have in the future interest in the computational analysis of immune receptor sequences. In short, immune receptors represent a key technology for biomedical personalized and precision medicine and computational bioinformatics and bio-machine learning. **immunoHUB will be a key component to ensuring that UiO remains competitive in the immune receptor research field. To render the need of UiO+OUS groups for an immunoHUB explicit, we have attached support letters of close to ≈20 research group leaders from ≈8 Departments/Institutes to this proposal.**

In general, the current shortcomings in the storage and computational processing of immune receptor data at UiO revolve around the common issue that each group has its own setup which, in the short-to-midterm, may not be sustainable given the exponential increase in sequencing data and cutting-edge analytical approaches. Thus, all UiO groups working on immune receptor data would benefit from joining forces to develop a common, standards-based and scalable solution for immune receptor research that matches the majority of each group's specific requirements, needs, and methodologies. The current IT challenges in immune receptor research at UiO may be summarized as follows:

- Immune receptor analysis falls in between many chairs: it is based on high-throughput sequencing data for which, in principle, hubs (such as the [GSuite HyperBrowser](#) co-developed by Geir Kjetil Sandve [IFI]) exist. However, immune receptor data storage and analysis have their own unique requirements and idiosyncrasies that differ from those by research groups working on for example transcriptomics analysis, variant discovery or genome assembly.
- As evidenced by the support letters, the research groups having a need for a centralized hub for immune receptor analysis (immunoHUB) are spread across different UiO Departments and Faculties and are thus very diverse. Therefore, there is a need for a hub that unites these many UiO organizational structures.

- High-throughput immune receptor analysis has only very recently become feasible for clinical and immunological studies such as those performed by the supporting groups. This means that software and methodology are in rapid development. It remains, therefore, very difficult for each group to stay on top of analytical possibilities, available software, and best practices. Furthermore, suitable storage solutions and leading methods software are as of yet not consistently available on the high-capacity computing resources.
- There is currently no organization/network/constellation in Oslo that has the capacity and authority to develop unified solutions or fill gaps in the computational needs of groups performing immune receptor analysis.

Typical workflow of immune receptor research: immune receptor research is based on large amounts of immunogenetic sequence data because the genetic sequence of an immune receptor encodes its disease specificity. Post sequencing, immune receptor sequence data is correlated with a disease or target pathogen (virus, bacteria, cancer) to detect disease-related patterns. Per sample, millions of immune receptor sequences may be generated thus creating immense sequence datasets that require standardized storage, annotation, and analysis tools. Thus, a typical situation and research process for a lab analyzing immune receptors at UiO is as follows:

- Discuss group-internally about what would be the most suitable hardware infrastructure to work with – for example, personal computers, Abel, Fram, UH-laaS.
 - Acquire the necessary quotas for storage and processing time
- Determine what is currently the most suitable software to process the immune receptor data
 - Try to get the selected software installed at the relevant infrastructure (which might not be given priority when asked by each small group)
 - Try to get the selected software to work together – in terms of format compatibility, matching assumptions, etc.
- Determine what kind of data quality control should be applied for a particular analytical need (which kind of analyses/reports should be generated, using which software)
- Decide on valid analytical approaches to answer the clinical/biological question of interest
 - Try to cater to collaboration and transparency for the computational processing and analyses at the chosen infrastructure, at least internally in a group and ideally to make the work reproducible by peers

In summary, there is limited coordination between the different research groups in terms of the above process – each group spends a considerable effort making decisions, getting the infrastructure they decided on operational and trying to perform the computational work according to best practices. This considerably reduces research productivity, efficiency, and output. In short: the combination of a rapidly (and very competitive) discipline, a multitude of different resources with different APIs and usage models, and the lack of distributed competence and effort to navigate in the vast space of IT choices are currently threatening UiO's world-leading position in immune receptor research. Given the current challenges and shortcomings, the project immunoHUB has the following Goals and Objectives:

- create a network of researchers and research support staff working on immune receptor data
- map, unite and facilitate existing computational tools (both UiO internal and peer-reviewed international) and services to better manage immune receptor data in existing infrastructures and servers
- develop new tools and services where there are currently "gaps" in the offer. The biggest gaps so far lie in immune receptor machine learning and high-dimensional computational analysis
- develop best practice routines for data management, including as much open access as possible, and links and collaboration to other relevant projects, such as those of the AIRR [adaptive immune receptor repertoire] community. Briefly, the AIRR community is an international scientific society of about 800 members with the core mission to standardize the generation and analysis of immune receptor research. Victor Greiff is substantially involved in the AIRR Community by sitting on both the Executive and Communications SubCommittee. Thus, many data standards established and ratified by the AIRR community can be imported during the creation of immunoHUB.

1.2: Hvilket kompetanseområde skal dekkes?

We envision immunoHUB to cover the following areas of expertise, listed in the order of regular workflows:

- Data collection: Methods and tools for efficient acquisition of immune receptor data, with the possibility of storage right to central (and secure) data storage. The goal is to find good solutions that can be reused without ending up in the trap of "one-size-fits-none".
- Data preprocessing: Methods and tools for pre- and postprocessing of immune receptor data from different standards (MIXCR, Adaptive Biotechnologies, IMGT), including best practices for up / downsampling and error filtering. Here it is particularly important to build up the collective knowledge of such principles among researchers who have less technical understanding of some of these issues.
- Formatting/standardization: Knowledge and tools for choosing the right formats as well as the choice of the most standardized encoding (e.g. [AIRR-compliant format](#), see above).
- Pre-analysis / visualization: server-based tools for fast and basic plotting of the immune receptor data sets, such as sequence quality statistics, unique sequences, overlap of sequences with public immune receptor databases (such as [vdjdb](#)) that store antigen-annotated immune receptor sequences. These are things that are often auto-generated on local machines and in the various specialty software suites, but which are not available on UiO servers today. Quick visualization of data sets is of crucial importance for the researchers who are part of groups supporting this application.
- Feature extraction and adaptation for different variants of computational immunology and machine learning: Here, the actual analysis work is performed, so this point will have to be delimited more closely depending on the research groups involved – but major analysis types involve: diversity analysis, network analysis, phylogenetics, and machine learning. The goal must be to standardize these workflows to a large degree so that results can be reproduced and shared.

1.3: Hvilke ressurs-/eInfrastrukturbehov skal dekkes?

Primary server services that enable rapid and reliable data flow and data processing.

2: Organisering

2.1: Hvem skal være ansvarlig leder?

Victor Greiff (IMM) and Geir Kjetil Sandve (IFI).

2.2: Hvem skal være datahåndteringsansvarlig?

Victor Greiff (IMM) and Geir Kjetil Sandve (IFI).

2.3: Hvor skal hub-en være lokalisert?

We suggest the hub to be located at IMMI within the organizational structure of the recently established UiO [Convergence Environment ImmunoLingo](#) (a UiO research flagship initiative) led by Victor Greiff and Geir Kjetil Sandve. The groups of Geir Kjetil Sandve and Victor Greiff have already started an infrastructure for immune receptor analysis consisting of UH-IaaS and Fram ([sigma2.no](#)) that will both contribute to and be able to benefit from the initiative. One possibility is that the budgeted developer is placed at USIT and/or the Centre of Bioinformatics (which includes the UiO node of ELIXIR Norway), to ensure close follow-up and contact with the UiO Convergence environment and immunoHUB leaders. Furthermore, we will disseminate efforts nationally through ELIXIR Norway, and we will interface with ELIXIR Norway on end-user experience and support.

2.4: Hvilke forskningsgrupper, fagmiljøer og lignende skal inngå som noder?

- Mat-Nat Faculty
 - Institute for Informatics
 - [Sandve](#) group
 - Institute for Statistics
 - [Haff](#) group
 - Department of Philosophy, Classics, History of Art and Ideas
 - [Haug](#) group
 - Department of Pharmacology

- [Andersen](#) group
- Faculty of Medicine
 - Institute of Clinical Medicine
 - [Greiff](#) group
 - [Sollid](#) group
 - [Qiao](#) group
 - [Bogen](#) group
 - [Jansen](#) Group
 - [Lund-Johansen](#) group
 - [Taskén](#) group
 - [Malmberg](#) group
 - [Munthe](#) group
- Oslo University Hospital (OUS)
 - [Flatmark](#) group
 - [Olweus](#) group
 - [Helland](#) group
- Oslo Cancer Cluster (OCC)
 - [Inderberg](#) group
 - [Wälchli](#) group
- Akershus University Hospital
 - [Holmøy](#) group
 - [Lossius](#) group
- ELIXIR Norway (UiO node, at the Centre for Bioinformatics, see support letter)
- Centre for Bioinformatics
- USIT, Avdeling for IT i Forskning
- Other UiO environments that are interested will be included, but we await a large-scale contact round until a possible grant is granted

2.5: Hvordan skal arbeidet i organiseres?

ImmuneML will be organized as a three-year project (+2 additional years if possible) with a separate project manager and a scientific board with representatives of above-mentioned academic communities and USIT. The board will meet regularly and will also initiate journal clubs and workshops with international guests to learn about best practices in immune receptor research (for example in conjunction with Norbis – National Research School for Bioinformatics, Biostatistics and Systems Biology) from other environments. It will also be relevant to contribute to relevant activities such as Software / data Carpentry.

ELIXIR Norway (UiO node) will provide 20% of a FTE of a senior engineer for a year in order to harmonize immunoHUB developments with the ELIXIR Norway infrastructure (see support letter).

The plan is that the work can be coordinated with the construction of a new, common infrastructure for the UiO:LifeScience Convergence Environment Immunolingo.

2.6: Hvordan skal gevinstene videreføres etter avvikling?

ImmuneML will deliver:

- a network of researchers centered on the computational discovery of immunotherapeutics and immunodiagnostics using high-throughput immune receptor data. Such a network will be useful even after UiO:Hub funding has stopped. To render networking easier, the following measures will be taken:
 - A website will be created with extensive information on services and resources, a clear point of contact for interested users and more. This will make it easy for researchers to find immunoHUB.
 - A forum for peer leaders should be established where they can exchange experiences and discuss learning points from the reports: slack (ensuing instant and constant communication), Basecamp (project management of immunoHUB construction and maintenance), Github (for tracking of issues).
- a centralized IT resource encompassing computational tools and services that will enable easier work with immune receptor data at UiO in the future. The goal is for these tools to be developed so that they can easily be phased into day-to-day operations after the project ends.

- best practice immune receptor data storage and analysis workflows. These will be documented (readthedocs, github, wiki) and made available openly so that as many people as possible can benefit from them also in the future.
- Workshops and courses will be held (possibly in collaboration with NORBIS) to instruct and teach immunoHUB usage as well as best practices in immune receptor research.
- Clear exit strategy (that is, who takes responsibility for the continuation of the infrastructure and the solutions that have been established after the competence hub has finished its work) that ensures that the research and collaboration dynamism will not be lost post-exit.
- Development and acceptance of immunoHUB will benefit greatly if it is implemented to take advantage of standardized infrastructure solutions (instead of in-house development efforts). ELIXIR Norway (<https://www.elixir-norway.org>) is a key organization providing Life science infrastructure to Norwegian researchers, providing both national solutions as well as competence and inroads towards international undertakings. This includes:
 - solutions for deployment and containerization (e.g., Bioconda, Docker)
 - workflow management (e.g., Galaxy, <https://usegalaxy.org>; Common Workflow Language, <https://www.commonwl.org/>)
 - web-based analysis platforms (Galaxy, <https://galaxy-uiio.bioinfo.no>)
 - project management and storage, including data transfer from sequencing facilities and long time data storage (NeLS portal, <https://nels.bioinfo.no>)
 - user authentication and authorization (Elixir AAI, <https://elixir-europe.org/services/aai>; NeLS identity provider)
 - national help desk
 - national and international training resources
 - competence and solutions for service operations (uptime monitoring, upgrades, etc.)

3: Budsjett

Inntekter:	2019:	2020:	2021:	Sum:
Fra fagrådet	kr 200.000	kr 1.110.000	kr 1.110.000	kr 2.420.000
Egenfinansiering	kr	kr 192.000	kr	kr 192.000
Annen finansiering	kr	kr	kr	kr
Sum inntekter:	kr 200.000	kr 1.302.000	kr 1.110.000	kr 2.612.000
Utgifter:				
Lønnsmidler, frikjøp	kr 200.000	kr 1.152.000	kr 960.000	kr 2.312.000
Anskaffelser	kr	kr	kr	kr
Kompetanseutvikling	kr	kr 100.000	kr 100.000	kr 200.000
Andre utgifter	kr	kr 50.000	kr 50.000	kr 100.000
Sum utgifter:	kr 200.000	kr 1.302.000	kr 1.110.000	kr 2.612.000

The costs are divided into:

- salary for a software engineer (senioringeniør, ltr 66):
- server or quotas (IT hardware)
- competence development: workshops, courses
- in-kind from ELIXIR corresponding to a 20% position

4: Vedlegg

Attached are letters of support of the research groups mentioned in Section 2.4.

IT-HUB Grant Review Committee

Prof. John Torgils Vaage

Professor

Head of the Department of Immunology

University of Oslo, Department of Immunology

✉ j.t.vaage@medisin.uio.no

☎ 0047 99713889

Date: 15 August 2019

Letter of Support for a UiO IT Hub: immunoHUB (project leader: Prof Victor Greiff)

Dear Grant Review Committee,

It is with great pleasure that I write this letter in support of the UiO IT Hub application led by Prof Victor Greiff on the establishment of an IT competence hub for computational immune receptor analysis called immunoHUB.

I hereby confirm that the Department of Immunology (Institute of Clinical Medicine, Faculty of Medicine) enthusiastically supports this IT HUB application with the Department of Immunology being the hub (physical and budget location) of the immunoHUB project.

Dr. Greiff is at the international forefront of computational immune receptor research. In fact, the Department of Immunology recruited Dr. Greiff for his outstanding contributions to the study of the antibody and T-cell immune receptor analysis (immunomics) using machine learning and high-dimensional statistics. Dr. Greiff is heading the recently established Convergence Environment ImmunoLingo underlining his competence for leading the immunoHUB project.

Yours sincerely,



John Torgils Vaage



Post address:
University of Oslo
Department of Immunology
Oslo University Hospital-Rikshospitalet
P.O. box 4956 Nydalen
N-0424 Oslo, Norway

Fagrådet for eInfrastruktur / Søker på "Life science data management hub"

Date: 18 August 2019

ELIXIR support for the application "immunoHUB"

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called immunoHUB for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. In my activity as regional coordinator of ELIXIR, and also in my capacity as scientific leader of the Helse Sør-Øst bioinformatics core facility, I have come to realize that there is significant user interest for the proposal of developing an immunoHUB, as many users in fact are in dire need for the proposed functionality, as some service projects on an individual basis have been served these organizations.

In light of this situation, ELIXIR recognizes the value to the community, and aims to support the proposal both by this letter of support, and also by contributing hours in kind to the proposal (estimated to a 20% FTE for one year for an ELIXIR engineer). The purpose of this would be to disseminate the resultant software solutions to both the regional and national community through the ELIXIR organization, in order to secure a more unified and efficient distribution, to the benefit of the overall user community.

Sincerely yours



Eivind Hovig
Prof. Dr. philos.



Professor Bjarne Bogen, MDPHD
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N-0424 Oslo
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<https://www.ous-research.no/bogen/>
<https://www.med.uio.no/klinmed/english/people/aca/bbogen/index.html>

Letter of support for an IT-UiO:HUB – immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called immunoHUB for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today because it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in immune receptor research. A coordinated effort to centralize and standardize immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

The undersigned is professor of immunology/senior consultant at the University of Oslo/Oslo University Hospital. His research group works with T-B cell collaboration and development of autoimmunity and B cell lymphomas. In our experiments, considerable amounts of B cell receptor and Ig sequencing data are generated. We are, however, in need of better analysis of the data. I therefore enthusiastically support the application of Sandve and Greiff.

Oslo August 9th, 2019



Bjarne Bogen
Professor of medicine (immunology)



Established by
the Research Council
of Norway



Sébastien Wälchli, Ph.D.

TO WHOM IT MAY CONCERN

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Date: 29 July 2019

Letter of support for an IT-UiO:HUB – immunoHUB: a central resource for immune receptor sequence data storage and analysis

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called **immunoHUB** for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today because it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in immune receptor research. A coordinated effort to centralize and standardize immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

As a scientist working with T-cell Receptors (TCR) and Chimeric Antigen Receptors (CAR) pre-clinical development at the Oslo University Hospital, I eagerly support this application. The implementation of **immunoHUB** will directly benefit my research by rendering both immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are crucial determinants in today's publishing landscape. Indeed our main interests are to (1) isolated therapeutic TCR from patient's samples and (2) design novel CARs from the hospital antibodies collection. Both activities heavily rely on sequence databases. The availability of such a central infrastructure for immune receptor storage and data analysis will save my group the efforts needed to set up and maintain local solutions (outdated Excel database and fasta sequences) and facilitate the transfer of information to collaborators.

Sincerely,



Sébastien Wälchli, Ph.D.

Johanna Olweus
Professor, M.D., Ph.D.
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Oslo, July 30, 2019

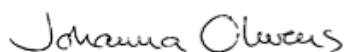
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Letter of support for an IT-UiO:HUB – immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called immunoHUB for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today because it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in immune receptor research. A coordinated effort to centralize and standardize immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

As a Professor and Director of K.G. Jebsen Center for Cancer Immunotherapy (JCIT) at the UiO, and Head of Department of Cancer Immunology at Oslo University Hospital, I give my full and strong support to this application. Identification of immune receptor sequences is crucial for the work of the the groups in JCIT and at my department to i) identify mechanisms and targets of immune responses to cancer in experimental clinical trials that we are involved in for testing of novel immunotherapies, and ii) identify novel T cell receptor and B cell receptor sequences that can be utilized as novel immunotherapeutic drug candidates in immunogene therapy. The implementation of immunoHUB will directly benefit our research by rendering immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are essential determinants to develop novel immunotherapeutic options in cancer and publish in the best scientific journals in this field. The availability of such a central infrastructure for immune receptor storage and data analysis will be crucial to save many groups, including mine, the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups, and contribute to giving UiO a competitive edge in the immuno-oncology space.

Sincerely,



Johanna Olweus

Date: 7 august 2019

Letter of support for an IT-UiO:HUB – immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called immunoHUB for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today because it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in immune receptor research. A coordinated effort to centralize and standardize immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

As a scientist working with immune receptor data at the University of Oslo, I enthusiastically support this application. The implementation of immunoHUB will directly benefit my research by rendering immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are crucial determinants in today's publishing landscape. The availability of such a central infrastructure for immune receptor storage and data analysis will save my group the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups.

Sincerely yours



Dag Haug
Professor of Linguistics



Your ref.:

Our ref.: Fridtjof Lund-Johansen

Date: July 27, 2019

Letter of support for an IT-UiO:HUB – immunoHUB: a central resource for immune receptor sequence data storage and analysis

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called immunoHUB for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today because it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in immune receptor research. A coordinated effort to centralize and standardize immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

As a scientist working with immune receptor data at the Oslo University Hospital I enthusiastically support this application. The implementation of immunoHUB will directly benefit my research by rendering immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are crucial determinants in today's publishing landscape. The availability of such a central infrastructure for immune receptor storage and data analysis will save my group the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups.

I am partner in the KG Jebsen Center for Cancer Immunotherapy. An important aim for the center is to develop T-cell receptors that target mutated peptides. In this line of work, immune-receptor analysis is fundamental. I also work extensively with auto-antibodies and antibody-based proteomics. One of the aims in this research is de-novo sequencing of antibodies by mass spectrometry (MS). Immune receptor sequence libraries are essential to map peptides from MS data into intact antibody molecules.

Oslo, Saturday, July 27, 2019



Fridtjof Lund-Johansen MD, PhD

To whom it may concern.

Professor Ludvig M. Sollid
Centre Director
KG Jebsen Coeliac Disease Research Centre
UiO FOCIS Center of Excellence
Department of Immunology
University of Oslo
Oslo University Hospital-Rikshospitalet
N-0372 Oslo
Norway

Oslo, August 5, 2019

Letter of support for an IT-UiO:HUB

I am writing this letter to support the application of Geir Kjetil Sandve and Victor Greiff for establishment of the UiO IT-Hub called immunoHUB. This initiative will facilitate standardisation of storage and analysis of adaptive immune receptor sequence data across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today as it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in this area of research. A coordinated effort to centralise and standardise immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

As a scientist working with immune receptor data at the I enthusiastically support this application. In my research done at the University of Oslo and/or the Oslo University Hospital, I have for many years pursued questions related to adaptive immune responses of autoimmune conditions; in earlier years being the director of the Centre of Excellence Centre for Immune Regulation and more recently as the head of the KG Jebsen Coeliac Disease Research Centre. Mostly, I work on the antigen receptors of specific T cell and B cells implicated in coeliac disease.

The implementation of immunoHUB will directly benefit my research by rendering immune receptor data storage and analysis faster and more efficient, standardised and reproducible, all of which are crucial determinants in today's publishing landscape. The availability of such a central infrastructure for immune receptor storage and data analysis will save my group the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups. Unreservedly, I support this very important initiative.

Sincerely yours,



Ludvig M. Sollid
Professor, MD, PhD
Centre Director



August 15, 2019

Letter of support for an IT-UiO:HUB - immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

I hereby fully support the initiative to establish the UiO IT-Hub, named immunoHUB, for immune receptor sequence data storage and analysis across UiO research groups.

The initiative is very timely as there is currently an intense interest in research on immune receptors, which is directly related to our understanding of biology and disease mechanisms. An in-depth understanding of the large repertoires of such receptors in health and diseases is therefore of fundamental importance as it will also guide development of novel diagnostic tool as well as therapeutics.

There are many research groups at UiO that are in the international forefront on studies related to immune receptors. These groups will surely benefit from having a central infrastructure in place for storage and analysis of large sets of immune receptor data. This directly relates to my own research on antibody repertoires. Establishment of immunoHUB is therefore a very welcome initiative that will secure a standardized way to secure such data.

Due to all these reasons, I hereby fully support the implementation of immunoHUB suggested by Geir Kjetil Sandve and Victor Greiff.

Sincerely yours,

Jan Tøtje Andersen





UNIVERSITY OF OSLO
Institute of Clinical medicine

Lørenskog, 13.08.2019

Trygve Holmøy, MD, PhD.
Professor of Neurology
Department of Neurology
Akershus University Hospital
Postboks 1000, 1478 Lørenskog
Borway

Letter of support for an IT-UiO:HUB – immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called immunoHUB for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today because it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in immune receptor research. A coordinated effort to centralize and standardize immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

As a scientist working with immune receptor data at the University of Oslo and Akerhsus University Hospital, I enthusiastically support this application. The implementation of immunoHUB will directly benefit my research by rendering immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are crucial determinants in today's publishing landscape. The availability of such a central infrastructure for immune receptor storage and data analysis will save my group the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups.

Sincerely,

A handwritten signature in black ink, reading "Trygve Holmøy".

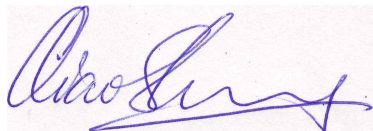
Trygve Holmøy
Professor of Neurology
And
Head, Division of Medicine and Laboratory Sciences
Institute of Clinical Medicine
University of Oslo
Norway

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My group in collaboration with the research groups of Professors Ludvig Sollid and Geir Kjetil Sandve have over the years sequenced and collected T-cell receptor data that constitute one of the largest databases of antigen-specific T-cell receptor sequence data in the field. This unique dataset is the foundation for several high-impact papers in journals such as *Journal of Clinical Investigation* and *Mucosal Immunology*. We have accumulated valuable knowledge in handling receptor sequence database of this magnitude and complexity. Our research groups have spent several man-years in designing tailor-made software to handle the data. Both the software and the knowledge needs dedicated funding so it can be maintained for the use by not only our research groups but also other research groups in the Oslo area that are increasingly applying receptor sequencing in research.



Shuo-Wang Qiao
Associate Professor,
Department of Immunology, Institute of Clinical Medicine
Oslo, 12-08-2019



UNIVERSITY OF OSLO
FACULTY OF MEDICINE

Institute for Clinical Medicine

Oslo University Hospital

N-0410 Oslo, Norway

Karl-Johan Malmberg, MD.PhD

Phone: +4745390926

e-mail: k.j.malmberg@medisin.uio.no

Oslo, August 16th 2019

Letter of Support of a centralized resource for immune receptor sequence data storage and analysis IT-UiO:HUB

I am writing to give my enthusiastic support for the initiative to establish a resource for immune receptor sequence data storage and analysis. My Lab is committed to the use of computational and cutting-edge analytic tools to better understand the function of human immune cells and to fast-track the translation of science-based innovation into new therapies and products. Therefore, we are very excited and supportive of the initiative to establish an IT-UiO:HUB. I believe that such a resource would be of tremendous help for all research groups seeking to address scientific bottlenecks concerning the regulation of the immune system and its implementation in disease settings.

Sincerely,

A handwritten signature in blue ink, appearing to read "K. J. Malmberg".

Professor Karl-Johan Malmberg, M.D, Ph.D.

To whom it might concern

Our ref.:

Your ref.:

Responsible:

Date: July 30, 2019

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As a scientist working with immune receptor data at the University of Oslo and the Oslo University Hospital, I enthusiastically support this application. The implementation of immunoHUB will directly benefit my research by rendering immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are crucial determinants in today's publishing landscape. The availability of such a central infrastructure for immune receptor storage and data analysis will save my group the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups.

In my research group, we have biological material from patients treated with PDL1 / PD1-inhibitors. We have several clinical studies ongoing, for patients diagnosed with lung cancer and mesothelioma, treated with checkpoint inhibitors. We collect both tumour material and serial blood samples for further analyses. We have good clinical follow-up data on these patients, and are eager to analyse immune receptors further, in order to understand why some patients respond very well, while others have no benefit of the treatment.



Åslaug Helland,
Oncologist, Oslo University Hospital
Professor II, University of Oslo

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As a scientist working with immune receptor data at the University of Oslo, I enthusiastically support this application. The implementation of immunoHUB will directly benefit my research by making the access to immune receptor data storage faster and more efficient, which is essential when developing new statistical methods for analysing these data. It will also make it easier to share promising new methods with potential users. Hence, the availability of such a central infrastructure for immune receptor storage will save my group the efforts needed to set up and maintain local solutions, and facilitate collaborative knowledge transfer with other groups.

16.08.2019, Oslo

Ingrid Hobæk Haff

A handwritten signature in black ink, appearing to read 'Ingrid Hobæk Haff', written in a cursive style.



UiO : **Institute of Basic Medical Sciences**
University of Oslo



ANDREAS LOSSIUS M.D., Ph.D.

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Dept. of Molecular Medicine
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Akershus University Hospital

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Letter of support for an IT-UiO:HUB – immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

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As a scientist working with multiple sclerosis and other neuroimmunological disorders at UiO and Akershus University Hospital, I enthusiastically support this application. Immune receptor analysis is key to understand the immunopathogenic mechanisms in these diseases and is anticipated to have implications for future diagnosis and therapeutic interventions. The implementation of immunoHUB will directly benefit my research by rendering immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are crucial to generate high quality scientific knowledge that will make an impact in the field. The availability of such a central infrastructure for immune receptor storage and data analysis will save our group the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups.

Oslo, August 1, 2019

Andreas Lossius

Oslo, 02 August 2019

To whom it may concern,

Letter of support for an IT-UiO:HUB – immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

Geir Kjetil Sandve and Victor Greiff propose to initiate a UiO IT-Hub called immunoHUB for collaborative and standardized immune receptor sequence data storage and analysis across UiO research groups. Immune receptor research is one of the most exciting areas in medicine and immunology today because it directly contributes to the understanding of disease mechanisms and to the development of novel therapeutics and diagnostics. UiO research groups are world leaders in immune receptor research. A coordinated effort to centralize and standardize immune receptor research is of decisive importance for UiO to remain at the top of the immune receptor research field.

As a scientist working with immune receptor data at the Oslo University Hospital I enthusiastically support this application. The implementation of immunoHUB will directly benefit my research by rendering immune receptor data storage and analysis faster and more efficient, standardized and reproducible, all of which are crucial determinants in today's publishing landscape. The availability of such a central infrastructure for immune receptor storage and data analysis will save my group the efforts needed to set up and maintain local solutions and facilitate collaborative knowledge transfer with other groups.

Our main interests as a translational research group in cellular immunotherapy performing both immunomonitoring of clinical trials and development of novel immunotherapies are 1) to follow changes in patient immune receptor repertoire pre- and post-treatment and 2) to isolate potential therapeutic TCRs from responding patients for the development of new therapies. These activities are indeed critically dependent on efficient immune receptor data storage and accurate analysis. A centralized and standardized infrastructure such as ImmunoHub would ensure the implementation and use of innovative, up-to-date, and efficient tools and facilitate collaboration between research groups.

Yours sincerely,



Else Marit Inderberg

To whom it may concern

Division of Cancer Medicine
Institute of Cancer Research

Oslo, August 17, 2019

Letter of support for an IT-UiO:HUB - immunoHUB: a centralized resource for immune receptor sequence data storage and analysis

I am happy to support the initiative from Victor Greiff and Geir Kjetil Sandve to establish a UiO IT-Hub (immunoHUB9 for immune receptor sequence data storage and analysis across UiO research groups.

This initiative is very timely as there is currently focus on a breath of different immune receptors, which is directly related to our understanding of structure, function and disease mechanisms. Furthermore, there is focus on the large repertoires of such receptors from different individuals which relates to immune responses and links to new strategies for cell therapy. In-depth understanding of specific antigen receptors is therefore of fundamental importance in health and diseases and as it will also guide development of novel diagnostic tool as well as therapeutics.

There are many research groups at UiO and OUH that are in the international forefront on studies related to immune receptors and a central infrastructure in place for storage and analysis of large sets of immune receptor data will be of great benefit. My group works with T cell signalling, regulatory T cells and tumor immune evasion mechanisms which includes work on different immune receptors and their interactomes. In the future, I anticipate that we will also go more into receptors from different individuals and their repertoires.

Establishment of immunoHUB is therefore a very welcome initiative that will secure a standardized way to secure such data.

Yours sincerely,



Kjetil Taskén, M.D., Ph.D.,
Group Leader, Department of Cancer Immunology,
Head and Director, Institute for Cancer Research, Oslo University Hospital

Professor of Medicine, Institute of Clinical Medicine, University of Oslo
Oslo, Norway

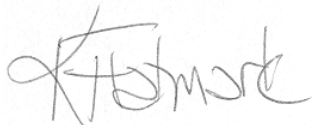
Email: Kjetil.tasken@medisin.uio.no / Mobile: +47-90860759

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Our group's focus is on translational research to develop novel therapy strategies for metastatic colorectal cancer. With introduction of immunotherapy in cancer medicine understanding the immune microenvironment has become increasingly important, particularly in colorectal cancer where only a subset of cases have had benefit so far. Immune receptor sequencing holds great promise in this regard by providing information on the tumor cell specificity of invading immune cells. This, in turn, provides information on the likelihood that immunotherapy could potentially unlock the adaptive immune system's ability to attack tumor cells. As our research group lacks previous experience and expertise in the analysis of immune receptor repertoires, streamlined tools and methods would greatly assist in our ability to answer the questions we are interested in.

Oslo August 5, 2019



Kjersti Flatmark, MD, PhD
Professor of Surgery, University of Oslo
Group Leader, Department of Tumor Biology
Consultant Surgeon, Department of Gastroenterological Surgery
Norwegian Radium Hospital, Oslo University Hospital
0310 Oslo, Norway
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Your ref.:

Our ref.:

Date: 31/7-19

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My research group (<https://www.med.uio.no/klinmed/english/research/groups/mucosal-immunity-in-gut/index.html>) studies the immune system in the human intestine. We have ongoing projects studying both B and T cells in the gut and single cell sequencing of the T and B cell receptor is a central part of our work.

I therefore highly support the immuoHUB initiative.

Best regards



Frode Jahnsen

*Prof. and Senior consultant in Pathology**Head LIIPAT, Dept of Pathology**Oslo University Hospital, Rikshospitalet**Phone +4723071444, Mobile +4793261235**Email. frode.lars.jahnsen@medisin.uio.no*



UiO • Det medisinske fakultet

Universitetet i Oslo

KG Jebsen Centre for B cell malignancies

Oslo, 11th August 2019

Letter of support and recommendation

I hereby strongly recommend the establishment of ImmunoHub, a new UiO-centralized resource and IT infrastructure for immune receptor analysis. This initiative will facilitate the Centre for B cell Malignancies analysis of Ig derived from malignant patient B cells and let us define the microenvironmental impact of V region mutations. Th cells recognize V region peptides and can support the proliferation of malignant B cells. The Immunohub will allow advanced and timely analysis of sequences.

Best regards,

Ludvig Munthe

MD, PhD, Professor.

Leader KG Jebsen Centre for B cell malignancies

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Head of Postgraduate Studies

Institute of Clinical Medicine

University of Oslo

Head of Research and Group leader - Dept of Immunology

<http://ous-research.no/ddi/>



KG Jebsen Centre for B cell malignancies

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