

Evaluation Report on the Program of Translational Medicine Sponsored by Stiftelsen Kristian Gerhard Jebsen

Overall summary, conclusions and recommendations

For the overriding issue as to whether the KG Jebsen Centers program has honored the name of Kristian Gerhard Jebsen, the assessment of the expert group is unambiguous: in a short period of time, the program has emerged as a central player in translational medical research in Norway. It has triggered an intense search for new and original work modes among Norwegian medical scientists and induced improvements in the interaction between health authorities and Norwegian universities. The program holds an important role in the Norwegian research policy landscape, and it has acted as a catalyst and a change-promoting agent for universities, health authorities and academics alike.

Since the inception of the program, many of the goals initially spelled out have been reached or are expected to be accomplished within the foreseeable future. The KG Jebsen Centers program is indeed unique, in that no such a program exists in other Nordic countries. It focuses on translational medicine, a research area of ever-increasing importance for future preventive and therapeutic health care. During our review process, we identified not only a large number of strong features of the program but also several issues of concern. The latter ones relate mostly to matters at host institutions which could be potential obstacles for the KG Jebsen Centers program to excel in years to come.

Our main recommendations are as follows:

- The KG Jebsen Centers program should be continued and strengthened contingent upon the available funds from all parties involved
- Center leadership is pivotal for success and requires more attention
- The duration of the KG Jebsen Center funding may require reconsideration
- Mid-term evaluation and application for extension should be merged
- Scientific excellence should be the overriding criterion for selection
- Networking of the KG Jebsen Centers at all levels needs improvement
- Establishment of a KGJ Foundation Fellows Program should be considered
- Exchange of knowledge regarding experience with media should be established across the Centers
- Host institutions have to improve their career development programs
- Protected time for research is mandatory for translational scientists
- More attention should be paid to space allocation to permit physical proximity of the groups at KG Jebsen Centers
- Current requirements in Ph.D. training are not commensurate with ambitious research goals

Introduction

Stiftelsen Kristian Gerhard Jebsen (hereafter the KGJ Foundation) commissioned an expert group – Professors Mats Benner (University of Lund), Olli A. Jänne (University of Helsinki), and Bente Klarlund Pedersen (University of Copenhagen) – to evaluate its KG Jebsen Centers program on translational medical research. The evaluation was aimed at including both scientific and organizational aspects of the program. Prior to the meetings with the leadership of the current and past KG Jebsen Centers as well as that of the host institutions, the evaluation group was provided with extensive background documentation from the KGJ Foundation, including up-dated bibliometric analyses and the 2018 annual reports of the existing Centers. For the meetings with the expert group, each Center had prepared a SWOT analysis that was discussed during the interviews.

The key evaluation questions that the expert group was asked to assess during their visit and comment on in their report were the following:

- Is the program on the right path, from both the KGJ Foundation's and the host institutions' point of view?
- Has the program been able to make a difference in Norwegian translational medical research?
- Has the program been capable of improving international visibility of Norwegian translational medical science and increasing international funding by Norwegian scientists?
- Has the research at the KG Jebsen Centers resulted in development of new therapeutic modalities?
- Have the host institutions established more robust research environments, facilitated collaboration between Medical Faculties and University Hospitals, and continued investments in the Centers throughout their duration?
- Has the program enhanced the host institutions' ability to prioritize their research areas?
- Are the host institutions (Medical Faculties and University Hospitals) in the right track with regard to their role in organizing and supporting translational medical research as well as in training future scientists to the field of translational medicine?

The evaluation group dealt with the above issues at its meetings with the leadership of the KG Jebsen Centers and that of the host institutions. In addition, Ph.D. (graduate) students and post-doctoral fellows from the Centers were interviewed separately. Each of the above key evaluation questions together with some additional issues are addressed in this report by the expert group.

The Program

The KGJ Foundation established in 2011, in cooperation with Norwegian Medical Faculties and respective health trusts (hereafter University Hospitals), the KG Jebsen Centers funding program to support translational medical research in Norway. The goals of the program were (i) to boost the quality of medical research in Norway; (ii) to facilitate research collaboration between Medical Faculties and University Hospitals; and (iii) to provide improved therapies to patients through the research conducted at the Centers.

During the period of 2011–2017, the KGJ Foundation contributed to the establishment of 18 KG Jebsen Centers in the field of translational medical research in Norwegian Medical Faculties/University Hospitals, with the total financial contribution being 348 million NOK (approx. 36.5 million €). Each Center was funded by the KGJ Foundation annually up to 4.5 million

NOK (approx. 0.47 million €), and the host institutions (Medical Faculties and University Hospitals) were anticipated to provide matching funds. The initial funding of all Centers is for four years, with a possible extension by two years contingent on a favorable interim evaluation.

The host institutions (Medical Faculties/University Hospitals) are invited by the KGJ Foundation to select within their region a limited number of proposals that are eligible to apply for funding as a potential KG Jebsen Center. The permitted maximal number of proposals from the four regions was in 2017 as follows: Oslo, 6; Bergen, 4; Trondheim, 3, and Tromsø, 3. By and large, the number of applications in each region exceeds the region's share; preselection of the applications that will be given the permission to send a proposal to the KGJ Foundation is carried out by regional committees.

The Advisory Committee of the KGJ Foundation (Professors Ole Sejersted, Carl-Henrik Heldin, Gitte Moos Knudsen, Stener Kvinnsland, and Ulf Smith) assesses the applications with the help of external reviewers and makes recommendations to the board of the KGJ Foundation pertaining to the Centers to be selected and funded. The composition and expertise of the Advisory Committee fit very well for different aspects of translational medicine. The Committee is also responsible for assessing the progress of the funded Centers and their eligibility for the two-year extension.

At the time of this evaluation (March–April 2018), all together eight Centers had received extended funding, and 12 (13) Centers were active.

The program from the KGJ Foundation's and the host institutions' point of view

In its 2017 call, the KGJ Foundation defines translational medical research comprising three different categories: (i) between basic research and patient-oriented research that leads to new or improved scientific understanding or standards of care; (ii) between patient-oriented research and population-based research that leads to better patient outcomes, the implementation of best practices, and improved health status in communities; and (iii) between population-based research and laboratory-based research to stimulate a robust scientific understanding of human health and disease. In short, the aim is to translate the findings in basic research more quickly and efficiently into medical practice and, thus, to meaningful health outcomes by taking research from the bench-to-bedside and back.

During its visits with the leadership of the Centers and host institutions, the evaluation panel (we henceforth) did not hear any complains about the program's focus area, that is, translational medicine. We fully agree and congratulate the KGJ Foundation for making this highly relevant and forward-looking choice; it is important not only for translational medical research but also for medical science at large in Norway. We recommend without any hesitation that the program be continued.

All host institutions were proud of their KG Jebsen Centers, and they appeared to be fully supportive in terms of matching the KGJ Foundation's funding – more often than not by providing new graduate student/post-doctoral fellow positions rather than unrestricted funds. Likewise, the Center directors were very appreciative and thankful for the support they had received; in particular, the flexibility of the KGJ Foundation funds was commented on in a highly positive fashion by many directors. The KGJ Foundation and its administration were considered as a very lenient, efficient and supportive patron. The leadership of the Centers perceived it as a knowledgeable and professional funder that takes ambitious measures to keep informed about the progress of the funded Centers, despite its very cost-efficient administration.

We did not hear any criticism on the focus area or the outcomes of the evaluation process, be it the preselection of the proposals by the regional committees deemed eligible to apply for KG Jensen Center funding or the final selection of the Centers for funding by the KGJ Foundation's Board upon the recommendation by the Advisory Committee. In a few instances, however, the host institutions felt that the Advisory Committee could have been more informative and transparent about the reasons as to why the applicants from their region were not successful. Thus, written evaluation reports from the Advisory Committee or the Foundation's administrative personnel were hoped for.

Almost all Center directors and the host institutions' leadership commented on the current funding scheme: the initial funding for four years with a potential two-year extension. The main issue was the duration of funding which was felt to be too short. Various longer funding schemes were suggested, such as 4 + 4 or 5 + 3 years of support from the KGJ Foundation. Should the funding period be prolonged, all seemed to understand that the number of KGJ Jepsen Centers would subsequently be lower. Whereas we do not have a strong position one way or the other on this issue, we recommend nevertheless that the Advisory Committee and the Board of the KGJ Foundation will discuss potential amendments in the current funding schemes.

Some critical issues were raised, especially for the prolongation of Center support. The timing of the evaluation was deemed critical, in that assessing Center progress after two and a half years may be necessary for practical reasons, but the time frame clearly had a detrimental impact at least on some of the Centers – especially those recently formed –, which felt pressure to deliver substantial progress after a relatively short funding period. In addition to the compact time frame, the decision-making process for prolongation appeared less than optimal. While we fully understand that there has to be a selection, the reasons for prolongation (or its denial) were less than transparent, and there may be a need for improved communication – possibly aligned with the mid-term review. The mid-term review – while sometimes reported to be of help and guidance –, appears a bit displaced and unclear in its alignment with the prolongation decision. We, therefore, recommend that the two – mid-term review and prolongation application – should be merged (and perhaps postponed to a somewhat later date).

The KG Jepsen Centers differ significantly in their size and composition; some are very large and dispersed, containing a large number of research topics and senior partners, whereas smaller ones comprise more focused research themes and only a few principal investigators. Our unambiguous opinion is that the quality, *i.e.*, scientific excellence, ought to be the overriding selection criterion. Should there, however, be competition between center applications of equal scientific merits, a more compact and focused proposal with partners of close physical proximity should be preferred. We also recommend strongly that the KGJ Foundation continues its practice to take no consideration of the geographical distribution for its support. Geography should not in any way influence decisions to fund, prolong, or terminate funding, as this would counteract the laudable goal of raising the quality of Norwegian translational medical research.

Translational medical research in Norway

There are other long-term funding mechanisms for (bio)medical research in Norway, but they are either quite intermittent or focused only on one component of translational medicine, such as basic research or clinical trials. In view of this, the KG Jepsen Centers program stands out clearly by its continued specific commitment to translational medicine. It has indeed found a unique role alongside the other funding sources, such as the Norwegian Research Council, the Medical Faculties and the health authorities. The KG Jepsen Centers have become in a short period of time a highly visible and well-advertised landmark of success at their home institutions. The high-profiled and consistent activity by the KGJ

Foundation has also brought about a healthy balance between public and private engagements in research funding and governance, and it has contributed to a plurality in medical research funding. A KG Jebsen Center designation is also an emblem that opens doors to multiple arenas. Collectively, the KG Jebsen Centers program is unique – no such program exists in other Nordic countries –, and it has a great potential for making a difference in Norwegian translational medical research.

The KG Jebsen Centers have been selected by the Advisory Committee of the KGJ Foundation after a careful evaluation of the applicants and their research proposals. In that respect, they are likely to represent environments with a great potential for conducting high-quality translational medical research along with the goals set forth by the KGJ Foundation. Our mandate did not involve an in-depth analysis of the research work by the Centers; we had access to the Centers' annual reports, current bibliometric analyses and lists of publications together with ample other documentation. In addition, all Center directors summarized briefly their research goals and accomplishments during the interviews. It is our collective understanding that most – but not necessarily all – of the past and current Centers have fulfilled most of the expectations set forth during the initial review process or will most likely be able to do so within the next few years.

Overall, we were impressed by the agility of university leadership to respond to external calls, and their ambition to encourage and support different groups to form new collaborative constellations, and to continue working with application groups that did not obtain KG Jebsen Center funding, in order to be better prepared for new calls in years to come. We were, however, less impressed by the current training of translational medical scientists within Medical Faculties and University Hospitals. We return below (on p. 7 onwards) to this issue that we consider very important for the future of translational medicine in Norway.

International visibility and funding of Norwegian translational medical science

The present and past KG Jebsen Centers have undoubtedly upgraded the international visibility of translational medical science in Norway. This development has taken place mainly through high-quality publications in top-tier journals, invited presentations at international meetings, and extensive collaboration of the Centers with international scientists and/or consortia. In this regard, it is highly laudable that the KGJ Foundation's policy permits KG Jebsen Center funds be transferred to international partners. There is a number of excellent biobanks in Norway, and their specimens have been used in a large number of international genome-wide association and other studies. It is, however, of some concern to us that the Norwegian scientists involved in these studies have only seldom possessed a leading scientific role in the utilization of the Norwegian biobank materials.

The funds from KG Jebsen Centers are not sufficient to recruit renowned international scientists to work at the Center's home institutions. On the other hand, the visibility of the Centers has permitted recruitment of excellent international Ph.D. (graduate) students and post-doctoral fellows who will hopefully stay in Norway as future translational medical scientists. Despite this, it is of concern that more often than not, a Ph.D. (graduate) student seems to have limited mobility, in that there is a strong tendency to stay upon graduation as a post-doctoral fellow in the same research group. We will return to the issue of graduate and post-doctoral training more comprehensively on p. 7 onwards.

With regard to enhanced international funding in Norwegian universities for translational medical research brought about by the inception of the KG Jebsen Centers program, we believe that this has not occurred to a greater extent. A number of scientists at KG Jebsen Centers had already funding from international sources, such as contracts from European Union and/or research funds from the European Research Council, prior to their inclusion into the Center in question. Most Centers belong currently to various European or international

research consortia and have, therefore, become more international. However, more extensive new international funding to support individual scientists (groups) at the Centers may not have occurred. We emphasized the importance of international funding at all our meetings with KG Jebsen Center directors. In any event, the KGJ Foundation is to be congratulated for raising the awareness and importance of international competition and networking.

Development of new therapeutic modalities

The goals of all KG Jebsen Centers were aimed to enhance understanding of human health and disease; to create new potential for therapy and standards of care that eventually leads to better patient outcomes; to implement best practices; and to improve health status in communities at large. Many of these goals have been achieved or are clearly under way. Likewise, novel diagnostic and prognostic tools have been developed at different Centers. In a few instances, the research work has entered to the stage, in which an investigator-initiated phase one clinical trial looks feasible. It should be pointed out, however, that we were unable to identify any dramatic breakthroughs in patient care emerging from current or past translational medical research at KG Jebsen centers. Perhaps the time since the inception of the program is still too short.

Research environments and collaboration between Medical Faculties and University Hospitals

One aspect of the successful implementation of the Centers is the coordinated support of regional authorities and universities. We found consistently strong alignment between regional authorities and universities – and were especially impressed with the commitment of the latter. This indicates that the KGJ Foundation has indeed been successful in creating linkages between the two different entities, and that the Center scheme has forged a close co-operation between academia and the health care system. This represents a vast improvement since the 2014 evaluation, when the commitment of the regional authorities was superior to that of the universities, and when many of the regional authorities acted as lead partners with universities operating in a far more reactive mode. It is thus clear that the relationship between the two partners is far more equal today, and the responsibilities for supporting and sustaining the Centers are shared, a remarkable feat given the organizational and financial differences between health authorities and universities.

A recurrent issue in our conversations with the leadership of Centers and host institutions was the localization of research activities, which varied between the Centers – from physical proximity to (continued) dispersion. By and large, the KGJ Foundation's support has not necessitated, or resulted in, significant physical reorganizations of research environments, which is understandable but also unfortunate: one of the most important elements in translational medical research is the eradication of physical boundaries for the scientists to interact. The same applies to multidisciplinary research which is also contingent on interactions and learning between traditions. We also noticed strong differences in this issue between Medical Faculties and University Hospitals: some were quite adept at enabling environments for close physical proximity of the groups, while others held a more passive approach.

Co-location and interaction are key aspects for successful research environments, and the same holds true to leadership – at both scientific and organizational level. With the complexity and multiplicity of the goals, continued risk of runaway partners, and incentives to pursue existing rather than novel research lines, the two-pronged leadership is pivotal to create coherence and direction. In comparison to the 2014 evaluation, we noticed a general upgrading of leadership, but it is still a somewhat underplayed dimension to the program. The approaches to the Center director's role differed significantly; there are several laudable and quite innovative models when it comes to inclusion, succession issues, provision of support and network opportunities, but also examples of passive and subdued management styles.

Both organizational and managerial issues should belong to the domain of the host organizations. Their leaving to the discretion of the Centers themselves may in the end hamper the impact of the KGJ Foundation's support. While leadership programs are no panacea, and they run the risk of becoming ritual nods to managerial stereotypes, it is nevertheless important that the KGJ Foundation highlights more forcefully the importance that an active leadership plays for the long-term stability and rejuvenation of integrative research environments.

Formal interaction between the directors of the KG Jebsen Centers takes place at annual meetings. These meetings appear to be successful and very welcomed by the Center leaderships but their attendance is limited, most often only a few senior partners are included. By contrast, there seems to be very little sponsored interaction between the Ph.D. students and post-doctoral fellows among the KG Jebsen Centers, both regionally and nation-wide. We recommend that the KGJ Foundation considers sponsoring an annual meeting for the Ph.D. students and post-doctoral fellows as well. At these grass-roots-level meetings, the students and fellows should present their research results and compete for a KG Jebsen award given to the best young scientist and/or presenter. A highlight of such a meeting could be a state-of-the-art lecture on a translational medical research topic delivered by a renowned international expert. Creating a network among the Centers at multiple levels would no doubt contribute to enhancement of the KG Jebsen spirit and to facilitate networking of Norwegian scientists at multiple levels.

Host institutions' ability to prioritize their research areas

To create a successful KG Jebsen Foundation Center in translational medicine necessitates interaction and co-operation between a number of research groups, from both the Medical Faculties and University Hospitals. By and large, the planning periods already involve the leadership of the host organizations and give them ample opportunities to recognize the strongest research areas in their domains, which also need to be supported by matching funds in case the applications get funded by the KGJ Foundation. In view of this, it would not be unexpected, if the mere application phase were to result in priority assessment at host institutions. We did not conduct in-depth discussions on this issue at our meetings. It was nevertheless clear that such developments towards priority assessments had taken place in a few instances and, not surprisingly, especially in Trondheim and Tromsø.

Host institutions' role in supporting translational medicine and in training future translational scientists

As already mentioned above, we were impressed by the home institution's support to their KG Jebsen Centers; in particular, as it applies to financial aspects, such as matching funds, excellent infrastructure, and continued support after the termination of a Center's tenure. Nonetheless, we identified a number of concerns that the home institutions need to pay attention to, in order to strengthen not only the future of Norwegian translational medicine but also that of medical research at large. The KGJ Jebsen Foundation could, in turn, use its clout in the negotiations with the home institutions, in order to ensure that substantial attention is directed to the issues mentioned below.

The number of Ph.D. (graduate) students in many of the Centers is very high (up to > 40!), and it clearly exceeds that of post-doctoral fellows. This is not an optimal situation. The standard requirement – with a few exceptions to the rule – for the three-year graduate training is to have a Ph.D. thesis that contains three research articles. It is easy to envision that, in order to meet this requirement, a large number of Center publications is needed (*e.g.*, for 20 Ph.D. students up to 60 publications in three years) which is bound to take the research work to a lateral as opposed to vertical direction. In other words, the establishment of ambitious goals leading to publications in top-tier journals is not really supported by the current Ph.D. thesis requirements.

We were pleased to learn that all Medical Faculties in Norway have an M.D./Ph.D. program and that in many, but not in all regions, this program is popular among the medical students. From the translational medicine point of view, it is important to train research-oriented medical students rigorously in basic sciences, since a prototype translational scientist is an M.D. with strong basic science training with board certification in a clinical specialty. We will return below to the career development of translational scientists as it relates to the support from University Hospitals.

Many of Ph.D. students appear to continue as post-doctoral fellows within the same Center, and likewise, many of the present post-doctoral fellows had followed the same path, in that their graduate training took place at the same Center. Only some Ph.D. students and post-doctoral fellows expressed keen interest in moving abroad for at least a year. This kind of immobility fails to support internationalization of the Norwegian science scenery, and it is seldom favorable to career development of post-doctoral fellows. However, a very positive progress – independent of the KGJ Foundation funding – has taken place in Oslo. Scientia Fellows is a post-doctoral research fellowship program in the field of health sciences; it was launched a few years ago by the Faculty of Medicine, University of Oslo. The program is co-funded by the Maria Sklodowska-Curie Program of the EU, and it permits both post-doctoral training of Norwegians abroad and recruitment of international post-doctoral fellows to Norwegian groups. The total number of trainee slots in this program is around 100; some of those coming from abroad are likely to select a KG Jebsen Center as their home base.

None of the host institutions has a clear-cut tenure-track system for career development of young group leaders. In some instances, however, home institutions have created permanent positions to young scientists at the KG Jebsen Center. It is also laudable that the leadership of a few KG Jebsen Centers has played specific attention to young and up-coming scientists and nurtured their development towards independence. Owing to the lack of a tenure-track system, the future of these talented young scientists is still insecure. In view of this, the KGJ Foundation should think about establishing a “KG Jebsen Fellows Program” to support career development of these researchers.

An M.D. scientist with strong basic science training combined with a clinical specialty is a must for a success in translational medical research. However, such a training does not suffice, in that this kind of person cannot be swamped with clinical responsibilities, but s/he also needs protected time for research. For the KG Jebsen Centers program in translational medicine to be capable of excelling also in years to come, it is mandatory that the University Hospitals create programs permitting outstanding translational scientists to have protected time for research. Even though a given KG Jebsen Center may comprise basic scientists and clinical investigators (with protected time for research) of complementary expertise, we stress nevertheless the importance of well-trained translational scientists for the success of the KG Jebsen Centers program. A corollary to this is that basic science research should be an inherent component of a KG Jebsen Center for translational medical research.

National visibility, knowledge dissemination and public outreach

New research discoveries within the KG Jebsen Centers need to be implemented and anchored in the health care system and in society as such, leading to changes that benefit the patients and the citizens alike. This requires focusing on dissemination of knowledge to lay audience through various media, and active participation in different networks that are likely to have an impact on health politics.

Some of the Centers have been very active and visible players in news media, for example, on television and in newspapers. Some had established excellent interactions with patient organizations, and at least one Center has a patient advisory board. Other Centers have

been less active regarding knowledge dissemination. It is commendable that a few Centers have continued knowledge dissemination and public outreach after the termination of their tenure as a funded KG Jebsen Center.

We recommend that some knowledge exchange regarding experience with media will be established across the Centers. This could take place, for example, at the annual meetings of the Centers. Since also the Ph.D. students and post-doctoral fellows showed interest in knowledge dissemination, it looks pertinent to establish some formal training in media handling for all personnel at the KG Jebsen Centers.

All Centers should have in their annual reports one page that describes the Center's "highlight of the year" and includes an informative picture in a format that appeals to the lay audience. The highlight pictures should, in turn, be shown on the homepage of the KG Jebsen Foundation and disseminated to key journalists, thereby contributing to the honor of the name of Kristian Gerhard Jebsen.

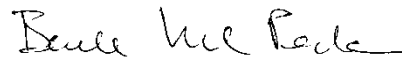
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