



Stiftelsen Kristian Gerhard Jebsen

**Evaluation of
The Kristian Gerhard Jebsen
Foundation's Support of
Translational Medicine**

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Lund and Stockholm, November 18, 2014

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Evaluation of the Kristian Gerhard Jebsen Foundation's Support of Translational Medicine

We, the undersigned, have been asked to evaluate the impact of the Kristian Gerhard Jebsen Foundation (the Foundation henceforth) and its support of centres in the area of translational medicine (K.G. Jebsen senter innen translasjonell medisn). We are honored by the and hereby submit our report. In the period from 2010 until 2013, the Foundation has supported 14 research centres in the area of translational medicine with a total sum of 223 million Norwegian Kronor. The initiative represents a major boost of translational approaches in Norwegian biomedical research, and the centres, together, represent a wide variety of areas and approaches within the overarching field of translational medicine.

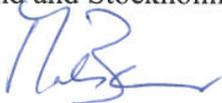
Our task has been to evaluate the impact of the Foundation's support, not in terms of the impact and progress of the individual centres funded, but rather the overall funding concept, its execution and implementation, and its general impact on Norwegian biomedical research. We will consequently broaden our analysis and discuss the general understanding of translational medicine and how it has been operationalized in this context. We will also make some remarks on how foundations may impact on university governance, on the interplay between universities and the health care system, and the workings of research groups in the Norwegian biomedical systems. All of these issues relate to the overall question of the impact of this specific research funding scheme.

Even at this early stage it must be stated that the Foundation has addressed a topic of global centrality to medical research and the clinical practice, and that its support has had an impact on the governance of universities in Norway and on medical research groups in the country, by offering a unique opportunity to form clusters of complementary skills and approaches. Translational approaches are critically dependent on a rapidly expanding methodological repertoire, requiring a mix of competences and collaboration over department, faculty or even university borders. Indicative of this insight is the formation of translational medicine centers binding bridging classic universities with medical faculties and schools of engineering as seen in many countries and contexts.

Even though we are aware of some such initiatives in Norway, bridging mechanisms of this kind seem to be uncommon in Norway. The Foundation's programme is therefore a necessary step in aligning biomedical research competencies and in bridging different organizational goals and interests. It is also a pivotal step in capitalizing on Norway's unique opportunities for translational approaches: the availability of biobanks – for instance through the large programme Biobank Norway – and the public health care system adjacent to its medical schools.

The evaluation team gratefully acknowledges the unfailing support of the Foundation's management as well as the prompt collaboration with the centres, faculty management and health corporations, in the site visits and through the provision of thorough reviews of their work modes ('SWOT'-analysis). We are also indebted to Dr. Fredrik Åström of Lund University for providing a bibliometric analysis to support our evaluation.

Lund and Stockholm, November 18, 2014



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Evaluation criteria

Specifically, the following evaluation targets were identified by the Foundation:

Visibility – the programme should honour the name of Kristian Gerhard Jebsen and associate it with innovation, internationalization, and a useful purpose.

The programme should add to the current support of Norwegian translational research in medicine.

International renown – the programme should elevate Norwegian translational research to a distinguished international level.

For the Foundation, the remit identified the goals of administrative lenience and efficacy, in particular highlighting if transparent and reliable procedures for selecting centres and interacting with the host organizations had been established.

For the host organizations, the asserted goal of support was to elevate their capacity for priority-setting. This involved embedding and governing research environments dedicated to translational medicine, engineering interactions between groups, and between universities and health providers, as well as institutionalizing interplay between laboratories and clinics.

For the centres, the goal achievement is stated in traditional academic terms – such as scientific impact measured in publications – but also in new clinical therapies.

These criteria and goals will guide the structure and content of our report. We will however start by stating some general observations regarding the dual goal of the programme: to stimulate translational research *and* to enhance the strategic planning of Norwegian research and health providers.

Translational medicine – past, present and future

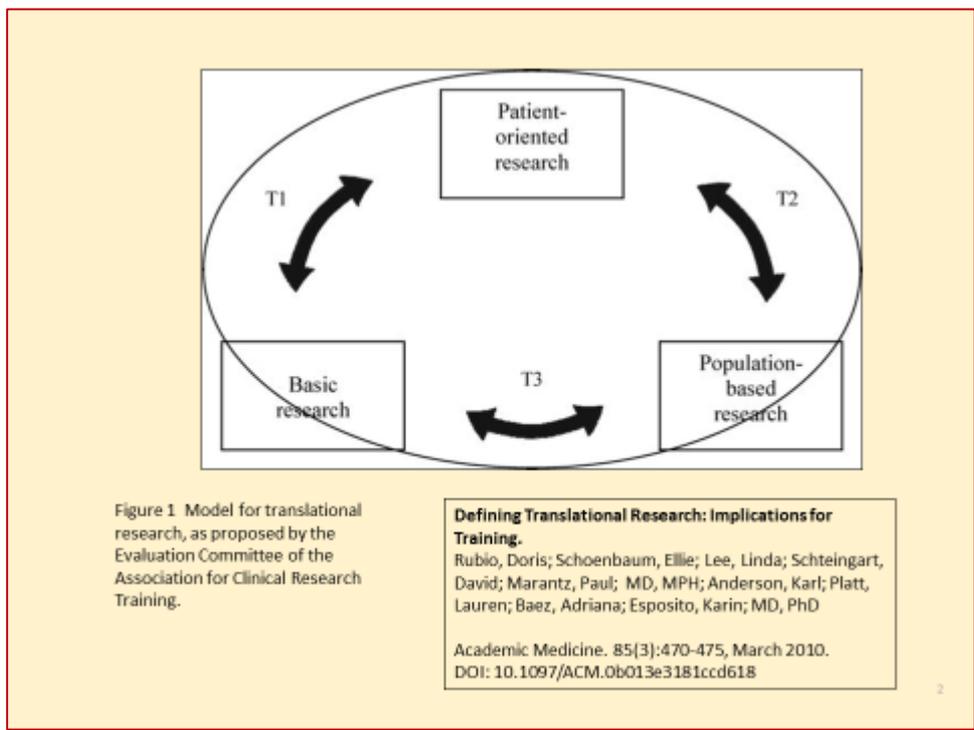
The explicit theme of the K.G. Jebsen Foundation is the support of medical research in centres directed towards translational research. This is a comparatively unique approach, which comes with another unique condition, matching funding with equal support from the respective medical faculty. The focus on translational medicine has parallels at internationally top institutions:

- Broad Institute in Boston jointly run by Harvard University and MIT, world-leading centre for large-scale genotyping.
- CHEM-H (Chemistry, Engineering of Medicine for Human Health at Stanford University (home of the 2014 Nobel Prize winner in Chemistry, W.E. Moerner).
- Joint Center for Translational Medicine, Caltech and UCLA “with the aim of facilitating development of new clinical therapies”.
- Center for Advancing Translational Sciences (NCATS) at the NIH “to transform the translational science process so that new treatment and cures for disease can be delivered to patients faster”.

Corresponding initiatives are emerging in Europe and Asia. Shanghai Tech is a university in the making with four faculties, Life Sciences (largest), Information Technology, Materials Sciences and Entrepreneurship. In Scandinavia, four universities, Karolinska Institutet, KTH Royal Institute of Technology, Stockholm University and Uppsala University have constituted SciLifelab “a national centre for molecular biosciences with focus on health and environmental research. The Centre combines technical expertise with advanced knowledge of translational medicine and molecular bioscience.

These scientific developments at the institutional level are partly a consequence of the changes in the corporate culture of “big pharma”, which in acts decided from commercial potential, have pulled out from the CNS area (high complexity), antibiotics or immunotherapies (consider the response to the current Ebola epidemic) as well as tropical diseases (uncertain financial return). Academic research and entrepreneurial initiatives in start-ups dictated by the medical need may become the source of innovation and eventually new therapies (Drug discovery in academia: the third way? Frearson J. and Wyatt, P. Expert Opin Drug Discov 5, 909-919, 2010).

In defining translational research we have followed the schematic suggested for training of scientists in the field (Figure). It outlines the significance given to genomics but also the passage from and between the categories, genomics, basic research and patient-oriented research. To be named translational, we find it essential that a research program should be multifaceted and integrating. The program should also be clearly goal-oriented, with an overriding patient-oriented perspective. Most commonly, this means forming a “center” with different competences. Translational medicine will therefore be distinguishable from the classic research council supported, in-depth research programs



In population-based research, weight is given to genetics in the understanding of common (chronic) disease. Heredity is largely derived from large numbers of common genetic variants which calls for collection of large numbers of patients. Two K.G. Jebsen “centers” are part of large international efforts to investigate genetic variants in common disease (type 2 diabetes and schizophrenia, respectively).

It is clear, however, that further population increases can only define genetic variations which, taken individually, carry very little weight. We are approaching a “post-genomic area” where disease origins will have to be investigated with other approaches.

We recognize the potential of using subpopulations in Norway for studying pockets of individuals with a higher degree of homozygosity (as has previously been defined in Sweden), particularly in smaller populations in the north of the country (The genetic structure of the Swedish population. Humphreys, K. et al. PLoS One 6, e22547, 2011). Norway also owns bio banks with pathologic specimens collected under many years that can be very useful in order to monitor changes in morbidity, for instance in cancer.

To use all available information in a meaningful way (translation) there is need for different competences, not traditionally available at a medical faculty. Bioinformatics, not only for analysing gene polymorphisms and heredity but also for “Systems Biology”, simulation and modelling. Innovations do not happen uniquely in the academic sphere. Consider computational modelling and simulation which borrows from computer gaming. Inexpensive devices have become engines in advanced calculations. Developments in epigenetics, DNA methylation, histone modification and RNA interference call for competences in mathematics, mathematical statistics on one hand, but clinical insight and observation on the other. Imaging technologies such as ultrasound and MRI are indispensable for clinical research in certain areas, whereas more exotic technologies such as PET (CNS studies and cancer diagnosis) or MEG (CNS) are research disciplines. Method development or applications require knowledge in physics and engineering. Understanding at a cellular level is greatly facilitated by new super resolution microscopy technologies, which to be used at full potential also requires not only specific investments but also expertise. An advanced instrument requires proper educational background and dedication.

In summary, the rapidly expanding methodological repertoire requires a mix of competences and collaboration over department, faculty or even university borders. Indicative of this insight is the formation of translational medicine centres binding bridging classic universities with medical faculties and schools of engineering (see above).

Foundations have a freer role in comparison with research councils, are often connected to a specific will or ambition, and do not have to adjust to the same extent as other funders to expectations and power relations in their respective constituencies. History abounds with examples of foundations (Rockefeller, Ford, Wallenberg) which have acted as change agents, for new areas, collaborative patterns, recruitment, and similar causes. Hence, foundations have been a critical part of research policy with its wider latitude.

Comments on impact of the Foundation's support

Retort on the specific comments on the evaluation remit and our observations.

Regarding **visibility**, the Foundation has quickly established a role as patron in Norwegian medical research. Its support has triggered intense search processes within Norwegian universities, and the label of a Foundation centre has become widely spread and appreciated as a token of visibility and impact. Becoming a centre was unanimously seen as a sign of visibility and excellence. The Norwegian research system has few visible organizational tops and the few 'slots' available for such efforts (in particular the Norwegian Centres of Excellence, SFF) target only few and very large scale operations. Of the seven centres with biomedical orientation, several address translational issues (cancer biomarkers, immune regulation, mental disorders, etc.), but there is certainly space for a increasing concerted efforts, in particular those operating on a smaller and more concentrated scale. In addition, centres of excellence schemes like SFF may be too large and 'negotiated' to meet the requirements for efficient translational approaches as the one outlined above, which depends more on the daily interaction between groups of complementary skills. An often mentioned ideal in task-oriented research of the type envisaged by the Foundation, is to develop clusters of relatively small groups – comprising 6-8 people – under visionary leadership (Hollingsworth and Hollingsworth 2000).

Hence, the Foundation's support aligns with the ideal size and composition of research groups and constellations for translational research. It has created a new form of interaction between research groups in Norway, and in the process fostered a healthy competition for visibility for this type of 'medium-sized' collaboration. To sum up, the Foundation has been very successful in raising the profile of translational approaches in Norway and has developed a visible profile in surprisingly short time.

Regarding **additionality**, Norwegian universities themselves run some organizations devoted to translational efforts, but not on the scale found elsewhere in the world. Even though there are a few of this type in Norway, such as the EMBL node in Oslo (Centre for Molecular Medicine Norway), there is certainly room for more organizational settings for linking basic science/engineering and clinical usefulness. Norwegian medical faculties seem to be relatively traditional in their organizational set-up, with organizational boundaries and recruitment practices reflecting traditional educational and clinical boundaries and specializations, and with few incentives or spaces for creative interaction. Another challenge for the country is the relatively weak articulation between faculties of engineering and medicine, with the exception of Trondheim. The Norwegian system is therefore in need of an array of collaborative incentives. The Foundation's support may trigger more organizational experiments as well as conjoined efforts by universities and the health care providers – it may even incentivize Research Council Norway to instigate flexible support measures for integrated approaches.

Hence, the programme clearly fills a void not only in the academic system but also in the Norwegian funding landscape. A healthy research system is dependent on a degree of pluralism in its research funding template. Block grants to the medical faculties, funding via Research Council Norway and resources channelled via the health care corporations provide the backbone of biomedical research, but there is still an obvious need for support that bridges different approaches and activities. Research Council Norway only runs a limited number of schemes addressing translational approaches. In addition, none of the large-scale programme run by RCN has medicine as its main part, and the recently launched strategy for health (Helse2030) is very broad in its focus, missing an opportunity to foster more tightly knit

approaches and instead venturing into inchoate “strategic programmes” with vague goals and overloaded organizational structures. There are, as mentioned, a few Centres of Excellence in medicine, but their composition and management also seem to motivate researchers to form large constellations, rather than the focused interaction within clusters of smaller groups that we have discussed earlier. Altogether, there is a clear value added in the Foundation’s programme.

When it comes to the **impact on host organizations**, it is important to first note that Norwegian universities have gone through a development from highly regulated relations with the state to more devolved responsibilities. Theoretically, this would free universities from traditional constraints to organize and distribute their resources. In reality, this is more often than not counteracted by universities’ tendency to distribute resources widely. Even though Norwegian universities control more resources on their own than their counterparts in most other countries, “free” and flexible resources are seldom available. Hence, concerted research efforts are critically dependent on the supply of external resources, but these external resources can also leverage internal resource deployment.

The Foundation’s programme has triggered search processes within universities, primarily from the bottom-up to form constellations, either entirely new or reformed. The universities have installed various forms of internal assessments of the constellations – just as was expected by the Foundation. The funding calls seem in parallel to have triggered interaction between universities and health corporations to meet the funding expectations set by the Foundation. This seems, according to reports from the universities and health care providers, to have functioned without severe frictions. Hence, the impact on leadership strategy and interaction between universities and the health care system seems considerable. The Norwegian research system has too little flexible resources, both internally and on the external ‘funding market’. Here, the Foundation’s programme has incentivized universities to free money internally to support their centres. While there may be a squeezing out effect here – raised by some informants – the Foundation has clearly succeeded in stimulating resource flexibility within Norwegian universities. The universities should also be commended for selecting programmes based on the medical need and current absence of diagnostic markers or treatment paradigms. The selected projects represent a variety of clinical areas, and incidence which ranks from very common chronic disease to rare diseases with distinct pathological acumens of principal interest.

The questions remaining concern how universities have selected, promoted and embedded translational constellations from a more long-term perspective. As discussed above, we find a relatively wide variety of approaches and interpretations of the concept of ‘translational medicine’. We would have expected universities to have developed a more coherent understanding of the concept of translational medicine, and also some considerations of how it may best be embedded in the academic structure, in terms of organization but also location etc. A few of the centres funded were loose collections of competencies and others functioned primarily as discussion clubs. While this may be laudable, it falls short of the expectation of the foundation to create high-impact, integrated and focused environments.

The evaluation group was exposed to relatively little evidence of potential changes in work modes and organizational structure to enhance a translational approach in a long-term perspective. The perspective was more responsive in nature, namely to adhere to the expectations of the Foundation to select and support funded constellations, and to deploy the resources while funds were available, rather than using the programme as a vehicle to

mobilize infrastructural support and alignments with complementary resources elsewhere. In particular, the supply of bioinformatics expertise constituted a bottleneck.

A few highly impressive examples of long-term realignments of facilities and positions were put forward but in general the impact on work modes and organization was limited. Here, we identify a clear potential for improvement, both in terms of specifications in the calls, the universities' search processes, internal resource deployment, and the dialogue between the Foundation and the funded centres.

Does the programme raise **the international visibility** of Norwegian biomedical research? In several cases, the centres supported were internationally renowned and reached visibility, either as active parts of large international consortia or as focused entities. However, our bibliometric survey indicates that the funded centres are relatively uneven in their impact profiles, with a few of significant international regard and others with more modest impact so far. We would expect the Foundation's support to further align competencies and thereby raise the visibility of the groups. This again would call for a more elaborated procedure of selecting and supporting centres.

Regarding impact in academic terms (**scientific impact**), there is a clear impact on search behaviour among researchers, and we witnessed several examples of enhancing existing collaborations or the forging of new ones. While there were a few cases of only limited impact or only a haphazard collection of competencies, we were overall impressed with the drive to form constellations which are novel/original, and which operate on the basis of logic of interaction and coherence.

A recurrent issue was the **time frame** of the Foundation's support. While a few reservations were made, the four year-period must be deemed sufficient to initiate collaboration; however the issue that remains is more long-term support. The SFF's of Research Council Norway may be too big and unwieldy to serve as a platform for the prolongation of the Foundation's centres. It is therefore of importance that the Foundation's laudable initiative is complemented by efforts to create long-term structures for collaboration and interaction. It is also important – see more below – that the Foundation uses transparent and stable criteria for success, both at the initial selection, in their monitoring and follow-up of programmes, and in decisions and evaluations of continuation or early discontinuation of centres after the initial period.

An issue not raised in the evaluation remit but which we want to highlight, is the importance of **leadership**. If programmes of the sort envisaged by the Foundation are to be successful, they are critically dependent on visionary leadership that can create coherent visions and directions for the clusters of participatory research groups. Even though attempts are being made to foster an integrated leadership approach – by the Foundation through the annual meetings and by the universities through leadership support – we found striking variation in leadership roles, from clear-cut to scattered. In some cases, leadership was devolved to a junior member when leaders had leave of absence. In other cases, leadership seemed to be run in a consensual manner, allowing for great variety in ambition and interaction. Neither of these solutions is satisfactory. We were also surprised by the lack of active scientific advisory boards in some cases. In sum, the Foundation should ensure that the role as centre leader is structured to enhance direction toward the set goals, collaboration and interaction, and that proper advice is secured from advisory boards.

Another issue not raised in the remit but of critical importance for some centres is the management of **intellectual property rights**. Norway dismantled the so-called professor's

privilege in 2003 and universities now own their intellectual outputs. While the issue of IPR management only surfaced in some cases, we found evidence of a need of more concerted efforts to bridge university based research and commercial exploitation, as well as the need to engage universities in the management of the centres to allow for successful commercial exploitation and returns to universities, in relevant cases.

As to the Foundation itself and its procedures. It is an eminent exponent of the virtues of foundations to act swiftly, with lenience and lack of bureaucratic procedures and time lags. Selection processes seem functional if, however, subdued in matters of articulating the goals of the programme. A foundation has opportunities to instigate change and be “unfair” in that process, and should therefore be open and clear-cut in its communication and selection. One obvious omission is thus the lack of performance indicators. This could include preliminary patents, patents, and relationships with health providers, alternatively expanding the science background and/or performance, or contacts with industry. This relates more generally to the vague conception of ‘translational’ in the selection and evaluation of centres. Such clear-cut guidelines would be highly productive for host organizations, applicants and the Foundation’s evaluation procedures.

In keeping with the format of the printed material, presentations and interviews, we consider the programme a success and recommend that it should continue to support translational medical research. We have set a number of recommendations to propel the selection procedures at both the university and the Foundation levels.

Our conclusions and recommendations

The focus on translational medicine should be enforced.

1. By definition, translational medicine is strategic and discovery-based, linking various scientific disciplines to a clinically useful purpose.
2. Properly tuned this scientific enterprise uniquely positions medical research in Norway on a very active international arena.
3. Valuable assets for translational medicine in Norway are the common patient registers and health care which represents potential for international collaboration.
4. The international outlook should be emphasized by temporary visiting scientists or Scientific Advisory Board appointments.
5. The research program should be goal-oriented, with clear milestones defined. High-risk programs may be encouraged, given that alternative strategies are defined.
6. Centre leadership needs to be enforced. Ideally, to be productive, a centre should not have more than 3 – 4 senior scientists. Programs that turn into “discussion clubs” or have “run-away” members should be discontinued.
7. Performance indicators such as provisional patents, patents, implementation of novel biomarkers and therapies or contact with commercial partners should be measurable.
8. Intellectual property rights should be guarded, not only to generate possible returns to the universities, but also to enable commercial partners to transfer innovations to clinical use.
9. An essential part in the translational process is adequate IT-capacity, either internal or through collaboration. IT should be seen in a larger context, also involving modelling and simulation. Contact with basic science/engineering can be fruitful.
10. Comparative biology studies in mice/rats, zebra fish, *Drosophila* or cellular model systems are encouraged.
11. Infusion of new technologies, for instance imaging is also potentially critical for reaching an international level. In case new instrumentation investments are required, this might need additional support through negotiation.

