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Editorial

Improving the Current Translational Research Structure in Academia for the Progress of Regenerative Medicine

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It is often difficult to facilitate the translation of an advanced therapy medicinal product (ATMP) slated for use in regenerative medicine from the laboratory bench into the clinic [1]. In order to allow clinical trials for such ATMPs to commence, regulatory agencies require good data establishing the safety and efficacy of such products in preclinical models [2]. For an academic researcher who is bringing such products to the clinic, it has become clear that specialized knowledge about preclinical in vitro and in vivo models, good laboratory practice (GLP), good manufacturing practice (GMP) and also good clinical practice (GCP) is a requirement in order to even attempt this process and expect a positive outcome. In spite of their highly promising and innovative approach of treating diseases, many of these novel ATMPs are facing the hurdle of only making it to the end of basic laboratory research, since basic researchers often shy away from the translational research aspect that is unfamiliar to them and can pose a formidable challenge [3]. Here arises the need of a "go to" entity that can moderate the translational research process and move such promising ATMPs forward from basic research, suggest the proper preclinical research path, carry it through the regulatory process, and, finally, initiate and complete the clinical research phase. For this reason, several national forward-thinking initiatives have already been established that focus on future explorations and investments in the field of translational medicine.

A well-known translational research initiative in the United States, for instance, is the National Institute of Health (NIH) funded Clinical and Translational Science Award (CTSA) network [4], with their mission of accelerating discoveries toward better health. The CTSA consists of a group of 60 academic centers around the US giving researchers tools, resources and collaborative academic partnerships to translate their basic research into clinical applications. It also incorporates trainees and fosters volunteers who would like to learn about participating in research. On the other side of the Atlantic, the Ministry of Education and Research (BMBF) in Germany supports translational centers and small and medium sized companies (SMEs) developing therapies specific to the field of regenerative medicine. The federal government of Germany has been largely investing in the progress of health research and biotechnology through the High-Tech Strategy (HTS) 2020 [5]. HTS is a national concept, initiated by the BMBF, which aims to enforce the collaboration between academia and industry, hoping to create an effective innovative research environment.

In spite of these outstanding national efforts as sources of financial and scientific support, it still remains challenging for a basic researcher to take the product and move it through the regulatory pathway. It would be desirable for the basic researcher in an academic institution to have a close at hand, experienced "go to" entity that could assess an ATMP for its translational value and ensure a successful translational research process.

Our continuous efforts at the Berlin-Brandenburg Center for Regenerative Therapies (BCRT), an example of an academic translational center, aim to establish such a "go to" entity in the institute's clinical development & regulatory affairs unit. The unit will moderate the dialogue between the basic researcher, the clinicians in Charité - university medicine Berlin and the BCRT integrated GMP facility [6]. to develop a path in order to move a product established in the basic research lab into the clinic. To ensure continued exchange of critical information between all parties and therefore the timely execution of the development plan, the unit will identify and assist young scientists from different basic research fields with interest in translational research to act as "translational ambassadors".

The "translational ambassadors" will communicate with their team in order to test the novel product, also called the "development candidate" in the preclinical *in vitro* and *in vivo* models for safety, toxicity and efficacy. Such testing often has to be carried out under GLP to satisfy the regulatory requirements. Manufacturing strategies under GMP conditions will then be worked out with experienced GMP personnel since clinical trials

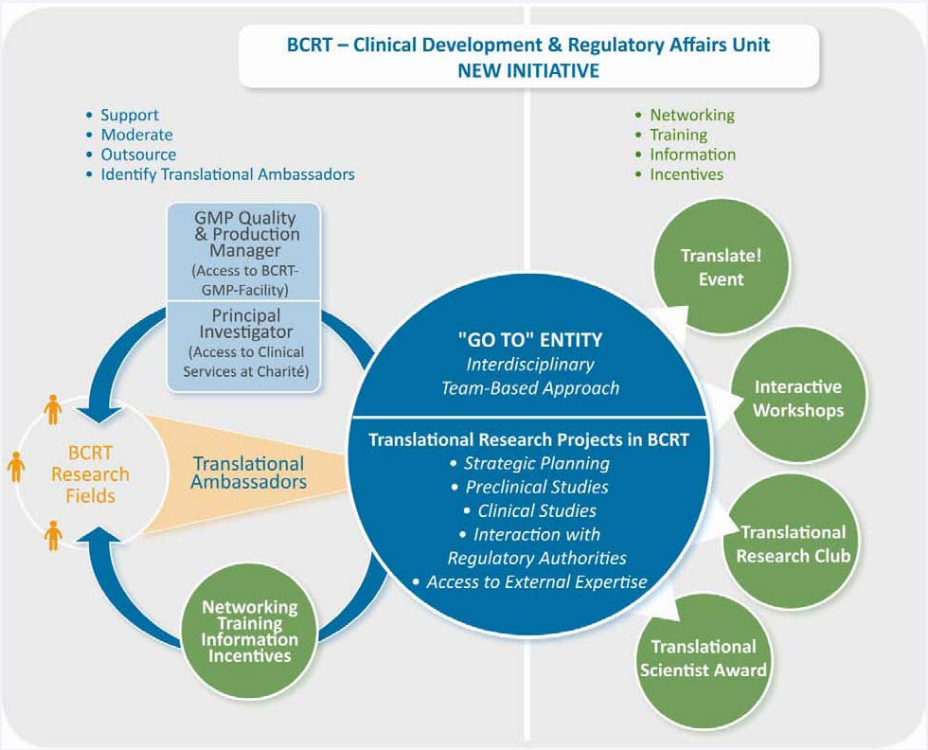

Figure 1 The "go to" entity, a new initiative by the Berlin-Brandenburg Center for Regenerative Therapies (BCRT) for improving the current translational research structure in academia to support the progress of regenerative medicine.

usually utilize a GMP manufactured product. The entity will assist in selecting the suitable clinician for each specific product, since the development of a good clinical protocol is dependent on the knowledge of the Principal Investigator (PI)/Sponsor with novel investigational products. After completion of the preclinical studies, the "go to" entity will supervise the clinical trial application (CTA) writing and submission.

The "translational ambassador" will be highly involved in writing the basic research description and the preclinical efficacy and toxicology data of the CTA. The chemistry, manufacturing and controls (CMC) section is preferably written by GMP facility personnel to satisfy the exact requirements stipulated by the European Medicines Agency (EMA) for product manufacturing [7]. The translational ambassadors will then work closely with the clinical trial PI to draft the clinical trial protocol. Finally, in order to move forward with a clinical trial application to the Paul-Ehrlich-Institute (PEI), the medical regulatory body for Biologics in Germany, the [8]. "go to" entity will determine how best to approach the PEI in a scientific advice meeting and which data will most likely be required to have a successful meeting. If after CTA submission clinical hold questions or other responses need to be addressed, the entity will carry out these items as well. Finally, product manufacturing for the clinical trial and transporting and shipping of the final product will be carried out by the GMP facility. The "go to" entity will then maintain effective communication channels with all the involved individuals during the conduct of the clinical trial. If some of the resources such as preclinical in vivo models or GMP manufacturing are not available at that center, the "go to" entity will communicate with other service providers who can provide the required resources. Creating such an "in-house translational research structure" has shown to be successful in other academic centers such as the Institute for Regenerative Cures (IRC), University of California Davis [9].

However, the question remains how can we encourage the young scientist to become a "translational ambassador" for his/her research group? A strategy had been developed in the BCRT and currently being reinforced by the "go to" entity to spark interest in translational research and provide incentives and efficient training for scientists conducting translational science. The strategy includes activities that are carried out in close collaboration with the Berlin-Brandenburg School for Regenerative Therapies (BSRT) and ranging from 1) the preparation of interactive workshops in translational research using problem-based learning, 2) forming the "Translational Research Club" to guide young scientists on how they can effectively integrate translational research activities in their daily work 3) announcing the "BCRT Translational Scientist of the Year Award" to improve awareness and increase participation in translational research, and finally 4) carrying out network-building activities through a series of events and conferences.

Overall, we believe that hurdles in translating a regenerative therapy into a clinical application can be accomplished in an academic center if a "go to" entity is established. The entity can support and drive the process of translation using an interdisciplinary team-based approach by recruiting young scientists in the different research fields. These translational ambassadors within academic institutions can develop the skills and the knowledge to contribute successfully to the future of translational research.

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