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How to Gain Expertise in Translational Research During Training

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Gastroenterology is an exciting field to pursue translational research in. Passionate gastroenterologists are well-placed to take knowledge obtained at the laboratory bench and apply it at the patient bedside because they have direct access to human tissue and data, which are essential for translational discoveries. How should a gastroenterologist who is in training proceed to embark on a career as a translational researcher?

What Is Translational Research?

It is difficult to define the concept of translational research exactly.[1] The United States (US) National Cancer Institute describes translational research as a "process by which the results of research done in the laboratory are used to develop new ways to diagnose and treat disease."[1] The US National Institutes of Health has a broader take, considering translational research as "(a) applying basic discoveries to clinical applications and (b) enhancing adoption of best practices in the community."[1] For the current article, translational research can be said to combine basic science and clinical investigations to translate scientific discoveries into clinical applications. It then follows that translational research requires an individual to acquire knowledge, skills, and infrastructure of both a basic scientist and a clinical investigator. Translational research not only brings profound intellectual satisfaction to a physician but is also essential for medical progress. It is worth noting that the number of physician scientists as a proportion of all physicians in the United States has declined from a peak of 4.6% in 1985 to only 1.4% in 2012.[2]

Understand Yourself: Which Research Model Is Your Interest?

Translational research is broader than studying a specific gene or protein. One needs to understand a range of disciplines from epidemiology to culture models, molecular biology, genetics, and, ultimately, clinical trial design and implementation. The models that may be used for translational research will involve some combination of 2-dimensional and 3-dimensional human cell culture models, animal models, and human material. Studying these disease models is very different from pure clinical research. You have to decide if studying some or all of these disease models is appealing and exciting. A brief apprenticeship in a laboratory and communicating with other translational researchers are highly recommended to help define your passion,[3] the best predictor for a successful career in research.

The Era of Multiple Mentors

By nature, translational research is multidisciplinary. What this means is that a "single" expert for all aspects of a proposal will be hard to find. Primary mentor(s) may need to be supplemented by additional collaborators from other fields, such as bioinformatics, engineering, and population medicine; these additional collaborators could develop into your mentors, depending on the direction that the project takes. Do not be afraid to seek mentorship outside your institution. Do not settle for mentor(s) simply because of local access. In this era of technology, many modes of communication (phone, email, electronic meeting platforms) can substitute for lack of physical meetings. While collaborating with researchers from outside institutions, maintain specificity in the questions that you ask. Set specific meeting times. If you rely on as-needed discussions, then the relationship and the idea may not endure.

Construction of a Biorepository

Biorepositories are a huge part of translational research to confirm the biological observations made in nonhuman models and to understand their relevance to human health. Recent updates in the consenting process allow the investigators to obtain permission for the specimens to be used not only for the impending projects, but also for other related projects.[4] Studying human material is limited in

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scope without knowledge of clinical information. Therefore, ensure that a priori, all the relevant clinical variables that may affect the disease process are included and linked to the specimens.

There are many useful guidelines available from the Early Detection Network on standardized collection methods (available from: https://edrn.nci.nih.gov/resources/standard-operating-procedures/standard-operating-procedures/serum-sop.pdf). Clearly understand which source of material will be suited ideally for your study. Not understanding these details at the onset can cause the project to fail in the future. Typically, you will need -80° freezer to store the specimens. Pick a freezer with a backup generator. If the freezer fails, the system should be able to send an alarm to the study personnel. The specimens should be well-organized in labeled containers. Simple but creative ideas such as pink tubes for blood and green tubes for tissue specimens can expedite retrieval, when hundreds of specimens need to be pulled.

To summarize, the need to invest time and money on the infrastructure required for high-quality tissue and data collections cannot be overestimated.

Key Steps for Success in Translational Research

1. Identify a unique area based on available expertise and your interests. You will have to focus on a unique area of clinical medicine to develop clear hypotheses and to enrich the populations from which specimens would be acquired.
2. Establish collaborations with experienced researchers in the field. They will not only be able to critique your manuscripts and grant proposals, but they will also help you to troubleshoot problems as they arise.
3. Laboratory experience is essential. The truth of the matter is that if you have practiced a technique yourself, then you will do a much better job of interpreting the data. Spending time in a productive laboratory for $\geq$12-18 months is extremely important for long-term success. During the laboratory experience, you will have opportunities to learn various techniques such as western blots, polymerase chain reaction, immunohistochemistry, genotyping, high-throughput sequencing, and so on, and also learn about interacting with basic scientists.
4. Build a team. You will have to seek expertise from varied disciplines (see The Era of Multiple Mentors).
5. Present your work often to the collaborators, either in individual meetings or in small groups. Take every opportunity to present to your peers as part of laboratory meetings, departmental conferences, institutional symposiums, and at national and international meetings. A poster presentation could serve as a nidus for a discussion that could lead to new experimental approaches. The feedback that you will receive and the questions that you will be asked will give you new insights into your work.
6. Become a part of the research working groups at your institution. Research working groups are researchers who share common interests and come together to discuss initiation of novel ideas and progress in those ideas. Being a member of these groups is incredibly helpful, not only to get valuable intellectual and technical input from your colleagues, but also to find new opportunities for collaboration.
7. Take baby steps. You cannot begin your career in translational research by leading a multicenter project of 3000 patients over 5 years with 10 different investigators. Aim big, begin small. You have to start with small projects that can be completed within a reasonable span of time, perhaps 6-12 months. This strategy will help you to learn the process, understand the limitations of various techniques, realize that data output will never be as clean as one would expect, and form relationships before you run out of money or time.
8. Be creative and frugal. Use your research funds judiciously. Be creative with solutions. For instance, to annotate stored biospecimens, commercial companies, which offer tissue-tracking software, may quote $15K to $20K, even $30K. Based on personal experience, a simple conversation with a local or regional database manager with previous experience in this field may have a tissue-tracking database built for less than $1K dollars. Managing your funds well can make research dollars last longer.

Acquiring Skills for Success

You cannot possibly have every skill to accomplish every aspect of your proposal, but try to learn the skills key to the success of your proposal.

Grant Writing

Grant writing skills are critical to secure funding. These are very useful and lead to huge improvements in one's abilities to articulate one's ideas. Almost all institutions offer such courses where they point out the commonest mistakes made during grant writing. A recent publication in the same section summarizes various aspects of grant writing.[5]

Statistical Courses

Every researcher will benefit from statistical courses, but you should not randomly select statistical courses to pursue. Identify how will the statistical course further your work. What strengths will it add? For instance, if sequencing is an important aspect of your work, you may want to take courses in bioinformatics to learn the interpretation and pitfalls of sequencing. If you want to focus on specific pathways, you may want to learn the techniques of pathway analysis. If you want to study biomarkers in populations, you may want to take courses in outcomes research.

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