Establishing a Successful Basic Science Research Program in Colon and Rectal Surgery

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Abstract

Although at first glance, the surgeon-scientist appears to be a rare breed in today's clinical revenue-driven world, with careful planning and mentorship this is still a vibrant career path. If one is considering this avenue, it is important to seize even small opportunities to pursue laboratory work during training—summers in college and medical school, rotation blocks, and dedicated time in the middle of residency. Publications and small grants during these times will lay the ground work for future success. When considering a faculty position, it is essential to identify a mentorship environment that has a track record for success—either in the department of surgery or anywhere in the university. Ensuring adequate support from the department of surgery chair and division leader is essential. Basic science careers take years for the return in investment to be manifested! Also critical is to secure extramural funding early in the faculty stint—first foundation grants and then National Institutes of Health–mentored scientist funding. Surgeons provide a unique perspective in basic science work and it is critical that we continue to support young surgeons in this career path.

Keywords
- surgeon
- K08
- basic science
- mentorship
- NIH

CME objectives: The goal of this article is to outline the key steps required for a successful career as a surgeon-basic scientist.

Even with the rapid changes occurring in health care today, the tripartite mission of clinical care, research, and education remains the cornerstone of the modern academic medical center. Although faculties have more diversity in how "success" is being defined in academic medicine, there remains a recognized advantage for the tenure-seeking junior professor who excels clinically and also maintains an active research enterprise. Historically, there has been nothing more valuable to an aspiring academic than the establishment and maintenance of a basic science research program. The financial and intellectual independence and intradepartmental collaboration and recognition of successfully maintaining one's own "wet lab" has not only been a direct route to a tenured position, but it has often provided more flexibility and wide-scale impact than has been possible in an exclusively clinically focused career.

Basic science research—the exploration of basic scientific principles through laboratory experiments—has historically been the "hard currency" of research. The vast majority of government research funding in the United States has been targeted to specific basic science questions thought to have real potential for improving our understanding and care of human disease. Similarly, demonstrating success in basic science research has been the most easily measured form of research productivity due to well-established metrics for quantity and quality of one's publications and funding sources.

Moreover, surgeons have been and remain uniquely placed in the academic medical center to facilitate and take advantage of ongoing basic science research efforts. An oft-cited perspective by Francis Moore, former surgeon in chief at the former Peter Bent Brigham Hospital in Boston, portrays the

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surgeon-scientist as an ideal "bridge-tender" that is able to shuttle new ideas from bench to bedside and back again.[1,2] Basic scientists exclusively understand biologic processes and laboratory techniques but do not have the clinical experiences to immediately connect new findings to the practice of medicine. In contrast, the typical clinician cannot afford to also maintain familiarity with often obscure basic science advancements that may not have an immediate application to clinical care. While difficult to be uniquely adept at both, a surgeon with an active clinical practice who understands the basic scientific principles at play maintains an environment in which to distribute and collect data to act as a liaison between these two complementary but fundamentally different worlds.

Within the surgical specialties, it could be argued that the colorectal surgeon is uniquely placed to act as an academic bridge tender. The limited anatomy of the practice of colorectal surgery is made up for with a diverse array of pathology that spans dermatologic diseases, autoimmune diseases, diseases of aging, and neoplasia. All of these pathologies offer several series of unanswered basic science questions ripe for further exploration. On the contrary, colorectal surgery is a relatively new addition to many academic medical centers in the last decade and has not yet firmly established its own tripartite mission in many of these institutions. Furthermore, colorectal surgery as a field is unique, in that surgeons can adjust their practice easily to their clinical effort. For example, young faculty committed to developing a career in basic science can scale back their clinical practice to focus more on anorectal surgery and colonoscopy to allow for substantial dedicated research time.

Basic science research remains a definitive pathway for a successful academic surgical career, but the hurdles of uncertain basic science funding support and increasing clinical productivity demands in academic medical centers make being a successful surgeon-scientist more difficult than ever before. This article explores the technical aspects of what is required of a surgeon to build a basic science research program, with a particular focus on how junior surgeons may have increasing opportunities to establish and maintain independent basic science research programs. In addition to the critical first steps needed to support basic science research as part of a surgical career, we also offer our own lessons learned through various basic science research efforts with a particular emphasis on how to avoid mistakes that can scuttle an otherwise promising start.

When and How to Get Started

Although a colorectal surgeon may not have the opportunity to develop their own basic science agenda until early after his or her first academic faculty appointment, the groundwork to be successful starts much earlier. Effectively exploring a basic science research question relies on marshaling one's own understanding of scientific principles, knowledge, and comfort with diverse laboratory techniques, and the financial resources to protect one's research time. There is a degree of luck involved, but often one's own efforts—going back to predoctoral training—may often provide the critical component to developing a successful research track.

The key point for aspiring surgeon-scientists is that when the opportunity arrives for one to devise their own basic science research plan as a faculty member, one must already have a curriculum vitae that supports the proposed research agenda. Being able to demonstrate a familiarity with the literature, laboratory methods, and understanding of the research funding process is critical. While formalized degree programs (e.g., PhD, Master of Science) may be helpful, they are not essential. Instead, what is most important for one to build before their first academic appointment is a track record of experience in support roles within basic science research. In the authors' opinion, nothing substitutes for bench-side experience. Thus, those interested in basic science research should take advantage of early laboratory experiences—college, medical school, residency, fellowship. All will provide opportunity for publication and/or successful submission of small individual grants from either the institution or professional societies. The American Society of Colorectal Surgeons, among other societies, is active in supporting medical student, resident and fellow research time. Although direct familiarity with the science, the methodology, and logistical workings of a basic science laboratory is important, a track record in publications and grants before beginning a faculty position is invaluable, as it is seen as a harbinger of future success.

Finding a Mentor (or Mentors)

Like all academic pursuits, no individual can be successful in a vacuum. There is strong recognition among successful researchers that arguably the most important determinant of early success is the strength of one's mentors. The consensus evidence from research on academic careers also suggests that mentored medical professionals are more confident, more academically productive, and more satisfied with their careers.[3,4] A good mentor can provide an early academic foundation with a wide variety of support mechanisms, and this diversity makes it difficult to delineate all of them in a short article. Some examples of the benefits of mentorship include identifying promising areas of research, including the mentee on institutional review or animal protocols so that the mentee does not spend excessive time on administrative tasks, introducing a mentee to other helpful faculty or logistical personnel, providing equipment and space for preliminary data, sharing preliminary data for a grant application, and providing critical feedback on research findings and reviewing grant applications. The value of these benefits—and the cost of not having them—to an early academic is hard to overemphasize. The mentoring available when evaluating one's first academic appointment should be an aspiring surgeon–basic science researcher's highest priority.

Conversely, a critically flawed mentor can easily destroy an otherwise promising research career. Not only can such a problem leave the early surgeon-scientist feeling unsupported, but funding agencies also place a high value on mentorship and research environment. Most competitive grant making bodies (e.g., National Institutes of Health [NIH]) evaluate mentorship and institutional support as critically or even more critically than they do the fundamental scientific exploration being proposed.[5] It is not uncommon for the NIH to give an overall low score to a grant proposal solely due to the review committee's concerns about an investigator's senior faculty support.

Given this constellation of needs in a mentor, it is understandable why early laboratory scientists often gravitate toward the senior scientist at their institution with the most name recognition. There is certainly value to this approach, and there is ample anecdotal evidence from the authors' own experiences that suggest a recognizable name can make the difference between a successful grant proposal and a failed one. However, such a reflexive move may not always be the best strategic choice for a mentor. Institutional celebrities are often decades into a research career and their priorities may not always align well with a junior faculty member. Ultimately, there are other factors that are as important as name recognition. Through our own research efforts, we have found a more balanced approach to mentorship selection that may produce a better match. ►**Table 1** highlights these features of good mentorship compatibility. In brief, finding an effective mentor requires identifying a "sweet spot" in available faculty colleagues who have enough seniority to one's own position that they are able to provide advice, equipment and personnel, and institutional heft while also having some investment in the mentee's own success. It is this symbiotic relationship that promotes productivity and academic success.

An important side note should be made on the practical realities of most academic medical centers. In our experiences, readily finding a mentor that *perfectly* suits one's own efforts has been an unusually rare occurrence. The limited availability of mentors in any given institution and the degree of "perfection" highlighted in the preceding paragraphs make finding all of these qualities in a mentor almost impossible. In the authors' opinion, the young faculty member should consider compromising the area of study if strong mentorship is not available in that area. A common workaround strategy that many report using with success is the model of multiple, complementary mentors. Many academic surgeons fall into such a multimentor model naturally given the tripartite demands of academic success. It is rare that one's clinical mentor would naturally coincide with the individual best suited to advise the mentee with their laboratory pursuits. Although it is essential that one's clinical mentor recognizes what it takes to be a successful surgeon-scientist.

Compartmentalizing the roles of mentors even further may have additional value. For example, even among laboratory mentors, there are senior faculties who have mastered grant writing, while there are others who readily pick up and

Table 1 Qualities of a good mentor and their rationale

Quality	Rationale
Promotes others	For the mentee, a mentor's own first-author publication record is less important than that of the latter's prior mentees. It is not uncommon to find a senior faculty member who has an exceptional publication record but has less success getting postdoctoral mentees or mentored junior faculty the same level of success. Mentors who have a track record with mentees receiving mentored grants are an added plus. The causes of such a failure are myriad, but what is important is the outcome. Avoid mentors who do not have a track record of bringing success to others.
Technically resourceful	New entrants to basic science research often find themselves without the equipment or personnel to successfully obtain preliminary research findings. A generous mentor can provide such resources at the most crucial times.
Socially resourceful	Mentors should already have an established social network of other senior researchers in the field. If an issue arises that a mentor cannot help out with directly, a good mentor will have someone they can call who can.
Common interests	Mentors do not need to have perfectly aligned research interests, but it is important that a mentor has at least a working knowledge and passion for one's own research topics. Advice, resources, and technical help are difficult to obtain if one's mentor is only vaguely familiar with the details of one's field of research.
Available	Academic faculties are routinely overwhelmed. It is important to ensure that one's mentor has the ability to dedicate an appropriate amount of time to mentorship.
Incentivized	Incentives for mentors take all forms from intrinsic altruism to need for mentored publications to well-defined institutional incentives for mentorship. The driving force of the incentive is unimportant. What matters is that a mentor wants a mentee to be successful and has some form of vested interest in the latter's success.
Experienced	The vast majority of advice comes through prior mistakes. A mentor needs to have made enough mistakes over a research career to help a mentee avoid them.
Extramural funding	An appropriate mentor must have extramural funding from the National Institutes of Health (R-series).

adapt novel laboratory techniques. With the ease of social communication today, it is probably inadequate to rely on one mentor to provide a mentee with all of these diverse needs. Instead, junior faculty should consider dedicating time and effort into nurturing an entire panel of mentors who synergistically provide the optimal support for an aspiring research scientist. Thus, a mentee should seek out the above-mentioned qualities as well as necessary roles (e.g., technical expertise, research writing, and clinical support) throughout his or her academic institution.

Following Trends in Basic Science Research

Many of our own mentors have commonly encouraged younger surgeon-scientists to keep abreast of the literature if one wants to engage with the greater academic community. This strategy has both direct and indirect benefits for the individual researcher. For example, grant proposals and manuscript submissions are often seen more favorably if one is able to clearly communicate how the relatively small advancement being proposed fits into a larger body of ongoing work in the field. Also, a working familiarity with current research and trends helps the individual researcher know which avenues are further worth exploring.

In practice, a comprehensive understanding of current literature is almost impossible. The volume of scholarly publications appearing weekly means that even regular reading of three or more journals a week would not adequately cover an entire field of interest. One could argue that for clinical research, the natural raising of clinical questions at the bedside and returning to the literature for an answer obviates the need for detailed scrutiny of newly released research findings. However, basic science research is just far enough removed from the daily practice of a surgeon that one can only remain engaged with ongoing work through a concerted effort.

There are several information technology tools that may offer assistance to the surgeon-scientist trying to remain abreast of new developments in basic science. Probably the most powerful is the evolving set of search tools available under the My NCBI feature offered through the National Center for Biotechnology Information, part of the National Library of Medicine and its PubMed.gov search portal (https://www.ncbi.nlm.nih.gov/account; Bethesda, MD). A similar service is offered in an automatically emailed query format via Google Scholar (http://scholar.google.com; Mountain View, CA). The features allow one to save a search string and then return to the site on a regular basis for updated publications in that search term. These features allow the busy surgeon-scientist to relatively quickly be presented with a set of electronic search results that demonstrate new publications in a narrow area of focus in a reasonable amount of time.

These features are best demonstrated with an example. Imagine that an early colorectal surgeon was interested in studying immunologic mechanisms observed in Crohn disease. Scientific research in this topic crosses many disciplines (e.g., cell biology, immunology, and genomics), and there is no clear small set of journals one may benefit from reading regularly. Instead, using My NCBI would allow one to save a search string that could provide a chronological update of recent work in this area. A saved search string that one could use to look at cellular binding proteins in mucosal inflammation might be “immune” AND “intestinal” AND “mucosa” AND “CD.”

Of course, further narrowing a string with an improved understanding of the literature would not only decrease one’s weekly or monthly repeat search time but also acts as a natural evolution of one’s original research question (e.g., narrowing the above search term from “CD” to “CD14”).

A newly evolving phenomenon in the research information technology landscape is the emergence of social network sites specifically dedicated to the promotion and sharing of one’s research. These sites borrow strategies from common social networking sites such as Facebook or LinkedIn but instill specific features relevant to research scientists. Two of the largest currently in existence are Academia.edu and Research Gate. In both cases, one creates an online profile that includes prior publications, personal background, and current research interests. The analytics behind these sites then use that data to not only present the user with other members that may be publishing in similar fields but also to publicize one’s own research to a large community of research scientists. The real impact of these sites remains to be seen, but the significant web presence afforded to the individual researcher likely demonstrates a new trend in research information sharing that the individual research scientist should consider engaging.

Basic Science Funding

The greatest hindrance to acting on a well-thought research question is ultimately lack of independent financial resources. With adequate research funding, departmental and institutional leadership will find myriad ways to ensure your research goals are met and that interruptions from other academic responsibilities are well managed. Without independent funding, basic science research can quickly come to a standstill. Not only will there be difficulty meeting the costs of experiments and laboratory overhead, but one’s own department may be less invested in ensuring the individual surgeon’s research success.

As already noted in this article, the surgeon-scientist must build a career trajectory that predetermines a successful outcome. This strategy also applies to seeking independent research funding. Building a successful track record of gaining outside funding not only builds one’s experience in this essential skill but it also provides career momentum when one returns back to the same or related funding institutions in the future. Researching funding is a cyclical and evolutionary process, and this section provides an overview of how one’s research funding needs to mature over his or her career.

►**Table 2** provides a rough timeline for the progression of basic science funding over a surgical career. The concept that underpins this approach to funded career development is that there should be recognizable elements of one’s early surgical

Table 2 Basic science funding over a surgical career

	Year		Approximate support
Trainee	−10	Undergraduate, medical school research fellowships	~$5,000/y
	−5	T32 research fellowship, advanced degree work (PhD)	~$30,000/y
Faculty	0	Unfunded experimentation of first independent research question	~$30,000/y
	2	Intramural/foundation grants	~$30,000–$50,000/y
	5	Career development "K" award (K08, K12, K30)	~$50,000–$75,000/y
	10	Independent investigator grant (R01)	> $100,000/y

Source: Adapted from Nelson.[6]

career (e.g., research efforts in medical school, residency) that influence one's early independent basic science explorations as a mentored junior faculty member. Once on faculty, there should then be a natural progression from unfunded preliminary experiments to foundation-supported work and then ultimately to larger faculty development awards that lead one to running a fully independent basic science research program.

One of the advantages to framing research funding in this manner is that it naturally fits with the conventional funding mechanisms available for basic science research. The first proven opportunity to receive dedicated time and funding to pursue basic science research as a practicing surgeon is by adding nonclinical years to one's residency training. Although the opportunities available to residents in their research years have greatly expanded in the last decade, proven approaches remain for those interested in basic science research. Funding methods vary by institution, but the format of basic science research remains relatively constant. For the aspiring basic science researcher, these research years provide an opportunity for funded basic science research under the mentorship of a senior surgeon-scientist. Historically, the questions one explores in this research interval away from clinical training help one to establish the research pursuits intended for independent inquiry at the end of residency and at the beginning of one's first faculty appointment. The most common form of funding during these years is the NIH's T32 institutional research training grant, but the paucity of these funding awards has led to several alternative funding options that include professional associations (e.g., American College of Surgeons, Association for Academic Surgery) and foundations (e.g., American Cancer Society).

After being appointed to a faculty position following residency, a similar process of small grant funding progresses with the key difference being an increase in one's research independence through a reduction in the amount of formal mentored oversight. This inflection point marks the critical moment in one's research career where with similar amounts of research funding as during one's research years, a surgeon-scientist needs to be able to demonstrate publishable results through independent experimental work. Early in one's first faculty appointment, support is derived largely from intramural sources (e.g., contractually provided research time, institutional research development grants) and foundation career development grants that resemble those sought as a research resident.

The capstone to basic science research success as an early faculty member is a "K award," one of many K series grants awarded by the NIH for basic science research. K awards represent formal recognition by one's peers and national grant-making entities that one has demonstrated a combination of successful preliminary data collecting, early publication, mentorship, and institutional support to have success as an independent basic science researcher. K awards are often seen as a key decision point for an aspiring surgeon-scientist. The successful application for a K award leads to the external financial support and the internal department recognition needed to lay the groundwork for one's own independent research program. While some surgeon-scientists manage to obtain funding through alternative means to continue basic science work, failing to obtain a K award is often seen as a major setback to a major career component in research.

The K award's importance is not just for its immediate contribution to one's research efforts but also because it often provides the springboard and momentum to reach the pinnacle of basic science funding support, an independent investigator grant. Most commonly called an "R01" when provided by the NIH, these large, multiyear grants provide the surgeon-scientist with the long-term financial security to build a multilayered and multidirectional research program to explore a broader field of scientific inquiry. In addition to its extrinsic benefits, achieving one's first R01 is a major milestone in any research-oriented career and remains the gold standard for gauging success along the research component of the academic's tripartite career requirements.

Finally, it should be noted that the career and funding pathway mentioned above may not be the only way to research success. The specific requirements of an academic surgical career today are somewhat less formalized than previously. Traditional sources of funding have not kept pace with the growth of medicine and more emphasis has been placed on clinical performance. Any aspiring surgeon-scientist needs to keep these traditional funding milestones in mind while also balancing their value versus where institutional and national trends are taking basic science research in the years ahead.

Models of Collaboration

One of the increasingly recognized realities of tripartite academic mission is that the increased demands on academic faculty are reaching a point where no individual can possibly excel at all three pillars of academic medicine. For the surgeon-scientist, managing these different academic pressures has led to several different models of collaboration. These vary considerably—largely due to institutional logistics and personalities involved—but the mechanism across all of these models is some form of responsibility sharing among multiple stakeholders that allows a basic science–oriented surgeon to be effective. Below we describe the three most common collaborative models in more detail.

"Independent" Basic Science Researcher

The classically funded, independent surgeon-scientist is historically the most common role for the academic surgeon. The limited increase in basic science funding and the increasing clinical demands on academic faculty have made this form of a surgical research career increasingly difficult in more recent generations. However, there are still notable exceptions that prove this form of career advancement is still possible. Steven Leach is one example who is currently the Paul K. Neumann Professor of Surgery at Johns Hopkins Hospital in Baltimore, MD, and will soon be leaving to be the founding director of the David Rubenstein Center for Pancreatic Cancer Research at Memorial-Sloan Kettering Cancer Center in New York City. Leach has been unusually successful as an academic surgeon in building a basic science enterprise at Hopkins using the unique and well-described features of Zebrafish embryology to demonstrate genetic mechanisms related to pancreatic cancer. The past 15 years have been very fruitful for Leach and his colleagues, and his NIH-funded research grants have provided him the opportunity to pursue his research interests full time with a relatively small clinical practice.

While Leach has been exceptionally successful at building his basic science research program, one could argue that the mission of the department would not be as effective without his clinical colleagues who take on a disproportionate amount of the patient care activities to balance faculty who spend most of their time in the laboratory setting. This phenomenon is by no means uncommon, but it is a balance that should be recognized by the early academic surgeon. If one hopes to build a robust and bustling basic science program as the primary sole investigator, it will take a combination of departmental support and likely scaling back of one's own clinical responsibilities to be successful.

Intradepartmental Partnerships

Rather than a department meting out clinical and research responsibilities like in the independent model mentioned above, another possible solution is for the individual surgeon-scientist to find another academic surgical collaborator with similar clinical and basic science research interests. At Emory University in Atlanta, GA, Christian Larsen, dean of the School of Medicine, and Thomas Pearson, Livingstone Professor of Surgery, have built two intertwined successful academic surgical careers by relying on each other for shared responsibilities. Larsen and Pearson met in general surgery residency at Emory and then worked together in Peter Morris' famed transplant immunology laboratory at Oxford University as postdoctoral researchers. Ever since, their contributions to clinical practice in transplant surgery and groundbreaking basic science work on the costimulation blockade in organ rejection have been impossible to distinguish. The two share each other's clinical responsibilities to allow the other to avoid research interruptions and have coauthored every major work produced by their laboratory.

The Larsen-Pearson Laboratory has been held out as a standout example of collaboration for academic medicine by the NIH. However, successful iterations of this model have been rare. The NIH has gone so far as to send behaviorists to study Larsen and Pearson's collaborative relationship to identify what has made their partnership last for their entire academic careers.[7] While the benefits of a close, deeply collaborative relationship with a surgical colleague are obvious, building a basic science research program on such a model seems to require finding the near-perfect counterpart for long-term success.

Extradepartmental Collaboration

Sometimes the best means of addressing the divergent demands of academic surgery is to get out of the department of surgery. Richard Schulick, Chair of Surgery at the University of Colorado School of Medicine, has routinely encouraged colleagues to "get away from the surgery and close to the research." While this advice has typically been used to guide how and where one sets up their physical laboratory space and research groups, it can also be applied to an important collaborative model that clinical faculty often fail to recognize early on. The definition of basic science dictates that the research question addressed should rise above solely surgical applications. Thus, there are likely other basic science researchers at any large institution who are interested in similar basic science avenues of research. Anecdotally, these researchers are often unaware of clinically oriented faculty with shared research interests. Schulick himself found extradepartmental collaboration via Drew Pardoll, director of tumor immunology, who ultimately worked with the former on many a major academic paper that leveraged Schulick's access and understanding of the inherent surgical issues in metastatic colorectal cancer to develop a prospective, translational trial of vaccine-based therapy for metastatic colorectal cancer. These collaborations are not just useful for their novel thought generation and shared resources, but these opportunities also allow for clinically active surgeons to find a basic science counterpart who is able to provide laboratory supervision for further coinvestigation. It would likely benefit the young academic surgeon to explore what possible extradepartment collaborations are possible. These could range from formalized mentorship and coinvestigation to more casual—but important—journal clubs and information sharing.

The benefit of the extradepartmental model is the extreme diversity of possibilities and high likelihood of finding research collaborators with common interests and potential work sharing. Unfortunately, the plethora of opportunities can also be daunting particularly in geographically dispersed university environments with limited physical and virtual interaction across departmental boundaries. There is also the difficulty of clinical and nonclinical faculty sometimes being driven by different department expectations in terms of productivity. These difficulties are not insurmountable, but one should be aware of them and take on collaborations carefully to maximize shared effectiveness.

Summary

Academic surgery remains in a period of flux that is reflected in the changes in the greater health care landscape today. However, an academic career that combines basic science research and a busy clinical practice still represents the gold standard for academic success. The relatively limited number of colorectal surgeons with established basic science research programs only enhances the value of the colorectal surgeon who succeeds in basic science. The surgeon-scientist's career track has never been easy, but with the appropriate combination of good mentorship, strategic career planning, and hard work, a surgical career that includes basic science research can be both personally fulfilling and a ready means of advancement in the academic medical establishment.

Our parting words of wisdom are to plan early! If you are considering this career field, demonstrate commitment to laboratory research at every chance—publish, obtain grants as early as college. When evaluating your first faculty position, plan early again. Establish your mentorship plan, clinical effort, and startup funding *before you sign a contract*!

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