**Title:** Critical roles of clinical laboratorians in translational research and applied sciences— experts’ insights and experiences

**Running Title**: Q&A: The role of the laboratorian in research

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Clinical laboratorians have been at the forefront of translating science into clinical practice, playing crucial roles in the development of techniques, instrumentation, and technologies that aid in patient care. Some noteworthy advances by laboratorians include the discovery of the Jaffe method for measuring creatinine, the Folin-Wu method for determining blood glucose concentrations, and Van-Slyke’s volumetric carbon dioxide gas analysis instrument. More recently, laboratorians have been instrumental in the development of assays for the detection of myocardial injury, informatics-based approaches for detecting laboratory error, and have stood at the forefront of omics-based approaches to diagnosis. In short, clinical laboratorians have been essential for the advancement of medicine and for providing timely, accurate diagnoses of medical conditions.

 The modern-day clinical laboratory looks dramatically different from labs of previous eras. The vast majority of laboratory developed tests have been replaced with FDA cleared instruments and assays. The implementation of laboratory automation has further mystifyed the testing process and has removed assay development from the hands of the laboratorian. The new laboratory structure has also necessitated a change in how laboratory directors are trained, requiring a greater emphasis on regulation and management, at times to the detriment of research and method development. Even in academic institutions, clinical laboratorians have limited protected time for research. Nonetheless, laboratory directors remain in a distinct position to impact patient care and to bridge the gap between research and clinical application due to their unique understanding of unmet clinical needs and technical expertise in laboratory testing.

The ever-changing landscape of the clinical laboratory and increasingly clinical/managerial role raises important questions about the future of the clinical laboratorian in research, development, and translation of laboratory testing. Furthermore, it requires that new generations of clinical laboratorians are trained and prepared to meet these needs. In this Q&A, international experts share their experiences building translational research programs and establishing leadership in scientific subspecialties with the goal of determining the future role of the clinical laboratorian in translational research.

***Please share your experience in building research programs and establishing leadership in specific scientific and clinical specialties?***

**Ann Gronowski**: My research program is pretty modest compared to others, in terms of size and dollars. I would say that I have had three main focuses: 1) diagnostics for maternal-fetal medicine; 2) general laboratory medicine; and, 3) industry-sponsored projects. My passion is maternal-fetal medicine and this is the area in which I have published the most and the area for which I have written small grants and requested funding. I have undertaken some industry sponsored projects which have allowed me accrue money that funds some of my own hypothesis-driven projects.

The general laboratory medicine-based projects have their roots in interesting observations made during clinical service responsibilities. These interesting observations have informed my maternal fetal medicine research and also lead to seemingly unrelated areas of research. For example, we recently published a study that examined the number and kinds of radioactive patient samples received by our hospital core laboratory annually. This grew out of a single event that occurred in the lab. It has resulted in improved safety for our lab staff, and improved communications with our radiation safety and oncology faculty—in addition to a publication.

**Fred Apple**: I owe my success in Clinical Chemistry to my mentors, Drs. Jack Ladenson, David Dietzler and Jay MacDonald, from my Clinical Chemistry fellowship training. Each provided doors to walk through and allowed me to pursue my passions in muscle biochemistry and toxicology. They also taught me that first and foremost was patient care, but to be successful in Laboratory Medicine in an academic setting one needed to focus on a primary research interest; and to pursue all the roads not taken until more questions arise that need to be answered. Professor Oliver Lowry took an appointment with me, and showed me the importance to learn and ask questions. It was clear that my need to balance clinical service, teaching, administrative roles, with my personal desire to initiate my own lab, was what I wanted. It was also clear that it involved more than a 40-hour week. Building a research program started with my own hands-on experimentation and testing/validations, one assay and one instrument at a time. You quickly learn studies require submitting grants, reagents and glassware cost money, and this concept of overhead/taxation hurt. I remember hiring my first research technologist with my first funding, a 2-year project pertaining to CKMB. I thought I was rich, and when right out to the local pub for a scotch. Over time 1 employee led to 2, and more, one technology led to others. At present my laboratory, the Cardiac Biomarkers Trials Lab of the Hennepin Healthcare Research Institute, has grown to 6 fulltime employees and a diverse array of applied research studies; my favorite being the investigator initiated funded and others in partnerships with industry. I got lucky. However, I never lost track of my hospital responsibilities in Clinical Chemistry, clinical and forensic toxicology and point of care testing; all my favorite subjects. You learn from other leaders, you listen a lot, but at the end of day, it is critical that we establish ourselves with a seat at the hospital table with other clinical service directors. Being creative is important but following the science with a continuing growth of clinical knowledge to explain why we bring up certain tests to address disease processes needs to be an ongoing educational process; one that needs to be built with other clinical colleagues who use the laboratories we direct. Leadership, surrounding yourself with common sense, engaging smart colleagues, especially in the pandemic world we practice in now, is the key to being successful.

**Mari DeMarco**: Experiences building research programs will vary widely based on factors like start-up support, availability of shared resources, mentoring support, time allotted for research and the type of your institution. It is important to understand your situation before looking to others for guidance. If you are at a small community hospital and want to grow a research program, reaching out to a leading scientist at a top-tiered research school may not yield the best advice. To better understand my perspective, I work in a 550-bed acute care hospital and while it is a teaching hospital it is far more on the clinical end of the spectrum than the research end. Within my own department few of my peers engage in externally-funded research, and none have independent labs. In that environment, it was critically important to build a research program that directly benefited the clinical lab. In that way, I could draw a direct line from my research program to innovations in the clinical lab. As structures were not in place in my department for someone with my career trajectory there were many barriers to overcome. Through these challenges, there are two lessons I have learned that I think are adaptable to various environments:

1) Advocate for yourself. As you build your research program you will hear a lot of “no’s” to your ideas, whether it be from an administrator at your site or grant reviewer. Keep moving forward. If you get a definitive “no”, don’t wallow in defeat—move on to the next challenge. However, if you see a path forward, no matter how small, be persistent, advocate for yourself and your vision.

2) Work with what you have. It took years for me to obtain the funding trifecta of personnel—operational—infrastructure support all working in harmony (i.e., money for people, consumables, and equipment). In the beginning it seemed like an impossible task to get these key pieces in place. There was a time I had funds to hire a trainee but did not have any of the analytical equipment needed for the research; from that followed a time when I had equipment, but my personnel budget couldn’t keep up. What has served me well is understanding that whatever stage I am at and resources I have, I must make it work. Looking back, a few of our key outcomes as a research lab were borne directly from budgetary constraints that forced me to look at a research challenge differently.

**Yusheng Zhu**: To build a clinical/translational reach program, a powerful research team is essential. Our team comprises principal investigators, technologists, post-doctoral fellows, nurses, and administrative staff. As a principal investigator, I oversee the research program, apply for funding, monitor the research activities and compliance with regulations, control budget, and work with sponsors. It is important to communicate with team members effectively. I have technologists who are dedicated to research projects. Postdoctoral fellows of our Clinical Chemistry Fellowship also directly conduct research as a key component of their training. In clinical studies, patient recruitment is always challenging. Research nurses are crucial to effectively select, enroll, and consent research subjects. Finally, our administrative staff aid in IRB application, funding management, and research reports.

**Paul Collinson**: Individuals working in laboratory medicine are in a unique position as they are not limited to a single patient or a single type of patients but have a whole hospital to choose from. They are also scientifically literate, aware of the latest developments in diagnostic laboratory testing and what is in the development pipeline. As such, they know what tests need validation and evaluation. The first thing is to keep an open mind and always be on the lookout for unusual aspects of an individual patients test results. It is essential to build relationships with clinical and scientific colleagues so that they know you are available to assist in a diagnostically complex problem and can support them in any research endeavor, no matter how small. Importantly, always be proactive in seeking opportunities rather than waiting for them to come to you. Once you have a reputation as a proactive investigator then people will seek you out. Accessibility and enthusiasm are the keys to building up research relationships.

**David Sacks:** Building a research program requires resources, particularly money. This needs to be obtained from the department chair, grants (intramural or extramural), or other sources, eg, collaborators. The specific approaches and resources needed for basic science and clinical research differ. Regardless of the research, one should integrate your program with the strengths of other departments and the institution. For example, if there is a Cancer Center, develop laboratory tests that support oncology. It is important to show others how you can help them.

Establishing leadership requires knowledge and expertise. Identifying good mentor(s) will considerably facilitate growth. Take advantage of opportunities that arise.

***How do you balance clinical and administrative demands and make time for research?***

**Ann Gronowski**: This can be very difficult, especially as your career advances and you assume more administrative responsibilities. Research is usually a team effort, so be sure to build a good team. Collaborate with other outstanding scientists. Engage trainees and teach them how to write IRBs, outline experiments and create first drafts of manuscripts. Make a list of ideas and questions as they occur to you, even if you do not have time to pursue. Students and trainees are often looking for projects, so when they come to you, you will have a list of potential projects ready and waiting for them.

**Fred Apple**: Balancing life and work have been never ending. Watching my 16-month-old grandson balance his minute-to-minute decisions has reinforced my professional thoughts, regarding the importance of finishing the task at hand, but without losing track of the multiple other challenges that need to be addressed before the end of the day. For me, patient care and providing quality and timely laboratory results has always been primary. As a medical laboratory director, I have always been fortunate to have outstanding laboratory professionals (administrative director, managers, supervisors, technologists) in my clinical laboratory who have always been empowered in operations as a team; understanding when the assistance of the medical director is required. Most important is rounding or huddling routinely with your staff to make sure they understand you have their backs when needed. This does free up time in your 12h plus day; allowing you to think and design and examine results from your research laboratory. Having a manager as a dyad-partner in your research laboratory with regulatory, IRB, budgeting, contracting, personnel responsibilities allow you, as a PI, to best optimize your academic pursuits.

**Mari DeMarco**: If you are starting a job and are interested in research, negotiate dedicated time for research activities as part of your contract. With employment contracts often dividing time between the broad categories of ‘clinical’ and ‘academic’, it is important to have a clear and detailed understanding of what each of those roles entails. Does the time breakdown seem reasonable based on the list of responsibilities? If you don’t know the answer, this is the perfect opportunity to reach out to your peers to get input. Knowing that there are always unforeseen demands on clinical time – like a broken analyzer or a new regulation requiring implementation – does the time split account for all of this? Regarding dedicated academic time, what percent of this time can you realistically carve out for research activities based on other academic responsibilities like teaching? If your responsibilities and the time divisions are in alignment, great! If not, reconsider if you will really have the time to build the type of research program you want while also meeting all of your other responsibilities, and what other options and avenues may be available to get the time you need.

**Yusheng Zhu**: This is a hard question to answer. We all have heavy clinical and administration responsibilities, and some may have teaching responsibility as well. I always put clinical duty first because it is a clinical chemist’s primary responsibility. Also, interactions with other clinical staff who directly manage patients can help me understand the clinical needs so that I get new research ideas. Therefore, I can connect basic and translational research with what is happening at the bedside. Making scientific advancements in medicine is also a clinical chemist’s responsibility, so I take any opportunity to conduct research. To have more time for research, I delegate some administrative work that does not require my immediate attention to other staff. Also, I try to manage my time efficiently. For example, I plan ahead, organize myself, and allocate my time according to the priority of the work.

**Paul Collinson**: This is probably the most difficult single thing to do. The usual factors are there, being organized, putting into place systems that make clinical and administrative tasks as streamlined as possible and the ability to delegate to others. Ultimately, and certainly at the beginning you will need to accept the fact you will have to sacrifice some of your own time and sometimes you will be doing things that are not immediately rewarding. You will have to accept the choice between evenings out and evenings in doing research.

**David Sacks**: That is a very difficult question to answer. The best opportunity to negotiate protected time for research is during the discussions before one accepts a position. Different institutions and departments have different policies regarding time for research. It is essential that the chair of the department understands the demands of research, particularly basic science, and supports faculty who want to devote time to that endeavor.

Having extramural funding considerably strengthens your position to carve out time for research. Department Chairs and universities in the US usually prefer funding from federal sources, eg, the NIH or NSF, as these have considerable indirect costs; these are funds that are paid directly to the university, and are in addition to the money that the investigator receives. The time demands of basic and translational research differ; the former usually requires more focused and protected time.

***Do you think that laboratorians should specialize within a focused area of research, or be more diverse in their research efforts? (How did you establish and focus on your research brand?)***

**Ann Gronowski**: In my opinion, laboratorians should do a bit of both. A good laboratorian should be asking questions about unusual cases and unexpected results they encounter in their clinical service. Investigation of unusual & unexpected situations can lead to discoveries that should be shared via publication. For this reason, I think that laboratorians often accumulate a diverse spectrum of research topics. I think this should be encouraged, not discouraged. However, those unusual cases may lead to just one or two publications in an area. I think it is also good for laboratorians to have one or two areas of research on specific topics that they can form and test hypotheses and really advance a particular area of science.

**Fred Apple**: The simple answer is yes. I was mentored to find a specialized area that you are passionate about and pursue all questions and directions of study. Become an expert on every facet of the specialized analyte/disease state and the analytical and clinical aspects of this analyte. Explore how you can partner with other experts in your field of choice and read the literature. This does not mean you cannot be a diverse research scientist, working with your residents and fellows during their training in the areas they choose to study and advance, as well as work with medical staff colleagues in your institution who will always be calling on you as a laboratorian to help solve their laboratory-based questions in their respective areas of research. At the end of the day, either direction can work, as long as your final product is quality and worthy of peer-reviewed publication.

**Mari DeMarco**: I see merits to both approaches, albeit for different circumstances. To build an externally funded research program specializing a specific area or select related areas is advantageous. It may be that you focus on an organ system, disease or analytical technique, for instance. The great thing is that this does not mean that you are forever stuck doing a narrow line of research. Think of researchers that you would identify as highly successful and that have built the type of research programs you would like to build—I would bet that you can readily identify their ‘research brand’ but you can also note an evolution of their research foci over the years.

When starting out it is important to build credibility in your desired areas of research. You can make that harder on yourself if you endeavor to tackle too many topics. For instance, in my research lab we focus exclusively on protein biomarkers with an emphasis on neurodegenerative diseases and clinical mass spectrometry. However, I rarely turn down an interesting clinical research challenge if it centers on a protein biomarker and can potentially be solved with mass spectrometry, no matter what disease state it relates to. This is how I fit in more research diversity into my lab without distracting from our core focus.

**Yusheng Zhu**: My research areas are very broad and evolve based on the clinical needs and research environment, but it is always in the realm of laboratory medicine. For example, my research areas include new assay development, telomerase biology, pharmacogenetics, hemoglobinopathy, clinical application of mass spectrometry, novel biomarker evaluation, and imaging mass spectrometry.

**Paul Collinson**: It is preferable to specialize rather than attempt to cover too wide an area. However, within the specialization there are always opportunities for diversity especially if there is the opportunity to use tests in a different way. The choice of specialization should be guided by your interests and by whether or not the field is already filled with experts. It is easier to start when there are few others working in your area of choice. There will always also be serendipity. In my own case, I was interested in the concept of rapid diagnosis using cardiovascular biomarkers. Developments in clinical treatment resulted in a switch from monitoring patients with myocardial infarction to proactive intervention hence a need for rapid diagnostic strategies. In addition, there is a need to have some laboratory space that you can call your own and then to obtain funding. This can be progressive, starting with small projects ideally using tests which are already in routine use and then progressing to grant applications and finally research collaborations.

**David Sacks:** Absolutely specialize. It is important to gain knowledge and establish a reputation as an expert in a focused area of research for a successful research career. This tenet applies to both basic and translational research. In basic science, investigators will contact you to collaborate for your expertise, reagents and experimental techniques. Similarly, if you are an expert in an area of translational research, people will approach you for your input into various undertakings, ranging from serving on panels and contributing to guidelines to speaking at conferences and performing peer review.

Sir Peter Medawar (Nobel Laureate in Physiology or Medicine) advised: “…any scientist …who wants to make important discoveries must study important problems”. I chose to address a common disease with debilitating complications, namely diabetes mellitus, where the underlying pathophysiology could potentially be elucidated. In this condition, if one asks consequential questions, the answers will be consequential.

***What have you found to be the most effective ways to form collaborations in academia and industry?***

**Ann Gronowski**: Most people are eager to collaborate if you come to them with an idea. The key is to be a good co-collaborator. Outline what you expect from your potential collaborator, follow through on what you promise, be clear on expected authorship order from the beginning, be generous on authorship, and make sure to see the project through to the end.

**Fred Apple**: I would offer that you not be shy to contact/communicate with a more senior expert in your field of choice. Pick up the phone; call this individual and talk with them to ask questions. Hopefully you’ll find that they are open to listen and work with you, to share their successes and failures that will be educational in your growth and approach to a problem. When you do initiate a collaboration, meet deadlines to complete study work, submit written reports on time, and when committing to draft sections of group authored manuscripts it’s important to be on time with the senior author’s request, as this establishes your reliability. Research collaborators like people who follow through on their commitments. It may sound corny, but it is what many people remember. Also, it is important to disclosure all industry collaborations, including advisory boards, consulting arrangements that may develop, and funding.

**Mari DeMarco**: From my experience, the most productive and beneficial industry collaborations have been spurred by non-industry related projects. That is, by establishing my lab’s expertise/resources/position in our focused area of research; it has put us in a great position to enable collaborations. As such, many industry collaborations grew organically from existing programs of research in my lab.

When discussing a potential partnership, think about what aspects of the study have high value for you—it could be anything from answering a scientific curiosity to advancing a new in vitro diagnostic or therapy. I would advise that you directly ask your industry partner to tell you what aspects of the project are of the highest priority for them and the key knowledge they hope to gain. Having a clear vision of everyone’s motivations will help develop study objectives that will lead to a strong partnership. If the motivations are not in alignment, maybe this is a project you take a pass on, and recommend a colleague who may have an interest in this topic.

Whether it be an academic or industry partner, ultimately the best way to secure more collaborations is to *be* a good collaborator. Did you respond promptly to queries? Did you follow through on specific promises you made? Did you help facilitate any paperwork or other administrative tasks that need to be handled? Is the research team in alignment regarding the results/outcomes that are planned for publication? Did you help ensure that expectations around authorship were clear for all involved? Did you prepare publications and/or project reports in a timely manner? Did you actively work to keep the lines of communication open?

**Yusheng Zhu**: To establish collaborations in academia, I attend as many scientific conferences, workshops, and symposia as I can. In this way, I can identify researchers who have knowledge and skills needed in my research. I have developed collaborations with two researchers for my imaging mass spectrometry studies: one has the animal model I need and the other has experience in imaging mass spectrometry. Another example is a collaboration with a researcher in bioengineering, developing a point-of-care assay for SARS-CoV-2 detection. Regarding industry collaboration, it is a good idea to reach out to IVD companies to show your willingness, expertise, and/or resources.

**Paul Collinson**: The most effective way to form collaborations is to acquire a reputation as someone with an interest in the area. It is also essential to meet and become friendly with others who are working in the field. This means attending meetings, presenting abstracts and papers and offering to collaborate on larger projects. Collaboration with industry follows the same general principles but is important that the collaboration is based on science and facilitation rather than financial. However, a willingness to collaborate and the ability to be able to fulfil the needs of that collaboration are essential.

**David Sacks:** Collaborations are essential to enhance productivity. This requires meeting and talking to people. In basic research, one should attend scientific conferences and talk to people at lectures, posters and social events. Don’t be afraid to venture outside your area of expertise. Collaborating across disciplines often produces synergism, enabling one to address hypotheses not possible with the techniques in one’s own laboratory. Get others excited about your work so they want to collaborate with you.

For industry collaborations, once you establish a rapport make sure you follow up and complete planned studies. Do good work, establish a reputation as reliable, and companies are likely to approach you for collaborations.

***What do you see as the role for laboratory medicine in research in the next 10-20 years?***

**Ann Gronowski**: Laboratory medicine will play an important role in several areas: 1) Detection of emerging infectious diseases. The COVID-19 pandemic has certainly elucidated the importance of laboratory medicine in the face of a pandemic. COVID-19 is unlikely to be the last pandemic and laboratorians will need to remember and apply the lessons they have learned. 2) Leveraging informatics and computational biology to improve diagnostics. Whether it is using machine learning for earlier detection of sepsis or synthesizing large amounts of patient data to detect analytical problems in in real time, I believe that data analytics will play an important role in advancing diagnostics. 3) Advancing cellular therapy. Laboratory medicine is playing an important role in treatment of neoplastic and non-neoplastic diseases through cellular therapy such as CAR T-cells. This important therapeutic work will continue to be driven by clinical pathologists in laboratory medicine.

**Fred Apple**: I am quite concerned about the role of laboratory medicine in research and development within academic and private and public hospitals and medical centers in the next 10 years. Moneys available for applied research are more difficult to obtain, not all chair-persons support applied research in place of basic science. Hospital administrators are looking towards sending specialized testing out to reference labs and not supporting the hiring of PhD and MD scientists to develop mass spectrometry and molecular based testing as a source of patient care testing and business opportunities.

**Yusheng Zhu**: Laboratory medicine always plays critical roles in research. The most recent example is the quick development of clinical assays for the diagnosis and management of COVID-19 patients during the pandemic. In the next 10-20 years, we will continue to develop new assays to meet clinical needs. We will discover novel biomarkers that can be used for the diagnosis and management of disease. We will continue to adopt new technologies/analytical tools such as mass spectrometry, next-generation sequencing, nuclear magnetic resonance, biosensors etc. Also, we will use machine learning and artificial intelligence for big data analytics.

**Paul Collinson**: There has been a spectacular increase in interest in the role of biomarkers in disease diagnosis and monitoring. The clinical laboratory is the place where basic and translational research is converted into useful clinical application at the patient bedside. This requires a graded approach commencing with proof of concept then translation into studies of clinical application and clinical utility. The most perfect biomarker will have no application if it must be immediately preserved in liquid nitrogen and measured using cyclotron. Laboratory medicine is the bridge that addresses the whole question of how a test may be used in routine clinical work. Any new test, no matter how appealing, must be meet two criteria: can I measure it in my laboratory and what will you do differently with the result?

**David Sacks**: I’m always reluctant to predict the future. Forecasting is traditionally based on the past. Clinical laboratorians have unique skills, which have been applied over the years to enhance patient care. For example, Jack Ladenson developed assays using monoclonal antibodies to measure creatine kinase MB and cardiac troponin which had tremendous impact on the diagnosis of myocardial infarction. Another important contribution by laboratory medicine has been standardization of assays. Similarly, working with clinicians, laboratorians have synthesized and interpreted published literature to generate guidelines for laboratory analysis in selected diseases. Both guideline development and improving accuracy of measurement have led to improvements in patient diagnosis and management.

The role of laboratory medicine in future research will depend on areas clinical laboratorians choose. An important challenge will be to convert large quantities of data, eg, from genomic or proteomic analyses, into an interpretable report that will allow practicing clinicians to make diagnostic and therapeutic decisions for their patients. Clinical laboratorians are ideally positioned to lead these endeavors. Clinical laboratorians should also apply their expertise to employ innovative technology to develop and, in collaboration with clinicians, evaluate new assays.