CONNECTING THE DOTS: THE IMPORTANCE OF AN INTEGRATIVE APPROACH IN TRANSLATIONAL MEDICINE

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In addition to being Program Director of the Specialized Certificate in Translational Science at the Altman Clinical and Translational Research Institute of the School of Medicine at the University of California San Diego, Dr. Laporte is Senior Director of Translational Pharmacology at Peptide Logic LLC, a San Diego-based biotechnology company that combines the advantages of synthetic peptides and recombinant antibodies to create innovative semi-synthetic biologics for pain and other pathological conditions. He is also Founder and Principal Consultant at Laporte & Associates LLC, a biotechnology and pharmaceutical R&D consulting company. Previously, Dr. Laporte was Director of Exploratory Pharmacology at Ferring Pharmaceuticals where he led teams that conducted or contributed to peptide therapeutics Drug Discovery programs resulting in eight New Molecular Entities spanning several Therapeutic Areas (Pain, Critical Care Medicine, Urology, Hepatology, Gastroenterology, and Reproductive Health), which were progressed to Development and are still actively developed internally or through licensees.

Please can you describe your background in the Biomarkers field. Are there any achievements you're particularly proud of from your career?

My answers to these questions require a prelude. I am a veterinarian with a Master's degree in anatomy and physiology and a PhD in pharmacology. This training allowed me to study health and disease at all levels of the biological organization continuum, from population to individuals (i.e., whole organisms), systems, organs, tissues, cells, organelles, and molecules—what I call vertical integration. My career in Drug Discovery in the pharmaceutical industry allowed me to put this academic knowledge into practice and, with my clinical training, to add another dimension that I call horizontal integration. It is the continuum from comparative anatomy (how similarly and differently human and other animal species are built), comparative physiology (how similarly and differently they function in health), comparative pathophysiology (how similarly and differently they malfunction in disease), comparative medicine (how similarly and differently disease manifests itself and is managed in human and other animal species), and ultimately comparative pharmacology (how similarly and differently disease in human and other animal species can be treated with drugs).

I believe that combining the vertical and the horizontal integrations is fundamental to the success of Translational Medicine (i.e., Translational Science/Research applied to Medicine), which is, in its essence, a discipline within the Biomedical and Public Health Research areas that "translates" Basic Science findings into medical applications (e.g., drugs, cell and gene therapies, diagnostics and other medical devices, health IT/digital health products, procedures, policies, education)—it is moving Science from bench to bedside and back! Using my approach of combining vertical and horizontal integrations greatly increases the odds for preclinical findings to translate clinically—the odds that medical applications of Basic Science ultimately work in patients!

Now my answers to your questions. Biomarkers constitute the most essential tool of Translational Medicine and are key to translating preclinical findings into medical applications that work in patients! I have devoted my whole 19-year-long career in Drug Discovery in the pharmaceutical industry to Translational Pharmacology, successfully turning 8 drug ideas into bona fide clinical candidate drugs currently in Development in a wide breath of Therapeutic Areas. In each case, the key to success was the identification of the right translational biomarkers!

Now, the Altman Clinical and Translational Research Institute of the School of Medicine at the University of California San Diego has given me the amazing opportunity to design, develop, and direct a Specialized Certificate in Translational Science. This is allowing me to contribute to the training of the next generation of biomedical R&D leaders, innovators, and entrepreneurs. I could not think of a more rewarding accomplishment!

You are presenting at the conference on developing a translational science program for San Diego's biomedical ecosystem. Why do you think there is such a demand for this sort of program?

The great advancements in biomedical science that have been made over the last 25 years, especially the omics revolution, have led to substantial strengthening of Translational Medicine, though the practice of Translational Medicine dates to the dawn of Medicine itself. While this resulted in the training of many highly skilled technical experts in a wide breath of sophisticated technologies, there has been a dearth of academic training opportunities in integrative biology and medicine. This was the province of classical anatomy, physiology, and pharmacology in the pre-omics era, where interactions between cells, tissues, organs, and systems—as well as interactions between form (anatomy) and function (physiology)/dysfunction (pathophysiology)—in health and disease were emphasized. In plainer language, while we have many dots experts, we have very few experts at connecting the dots! Let's call this "intellectual process" scientific and clinical integration.

An integrative approach is also essential to move a biomedical product from an idea to a marketed product as it allows to maximize the likelihood for preclinical findings to translate into the expected clinical manifestations in patients. The way that I practice and teach this integration is what I call the "white board exercise"—a term coined by Dr. Pierre Rivière, my most influential mentor. In essence, it is a "mini" due diligence exercise that you do when you are either looking for a new biomedical product idea or when you are developing a new biomedical product idea—the key point here is that you need to do this exercise at the idea stage to get its maximal benefit, which is de-risking; if you do it after you started your biomedical product discovery/design or development (i.e., bench or bedside work), you are already in damage-control mode! What this white board exercise consists in is asking yourself what new biomedical product is needed and why.

Practically, you start by defining what are the unmet medical needs to be addressed in the therapeutic indication that interests you—this exercise always starts (and ends!) with the patient; that is the secret of success in Translational Medicine. You then ensure that you have the best understanding of key aspects of this therapeutic indication: clinical presentation, natural history, pathophysiology, diagnosis, epidemiology, burden, and cost. Next, you review what is the standard of care and what is in the competition R&D pipeline (i.e., potential future standard of care). Now, you are ready to put together the Target Product Profile (TPP) for your biomedical product idea, the most critical part of the exercise; how will your product be differentiated (i.e., superior) to the standard of care and the R&D competition regarding the unmet medical need(s) that it is addressing for the therapeutic indication of interest? These attributes that your product needs to have then determine how it should be designed—e.g., for a drug, what should be its molecular target and its chemical modality. Once you have defined this, you then need to assess the relevant intellectual property (IP) space to define your freedom to operate (FTO) and your market exclusivity.

Finally, you conclude the exercise by defining your de-risking and translational strategy: what will be your in vitro molecular target and ex vivo tissue models and assays, in vivo healthy and disease animal models and assays, and, last but not least, efficacy and safety/toxicology biomarkers (which could end up being potential companion diagnostics and/or surrogate endpoints!). As for the practice of Translational Medicine itself, this white board exercise is best done by a multidisciplinary team involving scientists, engineers, physicians, and other professionals. Let's call this whole "intellectual process" Research and Development (R&D) integration.

Although the combined use of these two key integrative intellectual processes, scientific & clinical integration and R&D integration, is at the basis of most successes of Translational Medicine application to the discovery/design and development of biomedical products, there is a pronounced lack of academic programs providing such critical training. This forces new biomedical R&D professionals to waste years of productivity by having to gain this knowledge and these skills, often very imperfectly, the hard way: through years, if not decades, of trial and error! We have designed our new Specialized Certificate in Translational Science to address this critical unmet need of the biomedical R&D professional, be he or she still in training or already building his or her career. As Translational Medicine and the biomedical industry are themselves in constant evolution, our Certificate Program is constantly adapting and expanding to keep preparing professionals for the new challenges in biomedical R&D.

What are your priorities across the coming year and beyond?

We are going through the first edition/iteration of our new Specialized Certificate in Translational Science, which we have officially launched this summer, so we will focus this coming year on its marketing and on its fine-tuning as its first cohort of students will complete it. Meanwhile, in the back room so to speak, we are designing other graduate educational products to more fully meet the needs of San Diego's biomedical ecosystem; some will be added to the Certificate while others will be used to create a complementary Certificate. Our 5-year plan is to build of full-fledged Master's degree program in Translational Science.

Where do you see the future of the biomarkers field?

From my perspective, both as a teacher of Translational Science and as a drug discoverer interested in acute organ and system failure in Emergency and Critical Care Medicine, I see an exciting future in the application of Artificial Intelligence to multi-scale Translational Systems Biology to identify and validate better structural and functional biomarkers/biomarker panels to diagnose, monitor therapeutic interventions, and establish prognosis, especially for pathological conditions involving one or more organ or system failure, such as sepsis.

Why do you attend events like this? What do you look to achieve?

I attend events like this to stay abreast of the challenges faced by Translational Medicine at improving the success of clinical proof-of-concept trials (i.e., first-in-patient trials), which, taking drugs as an exemplary biomedical product, has remained at a dismal 30% on average over the last 15 years—though some Therapeutic Areas have been much more successful than others. What I hope to achieve through my contribution to the Congress this year is to raise awareness about our graduate educational program and to entice the biomedical community to engage in it either as sponsor of internships or scholarships, provider of Faculty, or, most importantly, provider of students!