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The Basis of Translational Physiology: From Molecules to Humans, a Wide Arc of Scientific Inquiry

Translational physiology, and for that matter translational sciences, has long been a buzzword discussed in multiple forums; however, often the term translational is equated to clinical or preclinical studies. Although these studies are translational, there is a much wider swath of scientific inquiry, especially within the field of physiology, that should fall under the rubric of translational sciences. Herein, I would like to put forth a vision of translational physiology and share with you some changes that are occurring within the American Physiological Society (APS) and Translational Physiology Interest Group (TPIG).

To paraphrase the APS, translation physiology is composed of studies that lead to new or improved methods of preventing, diagnosing, or treating disease; and clinical studies that lead to a better understanding of basic physiology (2). An arc with ends at A) fundamental basic discoveries and B) outcomes relevant to human health illustrates translational physiology. In mathematics, one can name this arc AB or arc BA since the order of the endpoints is unimportant to the fundamentals of the arc. So too in translational physiology.

A simplified example is the scientific and medical history of natriuretic peptides. Cellular, cardiovascular, and renal physiologists identified granules in myocytes that contain a natriuretic peptide (1, 6). This work eventually led to recent clinical trials indicating that neutral endopeptidase inhibitors are beneficial for the treatment of heart failure (3, 4). Those studies and most if not all of the studies within that 30-year time span demonstrate a translational arc from A to B: arc AB. However, this arc hides a second arc: arc BA. Before the development of neutral endopeptidase inhibitors, nesiritide, a recombinant B-type natriuretic peptide, was developed and used to treat heart failure since 2001. Ten years later, results of a large multicenter clinical trial (ACEND-HF) indicated that nesiritide is ineffective in a general heart failure population (5). The doubling back of arc BA is one of the contributing factors in the development of neutral endopeptidase inhibitors. This is also a clear example of the bidirectionality of translational physiology, as well as the unpredictable nature of research.

Identification of translational arcs in retrospect is quite simple. Observing an arc in real time is essentially impossible since one cannot unequivocally determine the future results of any experiment, and the time scale can be nearly as long as one’s career. Therefore, using the term translational physiology to label current research can be problematic. How then do we identify and promote translational physiology?

Identification of translational physiology must come from the physiologist. An argument can be made that all research supported by medically focused granting agencies is translational. Indeed most, if not all, physiologists funded by the National Institutes of Health indicate the translational quality of their work in the grant application. Additionally, most discussion sections of manuscripts tie the described finding to a clinically relevant end point. Then is it true that there is no need to identify and promote translational science? No, it is not true because the wide arc of translational studies is not always appreciated. Moreover, scientists, and physiologists are no exception, tend to fracture into groups based on the specific subject area studied or broader area(s) of focus, such as cardiovascular physiology. Therefore, it is important to revisit the motives behind the APS creating the TPIG. The mission of the TPIG, and thus the APS as well, is to bring the translational studies to the forefront of our meetings and to promote the interactions required to create translational physiology arcs (2).

This year, a change initiated by the steering committee of the TPIG and implemented by the APS was inserted into the abstract submission process. The change was a simple question: Is this work translational? Before the publication of this article, the TPIG will have statistics regarding the number of abstracts submitted that are considered translational. Alone, this data will be interesting to track over time, but that is not the intent behind asking this question. This year, the TPIG voluntarily gave up their assigned poster topic. Replacing this topic is a special 2-hour-long translational featured topic symposium filled with presenters who indicated their abstract represents translational physiology. Filling of this session will be managed by the TPIG, but the TPIG only receives abstracts from the other sections and groups. The TPIG 2-hour symposium will consist of short oral presentations and some posters. Organization of this symposium will follow a set of themes in such a matter that arc AB (as described previously) will be apparent within each theme. Each year, these themes will mirror the themes that the APS president puts forward for the annual meeting. However, the themes will be loosely structured since the programming committee will not know what abstracts are considered translational until after submission. The presentations in this featured topic will be in addition to the sections’ or groups’ regularly programmed activities. Most importantly, the presentation will be akin to an elevator pitch where the presenter quickly presents the problem in question, the central hypothesis, and most supportive data. The goal of this forum is not to duplicate the presentation programed by the section or group but to string together a translational arc that will act as a catalyst for further discussion between and among the attendees and speakers.

To summarize, translational physiology is a bidirectional arc that is inherently impossible to visualize in real time. The goal of the TPIG is to bring translational arcs into focus so that interactions across the disciplines within, and in the future beyond, physiology can in-
crease to bring about better health outcomes for humanity. However, this can only occur through increased interaction between all physiologists and non-physiologists along a topical arc to promote basic findings to the clinic and clinical findings to the laboratory.

References


