Stepping Into the Mix

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I was introduced to interdisciplinary research during my very first lab meeting in graduate school in 1991. Judith Rodin, my first advisor, was leading a MacArthur Foundation network on Health-Promoting and Health-Damaging Behaviors, including the role of stress. The network included diverse and broad thinkers such as neuroscientist Bruce McEwen and social psychologist Nancy Adler. The MacArthur networks provided a great model of how small interdisciplinary discussion groups could be highly collaborative and generative in promoting new ideas that stretch people out of their disciplinary silos, as well as support students in their training. Rodin started off the meeting talking about “allostatic load” — the cumulative physiological price of chronic stress — and how allostatic load might develop and present in someone who has depression versus post-traumatic stress disorder. Allostatic load helps to explain how a set of environmental inputs shape people’s psychological and homeostatic regulatory responses in complex ways, nudging them toward disease states. It was clear that this concept involved the perspectives and expertise of different groups — psychologists, physiologists, neuroscientists, and social epidemiologists. They all had a stake in understanding how allostatic load played out in organisms and in society. I was hooked on the idea of allostatic load.

I sought to find a cellular model of allostatic load — a cell system that registered wear and tear from an early age, long before diseases develop. The telomere — the protective cap on the end of chromosomes — was a good candidate and has been a useful biomarker (see main story on page 14). It is both a marker and a mechanism. It is mechanistic in that it explains how cells senesce or die. It serves as a proxy marker for cumulative exposure to stress mediators that include, for example, oxidative stress, insulin resistance, stress hormones, and inflammatory factors.

Scientists might argue for decades to come about how cell aging actually unfolds in humans and about whether the telomere is more marker or mechanism. Regardless, it seems highly predictive of most degenerative disease trajectories (early onset, worse prognosis, and sometimes earlier mortality). It is one of our few windows into the aging clock machinery.

I was lucky to find an ideal collaborator in Elizabeth Blackburn, who subsequently won the Nobel Prize for her research on telomeres and telomerase, the enzyme that protects telomeres. Blackburn was at first skeptical of the role of stress in cell aging, but was nevertheless open to and supportive of my research. She has since been integral to a tremendous number of human studies including many in the behavioral sciences.

I am also fortunate to work with extremely talented students and colleagues who are equally obsessed with the complex roadmap linking emotions and physiology.

A map is slowly emerging showing how telomeres are fitting into this integrative science. Having a clear understanding of how this life-long marker is shaped and protected could help the research paradigm shift toward prevention. Strategies for monitoring changes in telomeres could also be useful, and we often receive queries from people wanting to do just this — but there are few reliable options available. So we started a company to offer inexpensive telomere testing as a platform to conduct large-scale research and test the helpfulness of such testing for the public. This endeavor turned out to be an unsuccessful clash between our public, health-oriented goals and aspects of the business. We gave our shares away and moved on.

We are now writing a book about telomeres and their connection to aspects of health including social factors, with the hope that this integrative and interconnected view of health might be helpful to individuals and might encourage new models of prevention. It will also likely become a snapshot of a particular time in telomere research, as our understanding of aging and precision medicine is moving at a rapid pace.

Advice

Sometimes students want to know the best way to link up psychological processes of interest with biological mechanisms of health. Here are some tips and issues to consider for young behavioral scientists who want to collaborate with experts in biology and medicine and create interdisciplinary programs of research:

Keep asking yourself, “So what?” Make sure your best outcome will have implications, and not just for incremental science. Develop your intellectual support group where you ask each other this question in a challenging but helpful way.

Stay focused, flexible, and persistent. You should keep your focus on both your specific question as well as the big picture, and be open to changing your model or theory.Be prepared to withstand and overcome failures and rejections (in unreturned emails and in null results).

Secure pilot funding. Very little happens without money. For my first study with telomeres, the idea seemed "way out there." There was no evidence that telomeres were affected by lifestyle, much less by psychological factors. I tried three different funders before getting a small pilot grant. Securing small grants to add measures to the right types of ongoing studies is also a good model for starting off. Well-designed, small-scale proof-of-concept studies are a solid way to start testing a big idea, and small studies serve as a foundation for funding larger studies. The easiest sources are probably small pilot study grants associated with various research centers and training programs at universities and especially medical schools.

Be bravein approaching basic scientists, and realize thatwhat you bring to the table is invaluable. Psychological scientists are among the most highly trained methodologists — they will help design the best experimental and clinical paradigms. In most cases, basic science PhDs and MDs get only a small portion of the rigorous training psychologists get in research and statistical methodology. Don't expect them to have read Alan Kazdin's research-design textbooks.

Do your homework in the relevant physiology, which enables the dialogue to start. If you are putting together two (or more) pieces of the puzzle of mind-body health, you need to make sure that at least one of the pieces is solidly grounded — a known quantity you can operationalize well. That means if you are exploring new indices of biological health, you want to have excellent and reliable measurements of your psychological or social process or state.

Team science is the new science. You don't need to go to medical school to research a physiological system, but you do need to become a quasiexpert in that system. There are now many excellent doctoral programs that provide integrative training including the physiology in key regulatory systems, such as psychoneuroimmunology and neuroscience. If you did not get formal training in one of those programs, you can pick this up later on your own and through collaboration. In return, educate your collaborators about the relevant context and your own contributions to the proposed study.

Keep yourself strongly rooted in your primary area of strength. While you will stretch yourself to learn about other disciplines, you don't need to and cannot be the expert in everything. You actually *should* rely on having an expert basic science collaborator who has more in-depth knowledge of the relevant complex biological system than you yourself will be able to develop in your training.

How deeply will you dive?

This is a question you will likely wrestle with. Physiology is so phenomenally complex, and you need to decide on what level of analysis you will focus. The range is vast, from frank disease states, to autonomic-nervous-system and systemic biomarkers linked to disease, to cellular-level processes. Your research question will determine if you need a cell biologist collaborator or if simple access to medical records will suffice. For many health psychology projects, behavioral scientists do not need to understand the relevant molecular signaling pathways. That reductionist level of understanding is not critical if one is measuring only the level of physiological systems or biomarkers. But more and more, with the ability to link psychological mechanisms with big data such as gene-expression patterns, it will become important for psychologists to cross-train in depth in the relevant biological systems as well as develop closer and more interdependent relationships with the researchers who facilitate this new field of work.

Psychology in Precision Medicine

This is where I find myself today: I am collaborating on a meditation study with a mathematician-geneticist who can identify novel gene coexpression networks. The first, relatively easy step is collecting the RNA to get a transcriptome profile of participants in a well-designed study with highly stratified groups. Then there are new ways of analyzing networks that allow us to identify patterns of highly coregulated genes and how these may differ between groups or conditions. This can be used to identify and compare the most relevant (enriched) subnetworks in disease versus control states, as is now being done in medicine, but this can be applied to examining people before and after interventions, as we are doing in trials of meditation. This profiling is part of the larger field of precision medicine. This field is typically defined as the study of an individual's molecular-level signature — genetics and other "-omics" — and involves integrating information from clinical phenotypes. The hope is that this detailed picture will lead to individualized treatments of diseases such as cancer. These tools of precision medicine hold promise for drug development and treatment. They might lead us to better understand mental states and aging trajectories as well.

It may not be well recognized yet within precision medicine, but social and psychological factors are an integral part of precision medicine that cannot be ignored for long. It will be important for the new generation of psychologists interested in health to jump into the "-omics" as part of team science. We will surely contend with issues of replicability in this world of big data, and fortunately psychology is leading the way in tackling this issue as well. Systems biology is meeting psychology. We have the ability to use these integrative systems approaches to understand and characterize distinct psychological and behavioral states. I am feeling like a naïve new student all over again. It's very exciting!