COMMENTARIES

You Can Run, but You Can't Hide: The Academic Physician and Molecular Biology

In this issue of *Academic Emergency Medicine*, Drs. White and Sullivan provide a comprehensive look at apoptosis.[1] The article delves deeply into the cellular and subcellular molecular processes that contribute to "self-destructive cell death." For those academic physicians who are too old, or were too inattentive, to have received proper schooling in molecular biology, getting through an article such as this can be a daunting task. When I was in medical school in the early 1980s, adhesion molecules were the things that made my dirty dishes stick together when they piled up in the sink, and free radicals were non-incarcerated burned-out hippies.

The explosion of science in the field of molecular biology, particularly in the area of cellular injury, means that even for recent medical school graduates, keeping informed involves learning new concepts and terminology. Can the academic physician be ignorant of the recent advances in molecular biology and still function well? Perhaps, but each year the bar is set higher. Learning the basics of apoptosis today will make it far easier to understand future discoveries in molecular biology.

As one explores the field of molecular or cell biology, a pleasant paradox is found. Although the scientific methodology is becoming more complex and technical, some unifying themes of cellular function can make the science easier to understand. For all of its complexity, the cell has a finite number of ways to respond to stress. Investigators in the seemingly disparate fields of infectious disease, cardiac disease, stroke, and traumatic injury find that they are playing with the same molecules and biomolecular processes. This became apparent to me in my research on alcohol intoxication and traumatic brain injury, as I discovered that cellular reactions to a toxin (ethanol) are similar to that seen with applied energy (traumatic injury). Recognizing these similarities is an important function for the academic physician. We tend to become a bit resentful of the basic scientists, tucked away in their laboratories, churning out volumes of biomolecular information that we must try to understand. We forget that it is a 2-way street—the fuel for molecular biomedical research comes from our patients' disease processes and our observations of those diseases. Communication between biomolecular researchers and academic physicians is mutually beneficial—we learn more about basic cellular processes, and they gain insight into the clinical relevance and applications of their research.

Even if it is agreed that physicians need to keep abreast of the advances in biomolecular science, the logistics of this learning can be difficult. Since most of us will not have molecular biology journals on our nightstands or desks, we rely on review articles in our "normal" medical journals to provide biomolecular updates. A few suggestions for approaching such an article follow:

1. *You can't fake the fundamentals.* Whether we like it or not, a basic understanding of molecular biology is requisite to the current practice of medicine. Molecular biology can be grossly subcategorized into the study of genes and gene expression, proteins and protein function, and the interaction of other molecules, cells, and tissues with the proteins that are produced as a result of gene expression. If one has not gained this knowledge through medical training, it must be acquired, or at least accessible, through other means. We are fortunate in having more learning tools available to us than our predecessors, which is good, because we have a lot more information to digest. A current (i.e., not less than 5 years old) molecular biology textbook is a good place to start. Additionally, a number of sources of biomolecular educational materials for physicians are available on CD-ROM. Most medical journals, in a manner similar to that of *AEM*, offer review articles that address topics in molecular biology. The academic physician who can periodically learn the basics of new developments in molecular biology, and knows where to search for the details, will face fewer surprises and less bewilderment as new discoveries are made.

2. *Don't sweat the jargon.* Molecular biologists seem to have trouble with naming things, and especially in limiting the number of names for each molecule or process. Many molecules have multiple names and nicknames. Drs. White and Sullivan kindly point out that "RNA-activated protein kinase," or PKR, is the enzyme formerly known as DAI, p 68 kinase, PKds, or P1/eIF-2α protein kinase. Now we know where pop singer "Prince" took his cue!

Jargon is an inevitable part of hard science, and is not unique to molecular biology. As a physician, do you always go straight to a V/Q when you suspect a PE, or do you rely on the A-a gradient, D-dimer, or Duplex? I'll bet a molecular biologist would find that baffling. Many of us have experienced the same trouble with

computer jargon as we have with molecular biology. Yet, we find ways to make computers work for us. My suggestion for molecular biology nomenclature is to step back or regress when you are confronted with a new name, abbreviation, or symbol. For example, when I encountered the new abbreviation "CPP32" in White and Sullivan's article, my first thoughts were of the fretful robot in the *Star Wars* movies. After a few minutes of daydreaming, I reoriented myself, and realized that remembering the specific letters and numbers for this molecule was way more detail than I needed. Therefore, I regressed, thinking: very well, CPP32 is a caspase that is formed by neurons, and the authors already told me that caspases are a type of protease. Proteases are enzymes that degrade other proteins, and that can be bad for cell function, and can contribute to apoptosis. So, from now on when I see CPP32, I'm thinking—bad neuron enzyme that may contribute to apoptosis. And when the authors start talking about Nedd2, another neuronally-derived caspase similar to CPP32, I'm lumping old Ned in with CPP32. In this manner, you can simplify the jargon to a degree that is appropriate for the depth of understanding you need in the topic. Remembering all of your simplifications can become challenging, which brings us to the next suggestion.

3. *Take notes—even if you don't know what they mean.* Most of us are accustomed to taking notes when we attend a lecture or meeting to aid our recollection, decipher a difficult concept, or put foreign terms into our own words. This practice can be very valuable in simplifying a technical manuscript. For example, the first few times I saw "PARP" in the White and Sullivan article, I wrote "DNA repair enzyme" next to it. Substituting these words allowed me to make more sense out of the sentences in which PARP appeared. Combining the tactile sense of writing with the visual input of reading is a common method for enhancing learning. If I later return to these notes I have scrawled on the margins, they often make no sense to me, but the article usually does.

4. *Focus on the figures.* Textual descriptions of biomolecular processes can lead the reader in a downward spiral into the darkness. In many cases, the refreshing light that drives the darkness away is a well-designed figure. Since many biomolecular processes involve chemical reactions or cascades, they are often conducive to pictorial or schematic representation. Figures, by their nature, and if enforced by a good editor, are simplifications that can rescue the straying reader. Spending a few minutes to follow the arrows or trace the relationships between elements of a figure is usually time well spent. Also, the captions that describe the figure are often concise and simpler to understand than the accompanying text.

When it comes to molecular biology, you can run, but you can't hide. The head-in-the-sand approach does not work well when one of your patients presents with an Internet search result on his or her medical condition and asks your opinion on the molecular action of a particular drug. Even if you decided to ditch academic medicine and enter another career, you will still be bombarded by molecular biology information. Descriptions of molecular biology concepts as they relate to medicine regularly appear in newscasts, newspapers, popular magazines, movies, and novels. Your relatives, who used to ask about their rheumatism at the family reunion, will soon be asking how oxidant reactions may be contributing to their pain. The only defense will be a good offense. Articles such as White and Sullivan's "Apoptosis" will expand the academic physician's knowledge of molecular biology, and other basic science disciplines. Happy reading!

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Reference

1. White BC, Sullivan JM. Apoptosis. Acad Emerg Med. 1998; 5:1019–29.

Apoptosis: On the Verge of Clinical Relevance

Over the past few years we have learned a tremendous amount about gene expression as it relates to apoptosis and to cerebral ischemia. The process of apoptosis, as distinct from necrotic cell death, involves nuclear DNA as the primary target, with DNA fragmentation and chromatin condensation by activation of endonucleases and caspases. In apoptosis, there is preservation of membrane structures and cytoplasmic organelles. Necrosis, on the other hand, is characterized by lysis of membranes and destruction of cytoplasmic organelles with swelling of mitochondria and Golgi apparatus.

The apoptotic mode of cell death in the context of experimental cerebral ischemia involves several steps between the initial ischemia/hypoxic insult and frank neuronal death. Within this cell death cascade,