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Editorial

Translational Discoveries, Personalized Medicine, and Living Biobanks of the Future

From the age of Hippocrates and Galen to the pioneering work of the likes of Morgagni, Virchow, and countless others, pathology remains an absolutely crucial part of diagnostic medical science. The American Society of Investigative Pathology describes pathology as "the medical specialty that provides a scientific foundation for medical practice" (*http://www.asip.org/career/index.htm*). The NIH also recognizes the importance of the intersection between disease understanding and treatment advancements. With the rapidly changing field of translational research becoming a top priority for the NIH, pathology as a discipline demands closer, more synergistic interactions between the basic and medical research communities. Pathologists contribute fundamentally important expertise in both clinical research and preclinical modeling for the investigation of all human diseases, from embryonic development to aging, cancer, and dementia. This has been and continues to be one of the core strengths of academic and medical pathologists, a strength that is mirrored in the pages of *The American Journal of Pathology*.

Pathology's Contributions

Pathology is not a static discipline relying solely on the microscopic examination of tissue specimens. It is an evolving science that continues to incorporate the latest in scientific methods into its role in the identification and characterization of human diseases. Newer technologies such as mass spectrometry, advanced fluorescence-activated cell sorting capabilities, high-throughput sequencing, and other molecular techniques are changing the role of the pathologist, increasing our ability to characterize disease, and adding to the complexity of information that the discipline of pathology provides to the medical community.

In addition, the evolving science of obtaining and interpreting omics data—beyond genomics to transcriptomics, metabolomics, proteomics, and epigenomics—to arrive at new markers of disease state, prognosis, and therapy, as well as insights into the mechanism(s) of pathogenesis, means that today's pathologist must possess an understanding of computational biology to be an informed consumer of the enormous amount of data contained in a single omics data set. Pathology, therefore, represents a critical part of the research enterprise needed to improve health care and understand disease pathogenesis. It is the discipline, above all others, that provides the bedrock on which biomedical science progresses.

Pathology in the Ever-Changing World of Publishing

Journals represent the traditional gatekeeper of high-quality science within the framework of the highest-quality expertise in peer review, and this is equally true for pathology as for other disciplines. Traditional print journals have been the forum for presenting scientific advances and for obtaining peer review and input into scientific inquiry. This model, however, is evolving in the era of electronic information with electronic journals, alternative methods of peer review, and wiki-like discussions of research. This has been coupled with a proliferation of scientific journals, mainly electronic, aiding the dissemination of medical information.

The impact factor of many journals is also changing, owing to this dynamic flux in the publishing landscape. It is unclear whether the traditional impact factors are still an accurate measure of the true value of publication in a particular journal. This is illustrated by the strong influence of review articles on impact factor scores. Although reviews can drive dramatic changes in impact factor and provide an important service to the research community, the quality of primary science published in a journal is a truer measure of how successful a particular journal is viewed by the scientific community it serves. Where authors decide to submit their primary research is paramount to any journal's success. For pathology journals, the issue then becomes what is the balance of traditional pathological research and diagnostic methods, together with cutting-edge research and development articles, that provides what is needed for the modern pathologist?

Furthermore, how do we, as a journal, serve our constituents, including the membership of the American Society of Investigative Pathology in the case of the *AJP*?

Since I began my service as Editor-in-Chief in 2008, we have intentionally broadened the scope of the *AJP* by accepting more omics articles and articles seeking to integrate multiple scientific approaches with classical cellular and morphologic analysis to arrive at new pathogenic paradigms. As was true of my predecessors, we have continued to solicit high-quality Reviews and Commentaries. In addition, the *AJP* again began receiving Short Communications to facilitate the rapid publication of cutting-edge short research articles, which otherwise might be submitted elsewhere. I also broadened the Associate Editor pool and the editorial board to include scientists with expertise in emerging technologies and fields of research. These changes, I believe, are strongly reflected in the quality of science published in the *AJP* and in the high regard for this journal among research and clinical scientists.

As per the *AJP's* scope (*http://www.journals.elsevierhealth.com/periodicals/ajpa/aims*), we will continue to "accept manuscripts on the cellular and molecular biology of disease that advance the basic and translational knowledge of the pathogenesis, classification, diagnosis, and mechanisms of disease, without preference for a specific analytic method. Priority will be given to studies on human disease and relevant experimental models using cellular, molecular, animal, biological, chemical, and immunological approaches in conjunction with morphology." We will solicit high-quality Reviews that focus on emerging technologies in pathology and that offer a new synthesis of the pathogenesis of disease. We must be a journal for the next century by increasing our electronic presence and providing value-added content that allows dynamic interaction of the scientific community with the full data content published in the *AJP*.

Continued Emphasis on Translational Research

To emphasize the value of the translational data published in the *AJP*, we will continue to highlight major advances reported in our pages. Our Commentary and press release programs, together with the coordination of institutional media offices, helps to disseminate the forward-thinking advances appearing in the *AJP* and promotes many of the goals put forth by the NIH and other national agencies as they relate to translational medicine with the goal of improving disease diagnosis, treatment, and prevention.

One such example is the recent article by Liu et al[1] on conditionally reprogrammed cells (CRCs) from normal and cancerous biopsy specimens of human and rodent tissues. In an elegant series of experiments, Schlegel, Riegel, Albanese, and others at Georgetown University in collaboration with McBride at the NIH established a new method for propagating, in vast numbers, primary breast, prostate, and other types of differentiated epithelium without the need for passage through mice or the use of transforming oncogenes.[1] Termed the *Georgetown Method* by Rimm at Yale University in the accompanying Commentary,[2] this CRC culture system enables generation of the first inexhaustible patient-specific biobank of primary epithelial cells and cancer cells from the same patient.

This major breakthrough, which was also highlighted in the *NCI Cancer Bulletin* (*http://www.cancer.gov/ncicancerbulletin/012412/page6*, last accessed February 16, 2012) is timely, indeed, as it addresses the recent lamentations published in a letter to *Nature*, where Hyman and Simons[3] clearly articulate the need for generating more clinically relevant cell lines to allow for completely rewriting the rules by which human cells are used in preclinical studies.

One of the most exciting aspects of CRCs is their adaptability. For example, using this more flexible approach, CRCs may soon provide for the rapid screening of tumor cell drug sensitivity using a patient's own proliferating cells. Although the Food and Drug Administration will eventually need to be involved in the approval of such an approach, the Georgetown Method combined with phenotypically matched stromal cells may soon be the basis for truly personalized medicine. If successful, the CRC/stromal system represents a critical turning point/change in trajectory away from the more traditional paradigm of relying on genetic information to suggest indirectly possible drug treatments to a more applied approach of direct sensitivity screening.

Because the supply of a patient's cells is now virtually unlimited, new mechanistic, grafting, and omics studies can and will be performed to improve our understanding of the differences between a patient's normal and cancerous cells. The living biobank(s) that will arise from using this technology will also be used for a variety of basic and applied studies, such as to study the clonality of tumors. In short, the Georgetown Method makes possible a bench-to-bedside-and-back-again approach to personalized medicine on many different fronts.

A Future Trajectory of Growth

It is a credit to the stature and strength of the *AJP* that Liu et al[1] chose to submit their groundbreaking work to our journal. This pioneering work should be widely cited for many years to come, and I am thrilled that we had a hand in its peer review and publication. Similarly, Mori et al,[4] led by Mina Bissell at Lawrence Berkeley National Laboratory, have chosen to publish in the *AJP* details of their revolutionary new imaging techniques for viewing pathology tissue specimens. Please keep an eye out for this paradigm-shifting work, which is now

in press for publication in an upcoming issue of the *AJP*. It is clear that the *AJP* continues not only to excel but also to play a major leadership role in publishing top-tier, cutting-edge research. With the continued support of our readers and authors, we will maintain this trajectory well into the future.

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References

1. Liu X, Ory V, Chapman S, Yuan H, Albanese C, Kallakury B, Timofeeva OA, Nealon C, Dakic A, Simic V, Haddad BR, Rhim JS, Dritschilo A, Riegel A, McBride A, Schlegel R: ROCK inhibitor and feeder cells induce the conditional reprogramming of epithelial cells. Am J Pathol 2012, 180:599–607
2. Agarwal S, Rimm DL: Making every cell like HeLa: a giant step for cell culture. Am J Pathol 2012, 180:443–445
3. Hyman AH, Simons K: The new cell biology: beyond HeLa cells. Nature 2011, 480:34
4. Mori H, Borowsky AD, Bhat R, Ghajar CM, Seiki M, Bissell MJ: Laser scanning-based tissue autofluorescence/fluorescence imaging (LS-TAFI): a new technique for analysis of microanatomy in whole mount tissues. Am J Pathol 2012, (in press)