EDITORIAL

Coming into Focus

Computational Pathology as the New Big Data Microscope

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Significant advances in investigative pathology historically have been triggered by the development of new research tools. For example, new histochemical staining techniques in the first half of the twentieth century, electron microscopy and sensitive immunohistochemical and *in situ* hybridization detection procedures in the second half, and next-generation sequencing in the twenty-first century have all led to significant advances in diagnostic pathology as well as our understanding of disease pathogenesis.¹ We are now witnessing the emergence of computational pathology as a major driver of experimental pathology research and ever more refined disease classification.

What Is Computational Pathology?

Computational pathology has been variably defined to emphasize clinical decision making, scientific and clinical workflow, and/or microscopic image analysis.^{2,3} For the sake of this Editorial, we will define computational pathology as the development and application of data-analytical and theoretical methods, mathematic modeling, and computational simulation techniques to the scientific study of disease. This definition incorporates the NIH Working Definition of Bioinformatics and Computational Biology (<http://www.bisti.nih.gov/docs/compubiodef.pdf>, adopted July 17, 2000) and the generally accepted definition of pathology as the study of disease. Regardless of precise definition, computational pathology has gripped the imagination of the pathology community and is increasingly recognized as vital to the future of both diagnostic and investigative pathologies.

The use of information and communication technologies in the life sciences has entered a fundamentally new stage,⁴ and our discipline is beginning to embrace the change. The need for computational approaches to process signals from

microscopic images, molecular profiles, and a variety of omics platforms continues to grow, and pathology is ideally positioned to lead a systems-level integration of these new tools into clinical and research workflows.⁵ In the same fashion that pathology as a discipline is not defined by the microscope, the new domain of computational pathology is facilitated by recent technological developments in computer sciences and bioinformatics though not strictly defined by them. The development of computational pathology is in some ways similar to the early days of bioinformatics that arose from the intermixing of computer science and biostatistics.

The Future of Pathology

In the early 2000s, it was predicted that bioinformatics had only 10 good years before it would become obsolete.⁶ This prediction reflected the opinion that specific technological challenges in the field would be addressed within that time period and mission accomplished could be declared by 2012. In contrast, 3 years after the anticipated death of bioinformatics, opportunities remain for bioinformatics to address important biological and biomedical questions. In other words, the development of bioinformatics was the disruptive force that served as a conduit to new data-driven, quantitative approaches to science and medicine and, in our discipline, a growing emphasis on computational pathology.

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On a broader scale, concepts such as P4 Medicine⁷ have made a compelling case for a closer integration between population-level research and predictive, personalized, preventive, and participatory (P4) care delivery. Dare we add a fifth “P” for pathology in this scenario? Cost-effective use of personalized medicine is beginning to bear fruit,⁸ and it is time to lay down the welcome mat for precision medicine at the door of pathology. Too often, informatics training is conceived as simply learning how to use institution-specific commercial software systems rather than obtaining a deep understanding of data processing and analysis. In this era, a new generation of pathology trainees and investigators need to be ready to engage big data resources and statistical concepts with the same ease and familiarity with which they use the microscope. Computational pathology is poised to fill this need by becoming the Big Data Microscope that brings into focus the sometimes disparate fields of bioinformatics, systems biology, and molecular medicine. Nurturing this paradigm shift will dramatically and positively impact the future of P4 Medicine and biomedical research.

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