EDITORIAL

Advances in Experimental Neuropathology

New Methods and Insights

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The brain is unarguably the most complex and quite possibly the most fascinating organ in the body. It has inspired many generations of scientists to commit their own brain power to studying nervous system development, structure, and function. Unfortunately, the mysteries of the human nervous system defy easy exploration, but this has not deterred investigative pathologists in their quest to understand neurological disease pathogenesis. In this special Neuropathology Theme Issue of *The American Journal of Pathology*, we present four Reviews^{1–4} highlighting modern experimental and interdisciplinary approaches that have led to important new insights on the pathogenesis and treatment of diseases of the human central and peripheral nervous systems. These reviews emphasize the *AJP*'s commitment to publishing articles on human disease and relevant experimental models using cellular, molecular, animal, biological, chemical, and immunological approaches in conjunction with morphology to advance our understanding of the cellular and molecular biology of disease.

In an *AJP* Editorial⁵ I wrote 4 years ago to celebrate the 100th anniversary of the founding of the American Society for Experimental Pathology (predecessor of the American Society for Investigative Pathology) and its affiliation with the Federation of American Societies for Experimental Biology, I commented on the importance of integrating new experimental tools, systems biology, and informatics approaches into experimental and clinical pathology. It is with great delight to witness these approaches being rapidly integrated into neuropathology-related research and the early fruits of their utilization. The use of The Cancer Genome Atlas,¹ comparative oncogenomics,¹ conditional mouse mutants,^{1–3} and genome-wide association studies⁴ to examine rare human hereditary neuropathies,¹ tumors of the peripheral nervous system,³ and common degenerative diseases^{2,4} of the central nervous system has led to important advances in our understanding of these

diseases as described in the Review articles in this Theme Issue. Such advances would have been difficult to achieve without embracing modern experimental tools and approaches.

Three of the Reviews^{1–3} describe the use of animal models to investigate rare or difficult-to-study human diseases and emphasize the fact that animal models remain of fundamental importance in investigating human disease pathogenesis, despite improvements in our ability to collect, analyze, and interpret data from human specimens. Such animal models become particularly powerful when used in conjunction with actual human disease specimens as described in the articles by Carroll,¹ Luo and Huang,² and Tourtellotte.³ The potential discoveries of additional signaling cascades in malignant peripheral nerve sheath tumor pathogenesis,¹ mechanisms for improved efficiency of dopamine neuron replacement therapy for Parkinson disease,² and a fundamental pathogenic role for abnormal axon transport in hereditary sensory and autonomic neuropathies³ would unlikely have occurred without careful *in vivo* investigation of animal models.

The fourth Review in this Theme Issue, authored by Montine and colleagues,⁴ tackles the very topical and clinically important question of how to apply advances in precision medicine to the understanding and treatment of human dementia. This Review points out that a combination of methodologies—including genetics, biochemistry, and

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neuroimaging—will likely be needed to reach the goal of precision medicine for accurate risk stratification and alignment of therapeutics with the individual's molecular driver(s) of disease. Neuropathology and genomic pathology laboratories will play a critical role in both the discovery and implementation phases of personalized medicine approaches to human dementia.

It is my hope that this collection of neuropathology-related Reviews^{1–4} will prove both interesting and inspiring to *AJP* readers. We have much still to learn about the human nervous system and the myriad of pathogenic processes that lead to neurological and psychiatric diseases. By combining modern molecular techniques with interdisciplinary approaches and robust animal models, I am optimistic that significant advances will be made to further understand and treat neuropathological conditions.

References

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