

Preface

Molecular Pathology in the Modern Era: Revisiting Jacob's Spotted Sheep



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Editor

The Bible recounts the tumultuous story of the patriarch Jacob during his sojourn in the House of Laban in his quest to betroth the matriarch Rachel. Despite Laban's continuous trickery, deception, and debauchery in an effort to prohibit Jacob from claiming his due, whether in his marriage to Rachel or his earning of agreed upon wages, Jacob somewhat successfully prevails. Jacob, being attuned to Laban's malfeasance, proposes an odd request for wages. A rather obscure passage states the following: "Let me go through all your flocks today and remove from them every speckled or spotted sheep, every dark colored lamb and every spotted or speckled goat. They will be my wages."¹ The Materials and Methods section of the classic text continues, "Jacob, however, took fresh-cut branches from poplar, almond and plane trees and made white stripes on them by peeling the bark and exposing the white inner wood of the branches. Then he placed the peeled branches in all the watering troughs, so that they would be directly in front of the flocks when they came to drink. When the flocks were in heat and came to drink, they mated in front of the branches."¹ Finally, the Results section verifies that the experiment proves successful, "And they bore young that were streaked or speckled or spotted,"¹ where Jacob amasses the wealth that is due him.

Although many commentaries postulate this episode as an intended exercise using classical genetics, selective breeding, physiology, and epigenetics,^{2,3} it may be equally suggestive as a model of modern day molecular medicine in animals⁴ as well as in humans. Indeed, molecular medicine with respect to heredity probabilities, polymorphisms, recombination genetics, pharmacogenomics, pharmacogenetics, and the like in malignancy and other disease spaces has gained considerable popularity over the last decade with the current culmination of personalized medicine.^{5,6} Whereas years ago one would subscribe to the mantra "one gene one protein" hypothesis,

today's medical marketplace is seeing a paradigm shift in assessing multiplex interplays of factors that demonstrate pathway effects, which are taken into account in disease diagnosis, prognosis, therapeutic intervention, and patient management strategies.⁷

Molecular pathology, the discipline within pathology that focuses on the study and diagnosis of disease through the examination of molecules within organs, tissues, or bodily fluids,⁸ has evolved into the gatekeeper of molecular methodology with respect to its design, application, sensitivity, specificity, predictive value, interfering factors, and limitations to various disease spectra. The modern day pathologist is no longer limited to the microscope, paying homage to Leeuwenhoek's lens craftsmanship. Rather, the molecular pathologist is an all encompassing tour de force who is versed in molecular, cellular, and architectural aspects of tissue with respect to disease as well as its relationship to the multifactorial nature of its clinical presentation, variation, and polymorphism, which can often present confounding issues pertaining to diagnostic prowess.

The diagnostic methodological armamentarium has expanded considerably to include interrogation of nucleic acid—encompassing polymerase chain reaction (PCR) and its permutations (ie, real-time PCR), FISH, SNPs, and miRNA, among others—as well as protein assessment (ie, ELISA, Western Blot, IHC). Furthermore, the “omics” explosion, presenting a unique manner of high throughput technologies, will also further expound on disease from a biological systems approach.⁹ In addition, cellular and tissue microarrays^{10,11} hold additional promise for biomarker discovery, development, maturation, and application to various diseases.

To this end, the molecular pathologist may be likened to a modern day “molecular shepherd,” who will facilitate the evolution of the personalized medicine era and translate such into cogent, meaningful laboratory data toward the application to disease diagnosis, prognosis, and patient management for the betterment of mankind.

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