Through Evolution's Prism

OUR CELLS RELY ON COMPLEX MOLECULAR MACHINERY TO decode the genetic information we carry inside ourselves. Hundreds of molecular players must mobilize in a highly orchestrated manner so that the right piece of DNA can uncoil from its protective cocoon and the aptly named messenger RNA can be produced to deliver precise instructions for making the proteins needed to keep a cell running. And that's only stage one.

Scientists have borrowed a simple word from everyday speech—transcription—to encompass the steps required to generate the instructions to activate specific genes. Except that the biochemical process of "transcribing" a gene is so ornate that it's rather like having to whittle the pencil, make the paper, and assemble the components for a desk and chair before you can sit down to begin copying your roommate's lecture notes—each and every time.

This isn't a manufacturing process that an engineer would devise, if given the opportunity. Rather, this almost Rube Goldberg-like assembly could take hold only through a random trial-and-error process such as evolution. And that is one reason I have found transcription so fascinating for better than 30 years. What events initiate the process? How do the essential molecules assemble? Does the machinery vary? What cues enable RNA polymerase—the enzyme that makes messenger RNA—to latch onto the right snippet of DNA and begin assembling a transcript?

Nothing we study in biology and medicine would have a rational, predictable foundation without Charles Darwin's insights into evolution, the process of ceaseless experimentation that drives an organism's ability to adapt and survive over huge spans of time. Throughout this issue of the *HHMI Bulletin*, we consider different aspects of evolution: from how teachers introduce basic concepts to their students to the mathematical models used by HHMI investigator Jonathan Pritchard to gauge the impact of natural selection on human traits. We conclude with Darwin's magisterial prose, honoring the 150th anniversary of the publication of *The Origin of Species*.

Many Americans struggle with the fundamentals of evolution and whether to accept its tenets. As teacher Suzanne Black has discovered, focusing on relevant concrete examples is often the best approach. After all, without a firm understanding of evolution, scientists would have been utterly stumped by the new strain of influenza that is sweeping the world. The H1N1 strain of influenza is a mixed pot of genes drawn from viruses that infect pigs in Eurasia and the Americas, birds, and humans. By looking at changes in the proteins that dot the surface of the virus—changes that help the virus survive and adapt—researchers can assess its evolutionary path and map a vaccine strategy for the upcoming flu season. Likewise, each time a forensic scientist uses a sample of DNA from a crime scene to screen potential suspects, knowledge of evolution comes into play because each person's genetic signature is unique yet related and predictable in its relationship to other individuals. Such everyday examples have been compiled by colleagues at the National Academy of Sciences in the book *Science, Evolution and Creationism*, a survey of modern evolutionary biology written for the public. A free PDF is available at www.nap.edu/sec.

Barbara Ries

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ROBERT TJIAN

As a hard-core biochemist, I see the process of genetic inheritance through molecular eyes and, specifically, through the prism of transcription. My scientific journey has taken a path through evolution that began with trying to understand how genes got turned on (and off) in bacteria while I was a graduate student in the Harvard University laboratory of Richard Losick, now an HHMI professor. As a postdoc in Jim Watson's lab at the Cold Spring Harbor Laboratory, I studied a monkey virus called SV40 that does its damage by taking control of the genetic machinery of an infected primate cell. These early studies provided a path for discovering the huge family of regulatory proteins called transcription factors that govern how a gene gets activated. Thousands of such factors have now been found, along with a host of related molecules—all required to control gene activity.

Today, my lab group is trying to pin down the extraordinarily elastic orchestration of gene regulation in stem cells: What mechanisms allow the flexible capacity of genetic programs that define stem cells? What regulates the expression of genes specific to a particular cell type, such as muscle, liver, or neuron? Pushed by a highly creative group of graduate students and postdocs, we are finding surprising answers. We have also learned a major lesson: The machinery that has evolved is more elaborate, diversified, and convoluted than anyone anticipated. And that is a continuing source of wonder.