INTRODUCTION

What Is Epigenetics?

THE CELLS IN A MULTICELLULAR ORGANISM HAVE NOMINALLY IDENTICAL DNA sequences (and therefore the same genetic instruction sets), yet maintain different terminal phenotypes. This nongenetic cellular memory, which records developmental and environmental cues (and alternative cell states in unicellular organisms), is the basis of epi-(above)–genetics.

The lack of identified genetic determinants that fully explain the heritability of complex traits, and the inability to pinpoint causative genetic effects in some complex diseases, suggest possible epigenetic explanations for this missing information. This growing interest, along with the desire to understand the "deprogramming" of differentiated cells into pluripotent/totipotent states, has led to "epigenetic" becoming shorthand for many regulatory systems involving DNA methylation, histone modification, nucleosome location, or noncoding RNA. This is to be encouraged, but the labeling of nongenetic systems as epigenetic by default has the potential to confuse (see the related video).

So what is epigenetics? An epigenetic system should be heritable, self-perpetuating, and reversible (Bonasio *et al.*, p. 612). Whether histone modifications (and many noncoding RNAs) are epigenetic is debated; it is likely that relatively few of these modifications or RNAs will be self-perpetuating and inherited. Looking beyond DNA-associated molecules, prions (infectious proteins) are clearly epigenetic, perpetuating themselves through altered folding states. These states can act as sensors of environmental stress and, through the phenotypic changes they promote, potentially drive evolution (Halfmann and Lindquist, p. 629).

Some metazoans undergo genome-wide reprogramming of DNA methylation and histone modifications during gametogenesis and embryogenesis (Feng *et al.*, p. 622), which may suppress the activity of potentially deleterious DNA sequences. Furthermore, the activity of various populations of small noncoding RNAs (Bourc'his and Voinnet, p. 617) probably act as tags for these deleterious sequences. These small RNAs may also be involved in assessing parental compatibility at fertilization. Similar RNAs are likely to be important determinants in paramutation, where homologous DNA sequences communicate in trans to establish heritable expression states (Chandler, p. 628). Reprogramming is also critical for developmental phenomena such as imprinting in both plants and mammals, as well as for cell differentiation, and is linked to the establishment of pluripotency in gametes and zygotes.

A News Focus story by Kaiser (p. 576) examines efforts to treat cancer patients with drugs that reverse the abnormal epigenetic patterns found in tumors, and a paper in *Science Translational Medicine** describes the use of epigenetic markers to predict which liver cancer patients will respond to an anticancer drug that blocks DNA methylation. Papers in *Science Signaling* discuss signaling pathways that alter epigenetic patterning, posttranscriptional regulation of signaling molecules by microRNAs, and transcriptional networks. Articles on *Science* Careers trace careers embracing a translational approach to epigenetics.

– GUY RIDDIHOUGH AND LAURA M. ZAHN

*J. B. Andersen *et al.*, *Sci. Transl. Med.* **2**, 54ra77 (2010).

Epigenetics

CONTENTS

See also News Focus story p. 576; Perspective p. 598; Report p. 680; Science Translational Medicine, Science Signaling, Science *Careers, Video, and* Science *Podcast at www.sciencemag.org/special/epigenetics/.*

CREDIT: C. BICKEL/*SCIENCE*

Science

Published by AAAS

What Is Epigenetics?

Guy Riddihough and Laura M. Zahn

Science **330** (6004), 611.
DOI: 10.1126/science.330.6004.611