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EDITORIAL

Homage to the Chromosome

Biological organisms, unlike complex inanimate systems, contain information that regulates their day-to-day activities and, more remarkably, lets them produce new organisms from single cells. That this information resides in the chromosomes was established over 75 years ago when it was shown that the cytologically visible chromosomes were distributed at cell division, meiosis, and fertilization in the same patterns as were the genes detected by breeding experiments. Missing from the classical account, however, was any understanding of the nature of the information carried by the chromosomes. That gap was, of course, filled by later spectacular advances in molecular genetics, which showed that a gene is a segment of DNA whose linear sequence of nucleotides specifies the linear sequence of amino acids in a protein. Given the triplet code that predicts amino acids from nucleotides, anyone can read the book of instructions contained in the chromosomes. But just as a book is more than a random assortment of words, chromosomes are more than simple repositories of gene sequences. They must contain regulatory information for turning genes on and off and they must control their own replication, repair, and packaging, as well as the complex movements they carry out during mitosis and meiosis.

Today's issue of *Science* contains five review Articles and four Reports that focus on some of these global properties of chromosomes that cannot be predicted from a knowledge of gene structure and coding alone. Central to any genetic system is the mechanism for moving the chromosomes from place to place. In higher organisms, this involves interaction between the mitotic spindle and a specific part of the chromosome, the centromere. Pluta *et al.* (page 1591) summarize recent information on the (noncoding) DNA sequences at the centromere as well as the special proteins that bind to this part of the chromosome. Although centromeres have often been thought of as passive structures, McKim and Hawley (page 1595) review new evidence that suggests that centromeres take an active role in establishing the spindle and in controlling the molecular "motors" that move the chromosomes to the poles.

Zakian (page 1601) reviews recent studies on telomeres, the specialized ends of chromosomes. Most chromosomes have a repeated 6–base pair sequence at their ends, which is replicated by an enzyme known as telomerase. Telomerase is remarkable in that it is a ribonucleoprotein whose RNA moiety contains the template for the 6-base repeat. Like centromeres, telomeres contain specific proteins not found elsewhere on the chromosome. In a related Report, Chong *et al.* (page 1663) describe a human telomere-binding protein.

The review by Kelley and Kuroda (page 1607) deals with dosage compensation—the raising or lowering of overall gene activity on the X chromosome to compensate for the different number of X's in females versus males. In the fly *Drosophila*, the single X of the male works harder, whereas in the nematode worm *Caenorhabditis* the two X's in the female slow down. In both cases, special proteins coat the affected X chromosomes. In mammals, dosage compensation is accomplished in still another way, by overall inactivation of one of the two X chromosomes in each cell of the female. In her review, Barlow (page 1610) describes a similar phenomenon—gametic imprinting in mammals. In this case, single genes are inactivated instead of a whole chromosome, but only when inherited from a specific parent, sometimes the father, sometimes the mother.

This issue does not contain a review on chromosome replication, but the interested reader can find here three Reports dealing with the important first step in DNA replication, the formation of an initiation complex between DNA and a set of specific proteins [Gavin *et al.* (page 1667), Ehrenhofer-Murray *et al.* (page 1671), and Gossen *et al.* (page 1674)].

What are the common themes of these papers? First, they emphasize the importance and diversity of chromosomal proteins that serve both structural and regulatory roles, most often by interacting with specific but noncoding DNA sequences. Second, they underscore the extraordinary power of genetics to identify the genes that encode these chromosomal proteins. Finally, they provide novel molecular insights into some of the oldest and most baffling problems of chromosome structure and behavior. Chromosome research is alive and well!

Joseph G. Gall

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