lated recruitment of chromatin-modifying activities, such recruitment does not directly affect transcription and indeed is analogous to (although mechanistically distinct from) the bacterial mechanism in which activators modify promoter structure. In eukaryotes, the basic chromatin structure renders core promoters inherently inactive in the absence of an activator, whereas bacterial promoters are generally accessible to the polymerase. In my view, chromatin fundamentally affects the logic of gene regulation in eukaryotes, but fundamentalism is in the belief of the beholder.

The only disappointing part of the book is the brief section on higher eukaryotes. Unlike the rest of this book, and unlike Ptashne's previous influential monograph *A Genetic Switch*, this section covers many different phenomena (all very interesting and important) in a rather sketchy fashion. This subject calls for another book, although it is probably premature to write one at the level to which we have become, and wish to remain, accustomed.

In the grand scheme, the principles of regulated recruitment through weak, adhesive interactions between proteins are applied to other examples of enzyme specificity and regulation (such as splicing, proteolysis and signal transduction), where diversity, precision, and evolutionary flexibility are paramount. Some may consider this section to be a statement of the obvious, namely that protein-protein interactions are important in biology. However, I agree with Ptashne and Gann that this concept is fundamental to understanding specificity in biology, and is, in historical context, a revolutionary idea. Until recently, enzyme specificity and protein function were thought of in terms of precise active sites with near-unique substrate recognition. Regulation in this view occurs by allostery, a mechanism in which a signalling molecule alters the enzyme in a structurally precise manner.

In this context, the emerging picture that a great deal of biological specificity is mediated by simple adhesive interactions involving limited and modular protein surfaces is neither obvious nor intuitive. But the concept has the undeniable virtue of explaining the apparently contrary notions of precision and flexibility. In addition to the exposition of this major theme, the final section of the book and the afterword are full of interesting insights.

In *Genes and Signals*, Ptashne and Gann have written a unique book that is driven by ideas and broad concepts, yet is based on solid information. It is accessible to undergraduates with some knowledge of biology, yet it is also valuable to experts in the field. I highly recommend it. ■

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Science in culture

Seeing stains

Mary Osborn's immunofluorescence images of cellular structures.

Martin Kemp

Stains (and those who have pioneered their use) are the unsung heroes of microscopy — well known to microbiologists, certainly, but not generally enjoying a high public profile. New instruments for seeing ever smaller details seem to present more eye-catching examples of scientific advance.

The story began with the progress from the primitive microscopes of the seventeenth century, in the hands of such pioneers of discriminating seeing as Anthony von Leeuwenhoek and Robert Hooke, and the gradual refining of optical resolution to its theoretical limits. Then came the non-optical revelations of electron microscopes, as developed by Vladimir Zworykhin and others, and the molecular marvels disclosed by the scanning tunnelling microscope devised by Gerd Binnig and Heinrich Rohrer. Yet without selective staining and other marking techniques we would not be able adequately to differentiate key components in the tiny structures.

One of the most elegant and widely applicable techniques, immunofluorescence, has, as its name suggests, ingeniously adopted techniques from immunology. Albert Coons used it to reveal pneumococci in infected mouse tissues in 1942. But its power in visualizing intracellular structures was only realized in 1974 when Elias Lazarides and Klaus Weber (then at Cold Spring Harbor Laboratory in New York state) used it to reveal microfilament bundles in cells. The basic technique works as follows.

Given a protein (antigen) that is of interest, an antibody is made. Once the cell has been made permeable, the antibody invades and binds itself to the antigen. The unbound antibody is then washed away. A second antibody carrying a fluorescent marker (such as green fluorescein or red rhodamine) recognises the first, and the process of washing away the excess is repeated. It is rather like doubling the process in conventional photographic printing with 'hypo', in which the excess developer must be fully washed out if the image is to become clearly defined. The final step of immunofluorescence is to view the marked protein using a microscope with a light source and filter set.

A pioneer of the technique, Mary Osborn of the Max Planck Institute of Biophysical Chemistry in Göttingen, Germany, is the European winner of the 2002 L'Oréal/UNESCO Prize for Women in Science, awarded for international scientific excellence. She has also been in the vanguard of promoting the status of women scientists. Her work demonstrates that the results of immunofluorescence are both scientifically potent and visually beguiling to a high degree. Osborn, working at times together with Weber, has used immunofluorescence to

Colour coding: an immunofluorescence micrograph of epithelial and fibroblastic cells.

disclose microtubules and intermediate filaments as functional components in cells.

The story of the microtubules vividly shows how optical and electron microscopy need to work hand in hand, and how the greater magnification of the latter does not necessarily deliver fully coherent results when visualizing the structural continuities of forms that extend across the cell. In the late 1970s there was an acrimonious debate about the length and number of microtubules. Weber and Osborn were even accused of "painting white lines" on their images. Only when the same cell was visualized by the Göttingen group, both with immunofluorescence staining for tubulin and as a whole mount in electron microscopy, did the evidence of extended microtubules speak unequivocally for itself.

The intermediate filaments have proved to be particularly useful in routine pathology and cytology, acting as highly effective markers of cell type. As Osborn explains, "human tumours retain the intermediate filament typical of their origin. Intermediate-filament antibodies can be of particular use in certain differential diagnoses when the pathologist or cytologist is unsure of the diagnosis by conventional staining."

The micrograph shown here was made by Osborn in 1987, and shows a mixture of epithelial and fibroblastic cells growing in culture stained with antibodies against two intermediate filament proteins, keratin and vimentin. The keratin antibody decorates the intermediate filaments present in the epithelial MCF7 cell line (in green) whereas the vimentin antibody decorates the filaments in the fibroblastic HS27 cell line (in red), thus distinguishing the two cell types.

Alongside the technical achievements lies a sheer love of looking at the perpetually varied topography of stained cells. As Osborn says, "I can still stare down the microscope for hours. Not only because they are beautiful but also because every cell shows subtle differences in the arrangement and distribution of the three filament systems." ■

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