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The past as prelude

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This year the scientific community commemorates the 50th anniversary of the determination of the structure of DNA. Just half a century since that pivotal report, we are anticipating the completion of one of the grandest enterprises undertaken in the sciences—the sequencing of the human genome. The availability of this resource marks the completion of a unique period in scientific investigation and the beginning of a new era in genetic research. We thought it was time for a celebration—and a time for reflection.

Although the demarcation of an era of research is in some sense arbitrary, the last ten years have represented a period of particularly intensified molecular genetic research. *Nature Genetics*, launched in April 1992, has provided a forum for many of the important advances. To consider the salient developments that occurred during this decade of research, we asked researchers to look back over the past ten years and provide an account of progress in 11 different areas of genetics. To satisfy our curiosity, we asked them to speculate about the future as well. The summation, which we are delighted to present in this special supplement to *Nature Genetics*, is a ten-year retrospective

(1992–2002) that we hope will stand as a definitive record of much of the field during our first decade of publication. Each article has been peer reviewed to ensure accuracy and reasonably balanced coverage. Nonetheless, the formidable task of reviewing an entire field in the space allotted inevitably necessitates some omissions. Thus, the reviews, to some extent, reflect the authors' personal views of what mattered most.

In an attempt to explore how the focus of research in genetics has shifted, we categorized the content of *Nature Genetics* according to these same 11 areas of research for 3 different years (see figure). Obviously the topics overlap and therefore require artificial divisions. And, needless to say, the content of *Nature Genetics* cannot be presumed to reflect the field of genetics in its entirety. Nonetheless, some interesting trends emerge from the analysis.

Since at least 1997, genomics papers have appeared only infrequently in *Nature Genetics*. This is perhaps indicative of the field's success, as the important early technical advances, some of which appeared in the inaugural issue of *Nature Genetics*, quickly raised the expected level of analysis to that of a whole chromosome, if not the whole genome. Genomic studies advanced at a spectacular rate and provided the basis for many of the advances in genetics over the past ten years, as outlined in the review by Craig Venter, Samuel Levy, Tim Stockwell, Karin Remington and Aaron Halpern on page 219.

Trends in the subject content of *Nature Genetics*. 1992, $n = 155$; 1997, $n = 257$; 2002, $n = 201$.

A case in point is the field of human genetics, the continued success of which prompted the initiation and intensified efforts of the majority of genome-sequencing projects. As David Botstein and Neil Risch write on page 228, the identification of genes underlying mendelian disorders was due in large part to the success of the positional cloning approach. Translating this success to complex traits has not proved straightforward, but Botstein and Risch propose a possible approach. It is interesting to note that human genetics papers have come to account for a decreasing proportion of papers published in *Nature Genetics* over the years. This reflects the field's transition from the success of linkage and cloning of mendelian genes (at least the easiest ones) to the challenge of identifying the genes underlying complex traits.

The same trend is not true, however, for one of the most common heritable human diseases—cancer—the importance of which is reflected in the increasing proportion of our pages that cancer research occupies. As illustrated in the review by Allan Balmain, Joe Gray and Bruce Ponder on page 238, this field, perhaps more so than any other in the last ten years, has seen the greatest success in integrating different research fields. One such area of overlap with cancer research is the study of epigenetics, a field that is reviewed by Rudolf Jaenisch and Adrian Bird on page 245. Papers published in *Nature Genetics* ten and even five years ago predominantly described epigenetic phenomena, whereas increasingly we are seeing elucidation of the mechanisms that mediate these processes.

Genomic data have provided a plethora of tools for investigating evolutionary questions. As discussed in a review of molecular evolution by Ken Wolfe and Wen-Hsiung Li on page 255 and one of population genetics by Luca Cavalli-Sforza and Marcus Feldman on page 266, genomic data have afforded far greater power of resolution for the reconstruction of evolutionary histories. Ten years ago, both population and evolutionary biologists largely drew conclusions from the analysis of single genes and gene families, whereas these days we are accustomed to seeing investigations performed at a genome-wide level.

The last ten years have seen a continued emphasis on the use of tractable biological models to understand gene function. This is reflected in the fact that since 1997, almost one-fifth of the publications in *Nature Genetics* have reported studies in model organisms. As discussed by Andras Nagy, Norbert Perrimon, Suzanne Sandmeyer and Ronald Plasterk on page 276, technical advances have given geneticists the ability to exploit these models with increasing power and precision. Studies of model organisms have also revolutionized the field of development. The increase in the representation of this field in our pages reflects the growing importance of development to understanding the basis of human disease, as outlined by Kathryn Anderson and Philip Ingham on page 285.

Plant genetics papers appear less frequently than we would like in *Nature Genetics*, but we felt that it would be a serious omission not to include the field in which so many of the exciting developments in genetic and epigenetic research first occurred. The review of this field provided by Robert Pruitt, John Bowman and Ueli Grossniklaus on page 294 highlights the fact that studies of plant genetics have provided fundamental insights into genome regulation and the study of how the external environment is interpreted at the cellular level.

The final two reviews cover fields that are clearly maturing and look set to appear more frequently in the journal. The field of bioinformatics barely existed ten years ago. Today, bioinformatics departments are developing across campuses as the field co-evolves with the proliferation of biological data. Minoru Kanehisa and Peer Bork lead us through this evolution on page 305. Scott Patterson and Rudolf Aebersold argue on page 311 that 'global' approaches to biology began with proteomics. And it seems fitting to end this series with a review of proteomics—a field that is now making technological advances equivalent to those that drove the advancement of genomics during the 1990's.

And what of the future, you may ask. Well, we don't want to spoil the surprise, but a common theme emerges from all the authors' discussions of the future—the integration of different areas of research. The artificial barriers that we have imposed will become less meaningful, as already evidenced by the importance of epigenetics to cancer research, population genetics-based approaches to the study of human disease, our growing understanding of the links between development and cancer and the role that genomics and bioinformatics will have in facilitating and driving all twenty-first century genetic research.

A word of thanks goes to the sponsor, GlaxoSmithKline, whose generous support was essential in producing this supplement, the contents of which will be freely available online. Finally, we wish to express our gratitude—to the authors of this exciting series of reviews, to the authors of the roughly 2,000 papers we have published since April 1992 and to the referees who have reviewed many more.