

EDITORIAL: NAR SURVEYS THE PAST, PRESENT AND FUTURE OF RESTRICTION ENDONUCLEASES

In this issue, *Nucleic Acids Research* presents five Survey and Summary articles that describe the historical development of studies on restriction endonucleases and summarize much of our current understanding of this diverse and complex group of enzymes. The first of these articles, entitled ‘Highlights of the DNA cutters: a short history of the restriction enzymes’ (1), describes seminal studies on bacteriophage host restriction, details subsequent work on type I and type III enzymes that established the restriction-modification (RM) paradigm and summarizes other landmark events that led to restriction enzymes becoming a main driving force in the development of modern biotechnology and molecular medicine. Other Survey and Summary articles in this issue describe three of the major types of RM systems as they are understood today (2–4). The different types of RM systems—of which there are currently four—vary in their cofactor dependence, in the spatial relationship of DNA binding and cleavage sites and in the way in which endonuclease and modification activities are physically and mechanistically coupled to one another. The last of the Survey and Summary articles in this issue discusses RM systems in the broader context of toxin–antitoxin genetic systems, which exist in great variety throughout the microbial world (5).

With this issue, NAR enters its 42nd year of publication. The journal was founded during the period when restriction endonucleases began to be widely adopted for molecular biology research. An article in one of our first issues presented an early restriction map of the SV40 virus, which was an essential precursor to the sequencing of the viral genome (6). Another article from journal’s early years described a widely adopted method for restriction enzyme purification (7). In subsequent years, we published semiannual updates describing the popular REBASE database. Indeed, >10% of the articles published since the journal’s inception are indexed as dealing with RM systems in a significant fashion. The current collection of Survey and Summary articles thus builds on our long tradition of coverage of this field.

It is important to recognize that the structural protein folds, catalytic motifs and catalytic mechanisms that are found in restriction endonucleases and methyltransferases are also observed in a wide variety of other enzymes, including those responsible for the transfer of mobile DNA elements, the repair of DNA lesions and the maintenance of genome integrity. Several decades of detailed studies of restriction endonucleases (and of their corresponding modification enzymes) have motivated and informed investigations in these other areas of biology. At the same time, RM systems have provided the reagents required for the development of rapid and inexpensive genome sequencing technologies, powerful strategies for genome engineering, new methods for therapeutic gene modification and correction and novel protein- and cell-based medicines.

We hope that, as well as being interesting and informative, the current articles will remind our readers of the importance of basic research for the development of future therapies and new applications in biotechnology. In retrospect, the contribution of restriction endonucleases to modern molecular biology and biomedicine seems obvious and inevitable. However, it should be remembered that the original studies of phage restriction were driven purely by intellectual curiosity, and were supported by research infrastructures that valued discovery for discovery’s sake. The critical importance of such studies for creating new technologies for medicine and technology, as illustrated by >60 years of restriction endonuclease research, can be used as an example for all who believe in the importance of research and development for future generations.

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