
Preface

Virtually all aspects of cellular function, such as replication of DNA, separation of chromosomes during cell division, DNA repair, or gene expression, depend on the interaction of proteins with DNA. The nature of DNA-binding proteins is wide and ranges from structural proteins making up the nucleosome, enzymes modulating chromatin structure to enable, facilitate, or repress gene expression, transcription factors, and various cofactors. The biological significance of these associations in the context of gene expression, development, cell differentiation, and disease has immensely been enhanced in the past 20 years by the advent of a technique referred to as *chromatin immunoprecipitation*, or ChIP. The purpose of the ChIP assay is to identify genomic sequence(s) associated with a protein of interest, for example, your favorite transcription factor, in the genome. ChIP, then, has become the technique of choice to determine the genomic enrichment profiles of transcription factors, post-translationally modified histones, histone variants, or chromatin-modifying enzymes. In the ChIP assay, the protein of interest is immunoprecipitated from a chromatin preparation using specific antibodies. After stringent washes, the DNA is released and the sequences bound by the immunoprecipitated protein are identified. Sequence identification methods have rapidly evolved from dot- or slot-blots in the early days to polymerase chain reaction. Subsequently, the combination of ChIP with DNA microarray or high-throughput sequencing technologies has enabled the profiling of protein occupancy on a genome-wide scale. It has also promoted the appearance of new algorithms for mapping protein binding throughout the genome.

ChIP, therefore, is arguably a power tool. Nevertheless, it has for a long time remained a cumbersome procedure taking several days and requiring very large numbers (several millions) of cells. These limitations have sparked modifications of the assay and variations in DNA detection approaches to shorten the procedure, simplify sample handling, and make ChIP amenable to small cell numbers. As a result, the ChIP assay has become increasingly popular in several areas of molecular and cell biology. To illustrate this point, a PubMed search with the keyword “chromatin immunoprecipitation” brings up four publications in 1988 and a total of over 6,400 to date, including 1,578 publications in 2008 alone (see **Fig. 1**).

Release of this volume on *Chromatin Immunoprecipitation Assays* by Humana Press is, therefore, timely. The volume is devoted to recent developments in ChIP and related protocols, which have proven reliable in the literature and which I believe will remain current and of great interest to researchers for many years to come. The chapters describe protocols on subjects such as characterization of ChIP antibodies, ChIP methods for small cell numbers, fast ChIP protocols, and assays adapted to various species and cell types. Several strategies for the analysis of genome-wide data sets are also included. The book also extends beyond ChIP assays per se to include protocols on immunoprecipitation-based DNA methylation analyses, determination

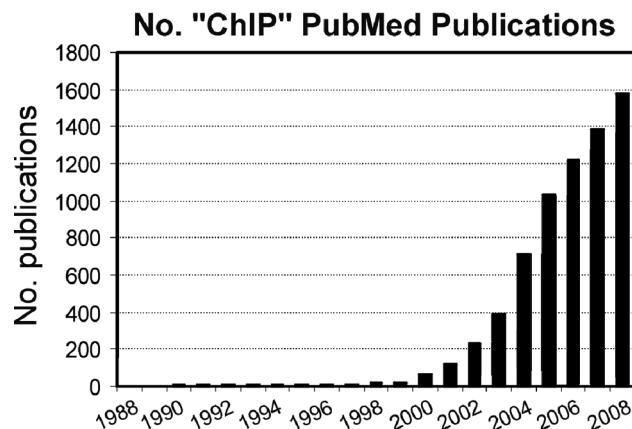


Fig. 1. Yearly number of PubMed publications responding to the search criterion "chromatin immunoprecipitation".

of spatial chromatin organization of large genomic regions, as well as RNA immunoprecipitation.

These protocols have been carefully detailed by researchers deeply involved in their development or improvement. All of the contributors and their teams deserve many thanks for their time, effort, and generosity. It has been fun to work on this project, and I wish to thank John Walker for his invitation to put together this volume, and the entire production team at Humana Press.

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Methods and Protocols

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