Number 12 March 20, 1978

Citation Classics

Huang R C & Bonner J. Histone, a suppressor of chromosomal RNA synthesis. *Proc. Nat. Acad. Sci. US* **48**:1216-22, 1962.

Chromatin isolated from pea embryos possesses the ability to carry out the DNA-dependent synthesis of RNA from the four riboside triphosphates. The present paper concerns the roles in such synthesis of the several components of chromatin. [The *SCI*® indicates that this paper was cited 679 times in the period 1962-1976.]

Professor Ru-Chih C Huang
Department of Biology
Johns Hopkins University
Baltimore. Maryland 21218

April 25, 1977

"There is an old saying: 'When you know nothing about Zen, a mountain is a mountain; when you know something about Zen, a mountain is no more a mountain; when you know more things about Zen, a mountain again is a mountain ' If one substitutes the word gene for Zen, the saying tells exactly of our knowledge about chromatin.

"The work selected as one of the most cited papers was done when little was known about the molecular approach to gene expression. The term chromatin as an interphase state of chromosome was beginning to be accepted as a biochemical working usage. The isolation and purification of chromatin was still approached with more art than science, until the pea embryo was chosen. From then on the procedure became more standardized and a 'pea popper' was installed in the basement of Kerckhoff Laboratory at Caltech to handle the mass quantity of preparation. The well defined genetic system of peas was actually not fully explored but the precision in the differentiated and synchronous state of germinating pea embryos helped to estabish the biochemical procedures.

"The desire to study the process of RNA synthesis was novel in the early 1960s. While chromatin as the genetic machinery can now be isolated intact, Michael Chamberlin, then a graduate student of Paul Berg, was able to obtain purified enzymes which would catalyze the polymerization reaction of RNA using DNA as the template.[1] Recognizing the significance of the combination, I went to Stanford, learned the procedure and upon returning to Caltech, applied it to chromatin studies. The results were not unexpected, namely that chromatin is rather inefficient in the support of DNA-dependent RNA synthesis, whether in a native or reconstituted form with either prokaryotic or eukaryotic RNA polymers. Because of the repressive function of the histones on RNA template activity, the named suppressor was used, which served its illustrative purpose although sometimes confused with the connotation of the prokaryotic system.

"The science of chromatin has gone from nothing → something → more things. The speculation of Stedman and Stedman in 1950[2] prompted the work cited, which apparently has generated a plethora of interest and studies on chromatin. Many controversial issues arose as further details were attended to. These have included the function of various chromosomal components, the fidelity of the RNA polymerases, and tissue specificity of the chromatins. However, the basic scheme that histone, being the major class of protein in the chromosomes, functions by blocking the transcription, remains unchallenged. It was a bold assumption and the experiments in 1962 provided important documentation.

"Today, not only the structure of chromatin has been revealed in microscopic details but also the function has been examined at a unique gene level. The devotion of the 1977 Cold Spring Harbor Symposia to this topic attests this progress.

"It may be added that during the midst of excitement of the work in 1962, I gave birth to a daughter, Suzanne. After seven days in the maternity ward at Pasadena, I was back at the bench and have stayed there ever since, even now as a full professor at Johns Hopkins. James Bonner too has continued to do work personally as well as inspiring others with brilliant ideas and thoughts."

REFERENCES

1. **Chamberlin M & Berg P.** Deoxyribonucleic acid-directed synthesis of ribonucleic acid by an enzyme from escherichia coli. *Proc. Nat. Acad. Sci. US* **48**:81, 1962.
2. **Stedman E & Stedman E.** Cell specificity of histones. *Nature* **166**:780-1, 1950.