CC/NUMBER 1
JANUARY 2, 1984

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Taylor J H, Woods P S & Hughes W L. The organization and duplication of chromosomes as revealed by autoradiographic studies using tritium-labeled thymidine. *Proc. Nat. Acad. Sci. US* **43**:122-8, 1957. [Dept. Botany, Columbia Univ., New York, and Biology and Medical Depts., Brookhaven Natl. Lab., Upton, NY]

Autoradiographs of chromosomes prepared after cells of Vicia (broad bean) had incorporated ^{3}H-thymidine into DNA in the cell cycle before division showed that both daughter chromosomes (chromatids) were equally labeled. After a second cell cycle without ^{3}H-thymidine, the labeled DNA in each chromosome was segregated so that one chromatid was fully labeled and the other was unlabeled Exceptions were produced by occasional exchanges of labeled and unlabeled segments between two daughter chromatids (sister chromatid exchanges) [The *SCI*® indicates that this paper has been cited in at least 680 publications since 1957, including 7, 29, 41, 42, 33, 36, 43, and 36 in 1957-1964, respectively, based on 1955-1964 *SCI* cumulation]

J. Herbert Taylor
Department of Biological Science
and
Institute of Molecular Biophysics
Florida State University
Tallahassee, FL 32306

September 15, 1983

"Soon after Watson and Crick published a proposed structure for DNA and a scheme for its replication,[1,2] Friedkin *et al.* synthesized ^{14}C-thymidine and showed that it was incorporated exclusively into DNA.[3] When preliminary attempts to follow the distribution of new DNA in chromosomes labeled with ^{14}C-thymidine failed to give a decisive answer, I realized that autoradiographic resolution with tritium, a low energy beta emitter, would allow analysis of individual chromatids. With enthusiasm but little knowledge of how to label thymidine, I joined Philip Woods at the Brookhaven National Laboratory for a summer project in 1956.

"A few days after I arrived at Brookhaven, we learned that Walter (Pete) Hughes was preparing ^{3}H-thymidine to study its lethal effects on cancer cells. We sought his assistance and he agreed to share the 'H-thymidine for the chromosome studies. We planned to grow *Vicia* roots in a solution of ^{3}H-thymidine for eight hours and then transfer them to a solution with colchicine and without ^{3}H-thymidine. Cells fixed within a few hours should show cells at the first division after their DNA was labeled during replication. Since colchicine blocks anaphase and cell division, but not chromosome reproduction in plants, the labeled cells which appeared after about 36 hours with 24 chromosomes would be at the second division after labeling of their DNA.

"The first half of our summer's work yielded no information, because the thymidine was not hot enough. Hughes soon had a second sample ready and we repeated the experiments, made the autoradiographs, and waited the two weeks necessary for the exposure. When the slides were developed, the dark grains were positioned over the red stained chromosome in many of the spread cells. In cells fixed a few hours after transfer to colchicine, both chromatids were fully labeled from end to end. However, some cells fixed after 36 hours had 24 chromosomes with one labeled chromatid lying beside an unlabeled chromatid in each metaphase chromosome. The segregation was occurring after the second replication and the only complication was an occasional exchange of segments between sister chromatids. Nevertheless, the result was convincing and many of our colleagues and visitors to the lab peered through our microscope during the next few days to see the first indication that the Watson-Crick scheme for DNA replication operated at the chromosome level. Reflection, however, revealed that we knew too little about chromosome structure to be sure that DNA chains were segregating.

"Our studies have been cited many times because they were the first significant studies with tritium-labeled molecules, which stimulated work on the structural organization of chromosomes, the time of replication of different parts of chromosomes, and the kinetics of the cell cycle. Sister chromatid exchanges which we discovered in these experiments were analyzed further to reveal the structure of chromosomes and these exchanges later proved to be good indicators for the effects of mutagens and carcinogens. A conference on this topic, the International Symposium on Sister Chromatid Exchange, to celebrate the twenty-fifth anniversary of the discovery and research on sister chromatid exchange as an indicator for mutagenic and carcinogenic agents, was to be held at Brookhaven National Laboratory, December 4-8, 1983. For a review of this field, see *Molecular Genetics."*[4]

1. **Watson J D & Crick F H C.** Molecular structure of nucleic acids. A structure for deoxyribose nucleic acid. *Nature* **171**:737-8. 1953. (Cited explicitly over 1,055 times since 1955.)
2. .....Genetic implications of the structure of deoxyribonucleic acid. *Nature* ***171***:964 -7. 1953. (Cited 535 times since 1955.)
3. **Friedkin M, Tilson D & Roberts D.** Studies of deoxyribonucleic acid biosynthesis in embryonic tissues with thymidine-C^{14}. J. *Biol them* **220**:627-37, 1956. (Cited 165 times since I956.)
4. **Taylor J H,** ed. *Molecular genetics.* New York: Academic Press. 1963-1979. Parts I-III.