This Week's Citation Classic


"H-labeled colchicine was used to identify the colchicine-binding receptor in cells. Colchicine-binding activity did not correlate strictly with mitotic activity but did correlate with sources abundant in microtubules. We suggest that the binding sites are the subunit proteins of microtubules. [The SCI® indicates that this paper has been cited over 595 times since 1967.]

Gary G. Borisy
Laboratory of Molecular Biology
University of Wisconsin
Madison, WI 53706

April 28, 1981

"Rosy said, 'It was all an artifact' He warned that I would never get my degree if I continued to study 'that colchicine-binding (expletive deleted).' "Rosy" was Joel L. Rosenbaum, now professor of biology at Yale University. At that time (1964), we were both doing research at the University of Chicago. Rosy was a postdoctoral fellow working on ciliary regeneration with Frank M. Child in the department of zoology and I was a green, second-year graduate student working with Edwin W. Taylor in biophysics.

On lazy summer days we would sit around Botany pond under a spreading ginkgo tree, shooting the bull and going over fresh results. It was on one of those days that I announced that in a survey of tissue types, I got my highest level of colchicine-binding in extracts of brain tissue.

"This was a most perplexing result. Colchicine was a drug known to inhibit mitosis in plant and animal cells by disrupting the formation of the mitotic spindle. 'A few years earlier, Taylor' had begun to study its mechanism of action and inferred that it exerted its effects by binding to a specific target site in dividing cells. Using "H-labeled colchicine, my project was to identify the target site at the molecular level.

"We first developed an in vitro colchicine-binding assay to quantitate the amount of the target molecule. It was quickly demonstrated that cultures of dividing carcinoma cells contained a lot of the colchicine-binding receptor. But there was no reason to expect the receptor to be present in the neuronal cells of brain tissue.

"To support the hypothesis that the colchicine-binding receptor was important in cell division, we attempted to correlate colchicine-binding activity with mitotic index. What a surprise, then, to find in a survey of tissue types that brain tissue, having the lowest mitotic index, had the highest specific activity of binding! How could anyone believe that colchicine bound to a component of the mitotic spindle if it also bound so well to neurons?

"This was one of those happy instances where investigation of a paradox led to a deeper understanding of the phenomenon in question. As further work showed, the reason brain tissue was so high in colchicine-binding activity was because of its high content of microtubules, a major structural component of neurons. Microtubules also form the framework of the mitotic spindle. The colchicine-binding receptor turned out to be tubulin, the subunit of microtubules. Colchicine inhibited mitosis by binding to tubulin, preventing its assembly into microtubules. Thus, Rosy's 'colchicine artifact' led to an understanding of the molecular mechanism of action of the drug, to the identification of the major component of the mitotic spindle, and to the discovery of the protein that microtubules are made of."