

Baserga R. Relationship of cell cycle to tumor growth and control of cell division; a review. *Cancer Res.* **25**:581-95, 1965.

The review article brings out the advantages of studying tumor growth in terms of cell cycle kinetics and opens the possibility of a new field of endeavor in biochemistry and cell proliferation. [The SCI® indicates that this paper was cited 236 times in the period 1965-1977.]

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"Since this was a review article, there was no startling idea that suddenly struck me, and the only obstacles I had to overcome were the comments of the reviewers. The idea of writing a review relating our recently acquired knowledge of the cell cycle to tumor growth came to me as I was moving from Northwestern University in Chicago to Temple University in Philadelphia. It seemed to me the right moment to make the point on the direction that my research was taking.

"I had started out doing research 13 years before, in Chicago, and at that time I wanted to find out the mechanisms in the metastatic spread of tumors. In a few years I came to the conclusion that there was very little mystery about the metastatic spread of tumors, and that the problem with metastases was essentially a problem of cell proliferation. That is, that tumor cells grow indefinitely while normal cells do not. Thus I slowly drifted from a study of metastasis into a study of the mechanisms that control cell proliferation.

"This was about the time when the studies on the cell cycle were receiving strong impulses from the discovery of the wonderful uses that one could make of (³H)-thymidine.

For a number of years, though, the cell cycle had been somehow the personal property of radiobiologists and I happened to stumble into it through my association with the Argonne National Laboratory. Cancer researchers were little aware of the cell cycle and its possible implications for tumor growth. In fact, a number of leading investigators in radiobiology simply refused to investigate the cell cycle of tumors on the ground that it was too difficult and complicated.

"Mort Mendelsohn and myself were probably the first to have the courage to tackle tumor growth in terms of cell cycle, and we found that tumors were amenable to a kinetic analysis. About this time, though, I felt that a kinetic analysis, while descriptive, really did not explain the basic mechanisms that control cell proliferation, and I therefore conceived the general idea that the cell cycle should be put in biochemical terms, rather than in purely kinetic terms. In writing the review, indicated above, I had exactly these two things in mind: 1) to show how the growth of tumors could be understood in terms of cell cycle kinetics, and 2) to point out that in the last analysis our understanding of life processes depends on our understanding of the underlying biochemistry.

"This review, therefore, was an attempt to open new fields of scientific endeavor. Since then our knowledge of the cell cycle has been extensively applied to basic and clinical studies of cancer drugs, and a whole field has developed on the biochemistry of cell proliferation that has been the object of a number of symposia, many reviews and even books. Personally I remember that when I was writing that review I felt elated about how much more we knew about cell division in 1965, than we did in 1950 when I started to be interested in biomedical research. Now in rereading that review I again feel how much more we know about cell division than we knew at that time, which is, I guess, another way of saying how little we know at any point in time, and how much more there is to know in the future."