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This Week's Citation Classic

Bollum F J & Potter V R. Nucleic acid metabolism in regenerating rat liver. 6. Soluble enzymes which convert thymidine to thymidine phosphates and DNA. *Cancer Research* **19**: 561-5, 1959.

DNA polymerase and thymidine kinase are described as soluble enzyme systems and correlated with DNA replication *in vivo*. [The *SCI*® indicated that this paper has been cited 291 times since 1961.]

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"The work Van Potter and I did on DNA synthesis in regenerating rat liver contained findings useful to scientists interested in DNA replication in eukaryotic cells. The primary focus of this paper was measurement of the actual increase in DNA polymerase in regenerating rat liver. Regenerating liver had already been well studied for *in vivo* incorporation of DNA precursors, so it was of interest to compare our new findings with the earlier work. The final result was a mixture of new findings correlated with old findings; what editors call a 'timely' piece of research. I also sense that many in vestigators had been unsuccessful in demonstrating enzymatic DNA synthesis in eukaryotic systems at that time and our work (and that from E. S. Cannellakis' laboratory at Yale) opened the door on this subject.

"In proper perspective it should be mentioned that the work was done in Van Potter's laboratory, University of Wisconsin, where I was a (rather fresh) USPHS postdoctoral fellow. The clever experiment in the paper was his idea. The problem was to correlate *in vivo* results with *in vitro* results without embarking on a tedious statistical study. Simple enough to Van Potter! Just inject ^{14}C-Orotic acid two hours before sacrificing animals for enzyme assay. Then isolate ^{14}C-DNA from nuclei to estimate *in vivo* rate of synthesis and measure ^{3}H-deoxynucleotide incorporation with the cytoplasmic extract and exogenous DNA template. The same rat was used for *in vivo* and *in vitro* measurements of capacity for DNA replication. The relation was remarkably good during the induction phase and is called the 'Correlation Curve' in the paper. The correlation was not perfect, however, and the deviations still require explanation. I think Potter's clever experiment and our unorthodox use of cytoplasmic extracts in these may have excaped the comprehension of many readers.

"I clearly remember the day Van Potter called me into his office, drew his conception of the 'Correlation Curve' out of thin air and chalk on a very small blackboard he kept there and said, 'If what we already know is true, this will be true. If we make this demonstration, and publish it, I think anyone will understand that our findings correlating DNA enzymology and DNA replication are correct.' We made the demonstration, I think his perception was accurate, and I learned more than DNA enzymology from this experiment."