

This Week's Citation Classic®

Vogt P K. Avian tumor viruses. *Advan. Virus Res.* 11:293-385, 1965.

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This paper was the first comprehensive review of the then-emerging field of avian RNA tumor viruses. Evidence available at that time indicated broad oncogenic activity of these viruses; several were shown to transform cells in culture. These were found to be defective for replication but not for oncogenicity. Avian tumor viruses could be classified according to immunological criteria and to host range. All showed an intriguing sensitivity to inhibitors of DNA synthesis and DNA transcription. [The *SCI*® indicates that this paper has been cited in over 175 publications.]

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The useful life of a review paper is often short. Less than a year may elapse before the information, so laboriously and assiduously compiled, becomes obsolete. It is, therefore, surprising that a review on avian tumor viruses written in 1965 should have become a *Citation Classic*. An explanation for this unexpected impact and longevity should probably be sought in the general state of the field of retroviruses (then known as RNA tumor viruses) in the early 1960s. It was a time of excitement as well as challenge. Some fundamental but also some puzzling discoveries had been made that presaged the future developments of the field. A critical, reflective reader could deduce from a review of the existing facts an outline of important questions on viruses and cancer that had become answerable. Several observations had converged to suggest that RNA tumor viruses are unique and interesting pathogens.

The spark that set the field in motion was H. Rubin and H.M. Temin's development in 1958 of a quantitative focus assay for the oncogenic transformation by Rous sarcoma virus.¹

I joined Rubin's laboratory at the University of California at Berkeley in 1959 and after three formative years accepted a faculty position at the University of Colorado at Denver. My interests at that time focused on the cell biology of avian retroviruses. A basic outline of virus replication, virion composition and structure, and strain differences and classification emerged from the work of several laboratories. The discovery of a helper virus was followed by that of defectiveness of Rous sarcoma virus. The properties of the defective virus, incapable of producing infectious progeny but capable of transforming infected cells, suggested for the first time that at least some replicative viral genes were not essential for transformation and that there perhaps existed specific oncogenic information in the viral genome. Defectiveness foreshadowed the discovery of oncogenes that was to occur several years later.²⁻⁵ Also on the horizon appeared the first clues for reverse transcription and of the provirus hypothesis. An unexpected and puzzling sensitivity of Rous sarcoma virus infection to inhibitors of DNA synthesis and DNA transcription had been found. But there was still much uncertainty about the significance of these observations and about the conclusions that could be drawn from them. These doubts were dispelled only with the discovery of reverse transcriptase.

In the early 1960s the retrovirus field was young, promising, and sometimes perplexing. Over the past two decades it has grown and matured. A recent volume devoted to this viral group encompasses almost 1,400 pages.⁶ It was quickly followed by an equally ponderous and extensive supplement. Initially a somewhat esoteric subject, the retroviruses are now part of mainstream biological research. With reverse transcription and oncogenes they have greatly influenced the course of molecular biology and of cancer research. With the AIDS virus they have become household words.

1. Temin H M & Rubin H. Characteristics of an assay for Rous sarcoma virus and Rous sarcoma cells in tissue culture. *Virology* 6:669-88, 1958. (Cited 515 times.)
2. Hanafusa H, Hanafusa T & Rubin H. The defectiveness of Rous sarcoma virus. *Proc. Nat. Acad. Sci. USA* 49:572-80, 1963. (Cited 285 times.)
3. Toyoshima K & Vogt P K. Temperature sensitive mutants of an avian sarcoma virus. *Virology* 39:930-1, 1969. (Cited 140 times.)
4. Duesberg P H & Vogt P K. Differences between the ribonucleic acids of transforming and nontransforming avian tumor viruses. *Proc. Nat. Acad. Sci. USA* 67:1673-80, 1970. (Cited 170 times.)
5. Stehelin D, Varmus H E, Bishop J M & Vogt P K. DNA related to the transforming gene of avian sarcoma viruses is present in normal avian DNA. *Nature* 260:170-3, 1976. (Cited 455 times.)
6. Weiss R, Teich N, Varmus H & Coffin J, eds. *RNA tumor viruses*. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, 1982. 1,396 p.