

Peyton Rous: father of the tumor virus

In 1910, Peyton Rous identified a transmissible avian tumor virus, a discovery that began the journey from tumor virus biology to tumor biology itself.

Peyton Rous loved wild flowers. A self-proclaimed disciple of Carl Linnaeus, he published a short-lived column in the *Baltimore Sun* at the age of eighteen called “Wild Flowers of the Month.” With that column, however, his career as a nature writer began and ended. But botany’s loss was cancer biology’s gain.

Lessons from the Plymouth Rock hen

In 1909, fresh out of medical school and with only 2 years of research under his belt, Rous joined the staff of the Rockefeller Institute and was promptly put in charge of the laboratory for cancer research. Soon thereafter, he was given a barred Plymouth Rock hen that had a large tumor growing on its breast. Recent descriptions of unusual transmissible growths in various animals had sparked his attention, so Rous attempted to transfer his chicken’s tumor. When he injected small pieces of the growth into hens from the same bloodline, but not chickens of other varieties or birds of other species, they too developed tumors (1). Although avian cancers were by no means a new discovery at that time—fibromas, myomas, carcinomas, and sarcomas had all been described in birds—they had never been successfully transmitted from one bird to another.

Close examination of Rous’ tumor revealed a spindle-cell sarcoma that looked like a classical neoplasm except that, unlike most neoplasms described at that time, it was transmissible. Rous later found that adoptive tumor formation did not require transfer of intact tumor cells, and could be achieved using cell-free filtrates that passed through a Berkefeld filter (to exclude bacteria) or supernatants from emulsified tumor cells (2). He thus concluded that the tumors were caused

by a filterable agent, as viruses were then known. He published these findings in a pair of seminal articles in the *Journal of Experimental Medicine* in 1910 and 1911 (1, 2).

Rous, however, did not report the first tumor virus. A Danish duo, Ellerman and Bang, beat him to the punch in 1908 by demonstrating that a filterable extract could transmit leukemia among chickens (3). However, the scientific community largely ignored this finding, as leukemia was not recognized as a neoplastic disease until after 1930. Rous’ work, although not ignored, was met with some indifference. The prevailing attitude was that tumors that could only grow in chickens must bear little resemblance to human cancers (thought to be noninfectious in origin) and were unlikely to provide any useful information. Rous was eventually vindicated and his discovery earned him a Nobel Prize in 1966 (he noted the work of Ellerman and Bang in his Nobel lecture) (4).

Cancer biology blossoms

Rous went on to confirm that other avian tumors could also be transmitted and thus the original tumor was not an oddity (5). Soon thereafter, he left the study of Rous sarcoma virus (RSV), as it became known, to pursue other scientific endeavors. But RSV strains have been studied in laboratories ever since.

In 1958, Howard Temin and Harry Rubin developed the focus assay, in which RSV-infected cells were overlaid with agar to keep progeny virus localized (6). This technique allowed for the separation of individual viruses and was critical for the identification of spontaneous and temperature-sensitive mutant viruses, which were the key to the identification of *src* (for “sarcoma,”



Peyton Rous at his microscope (1923). Photo provided by The Rockefeller University Archives.

later *v-src*) as the RSV gene responsible for the transforming potential of the virus (for review see reference 7). This later led to the discovery of *c-src* as the first cellular protooncogene, and the identification of the *src* homology domains (SH2 and SH3) as mediators of protein–protein interactions. Meanwhile, characterization of RSV as an RNA virus provided the first evidence of the existence of reverse transcriptase.

Reflecting on his career in his Nobel Prize lecture (4), Rous credited Linnaeus with opening a wide door for him into natural history, which eventually led him to his study of cancer. Rous, in turn, opened a wide door for countless others into the field of tumor biology.

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