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Svoboda J. The tumorigenic action of Rous sarcoma virus in rats and the permanent production of Rous virus by the induced rat sarcoma XC. *Folia Biol. Prague* 7:46-60, 1961.
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A chicken Rous sarcoma virus strain inoculated into rats produced a tumor that harbored and replicated the viral genome in a noninfectious state. Infectious virus was rescued by inoculation of intact cells into chickens. The similarity of this situation with lysogeny and phage integration was put forward. [The *SCI*® indicates that this paper has been cited in more than 125 publications.]

Chicken Tumorigenic Virus in Mammals

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Attempts to transmit chicken Rous sarcoma virus (RSV) strains into mammals were inspired by the discovery of immunological tolerance, the codiscoverer of which was Milan Hašek. Although immunological tolerance to RSV antigens was never obtained after inoculation of virus into newborn mammals, these experiments revealed pathogenic and oncogenic activity of the virus in mammalian hosts and were published for the first time by Russian workers.[1,2]

In the early 1950s, I was working at the Central Biological Institute in Prague as a volunteer university student and Hašek became my supervisor. He prompted me to study immunological tolerance to RSV in foreign avian species,[3] but, with his temperament, he strongly opposed the idea of using mammals. Nevertheless, I did the experiments, because immunogeneticists dominating the department despised outbred Wistar rats and, therefore, experimental material was easily available.

As a PhD student, I obtained a tumor, XC, in rats, which provided the first conclusive evidence that an RNA-containing virus (now retrovirus) of chicken origin was the etiological agent of mammalian tumor formation. In fact, I did not believe that, without some treatment with potentially virus-inducing agents, it would be possible to recover any viral activity from XC cells. Therefore, in the first experiment, I injected an X-irradiated XC cell suspension into chickens, where sarcomas containing virus oncogenic for chickens appeared rapidly. However, when I repeated the experiments using untreated, intact XC cells, I again obtained virus-producing tumors in chickens.[4] Then I repeatedly passaged the XC tumor suspension in newborn rats and found that the amount of XC cells required for tumor induction in chickens did not change during the passaging, thus showing that the replication of the viral agent followed that of the mammalian cells.

In the accompanying paper, I provided evidence that only constantly high numbers of structurally intact XC cells were required to produce tumors in chickens and that there was no viral activity in cells disrupted by freezing or in extracellular material obtained after XC tumor trypsinization.[5] I also performed a series of control experiments showing that RSV did not infect rat tumors of nonviral etiology, nor did it act in synergy with a chemical carcinogen in producing tumors in rats, nor, finally, was any viral activity found in healthy organs of XC tumor-bearing rats. These experiments therefore provided evidence of a general noninfectivity of the chicken tumor virus for mammalian cells and excluded the possibility that the virus genome, which transformed XC cells, might spread by reinfection. XC tumors, therefore, arose by a rare infection of rat cells that became transformed and consequently acquired selective advantage.

The stability of viral genetic information in the XC cell population in the absence of reinfection and the low frequency of infectious virus induction (later called virus rescue) indicated that "virus is present in the tumor cells (XC) in an incomplete form—probably as nucleic acid as in lysogenic infection of the bacterial cell by prophage" and remains "permanently integrated in the tumor cell." For all these reasons, the XC cell model looked very promising to me for elucidating the nature of the oncogenic viral genome in transformed cells, and I put into it all my youthful enthusiasm.

1. **Zilber L A & Kryukova I N.** Haemorrhagic disease of rats caused by Rous sarcoma virus. *Vop. Virusol.* 4:239-43, 1957. (Cited 30 times.)
2. **Svet-Moldavsky G J.** Development of multiple cysts and of haemorrhagic affections of internal organs in albino rats treated during the embryonic or new-born period with Rous sarcoma virus. *Nature* 180:1299-300, 1957. (Cited 60 times.)
3. **Svoboda J & Hašek M.** Influencing the transplantability of the virus of Rous sarcoma by immunological approximation in turkeys. *Folia Biol. Prague* 2:256-64, 1956. (Cited 15 times.)
4. **Svoboda J.** Presence of chicken tumour virus in the sarcoma of the adult rat inoculated after birth with Rous sarcoma tissue. *Nature* 186:980-1, 1960. (Cited 195 times.)
5. **- - - - - - - -.** Further findings on the induction of tumours by Rous sarcoma in rats and on the Rous virus-producing capacity of one of the induced tumours (XC) in chicks. *Folia Biol. Prague* 8:215-20, 1962. (Cited 50 times.)

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