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Lane D P & Crawford L V. T antigen is bound to a host protein in SV40-transformed cells. *Nature* 278:261-3. 1979.
[Depanment of Zoology. Imperial College London; and Department of Molecular Virology. Imperial Cancer Research Fund. London. England]

The oncogenic activity of the small DNA tumour virus simian virus 40 (SV40) is due to the activity of the virally encoded T antigen protein. This paper showed that in virally transformed cancer cells the T antigen protein was tightly and specifically bound to a 53,000 molecular weight host protein. [The *SCI*® indicates that this paper has been cited in more than 740 publications.]

Viral Oncogene Binds Host p53 Protein

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The ability of small viruses to cause cancer has provided a potent model system with which to understand the human disease. It became clear in the early 1970s that the RNA tumour viruses performed this remarkable activity through their ability to capture and alter the expression of host genes that promote cellular growth.[1] The activity of the oncogenes encoded by the small DNA tumour viruses, such as simian virus 40 (SV40) T antigen, posed more of a mystery, since these genes were not clearly related to any host gene. It is now clear that these viral oncogenes work by binding to and altering the activity of host proteins that normally act to inhibit cellular growth.[2]

This paper described the first such protein complex to be identified when we found that a specific host protein, now called p53, bound to SV40 T antigen. The p53 protein we thus identified has turned out to be enormously important since somatic mutations in the p53 gene occur in the majority of human tumours,[3] and germ line mutations result in an extraordinary incidence of cancer in affected individuals.[4] The normal function of p53 protects us powerfully from developing cancer.[5]

I carried out the experiments described in this paper during my first postdoctoral fellowship at the Imperial Cancer Research Fund (ICRF), working in Lionel Crawford's laboratory on the fifth floor of the ICRF building in Lincoln's Inn Fields in London. I remember it as an extraordinarily exciting time. I had got the position with Lionel in the summer of 1976 after completing my PhD studies with Avrion Mitchison at University College. Lionel went off to the US to work with George Stark and discover splicing in small t of SV40, leaving me in charge of his lab and his wonderful technician Alan Robbins. After a few months Av called me up and advised me to apply for a lectureship at Imperial College in London. Life now had a highly charged quality as I rushed around London on my motorbike doing my research at ICRF, teaching at Imperial College, and at the same time talking to Lionel across the Atlantic and trying to write up my PhD in a house with no heating. But the lab work went wonderfully well, and amid this chaos Alan and I were able to immunopurify enough T antigen from SV40-infected cells using crude tumour bearer sera to see the protein as a commassie stained band on a gel. This allowed us to make highly specific anti-T sera,[6] and with these we were able to show, when Lionel returned, that T was bound to a host protein of 53,000 molecular weight in SV40 transformed cells. It was a tremendously exciting observation, and though in good tradition our paper was at first rejected by *Nature,* they eventually took it after revision.

The work is often quoted because p53 has turned out to play a critical role in human cancer. Whole meetings are now held on p53 with hundreds of participants. The function of pS3 seems to be to induce apoptosis or growth arrest in cells in which DNA has been damaged, helping to protect the organism from the growth of mutant, potentially cancerous cells.

Lionel and I have continued to work on tumour viruses and p53. Lionel is a Fellow of the Royal Society and I was recently awarded the first Charles Rodolphe Brupbacher Prize jointly with Arnie Levine of Princeton, who described his independent identification of pS3 shortly after our paper was published.[7]

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