

The data on the presence of SV40 sequences in human tumors are provocative and intriguing but they fall short as evidence for causality.

The positive findings are inconsistent and the data do not allow an estimate of the strength of the association.

Prevalence of SV40 sequences in 24 studies of mesothelioma, conducted between 1994 and 2002, was examined. The prevalences varied over a wide range. Several of the recent studies are negative or have low prevalence.

SV40 Sequences in Mesothelioma: A Summary

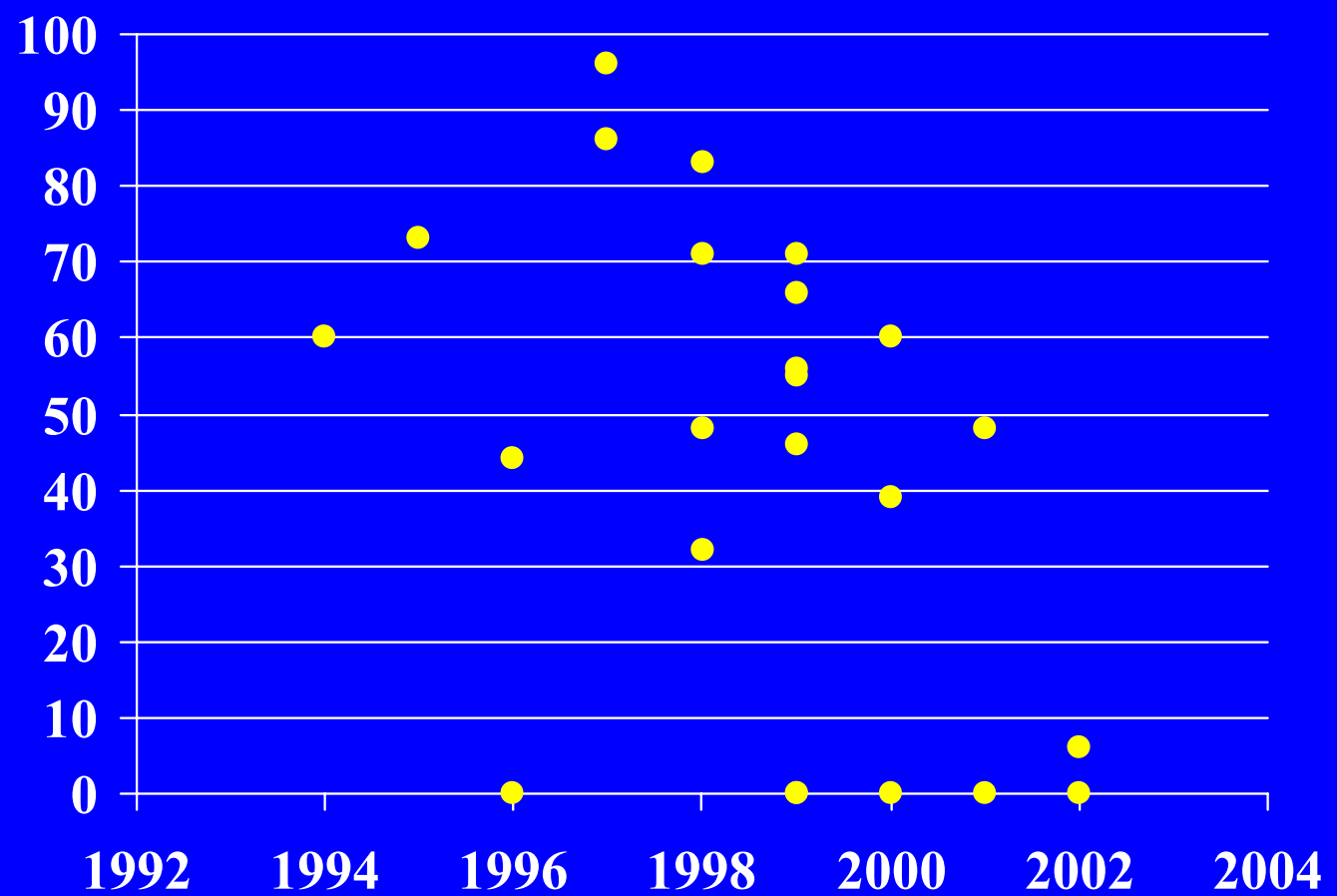
<u>Year</u>	<u>Investigator</u>	<u>Reference</u>	<u>Prevalence</u>	<u>Percent</u>
1994	Carbone et al.	Oncogene 9: 1781-1790, 1994	29/48	60
1995	Cristaudo et al.	J Environ Pathol Toxicol Oncol 14: 39-34, 1995	8/11	73
1996	Strickler et al.	Cancer Epidemiol Biomarkers Prev 5: 473-475, 1996	0/48	0
1996	Pepper et al.	Thorax 51:1074-1076, 1996	4/9	44
1997	DeLuca et al.	Nature Med 3: 913-916, 1997	30/35	86
1997	Carbone et al.	Nature Med 3:908-912, 1997	49/51*	96

1998	Testa et al.	Cancer Res 58: 4505-4509, 1998	10/12	83
1998	Pass et al.	J Thorac Cardiovasc Surg 116:854-9, 1998	30/42	71
1998	Mutti et al.	Dev Biol Stand 94: 47-53, 1998	8/25	32
1998	Galateau-Salle et al.	J Pathol 184:252-7, 1998	10/21	48
1999	Mulatero et al.	Thorax 54: 60-61, 1999	0/12	0
1999	Mayall et al.	J Clin Pathol 52: 291-293, 1999	5/7	71
1999	Shivapurkar et al.	J Cell Biochem 76: 181-188, 1999	61/93	66
1999	Ramael et al.	Eur Respir J 14: 1381-6, 1999	14/25	56
1999	Hirvonen et al.	Mol Carcinogenesis 26:98- 99, 1999	0/49	0
1999	Cristaudo et al.	Anticancer Res 20: 895-898, 2000	10/18	55
1999	Dhaene et al.	Virchows Arch 435: 1-7, 1999	13/28	46

2000	Emri et al.	Anticancer Res 20: 891-894, 2000	0/29	0
2000	Strizzi et al.	Anticancer Res 20: 885-890, 2000	9/23	39
2000	Procopio et al.	Genes, Chromosomes & Cancer 29: 173-179, 2000	50/83	60
2001	Toyooka et al.	Cancer Res 61: 5727-5730, 2001	32/66	48
2001	International SV40 Working Group	Cancer Epidemiol Biomarkers Prev 10: 523-532, 2001	0/25	0
2002	Gordon et al.	Oncol Rep 9: 631-634, 2002	2/35	6
2002	Hubner and Van Marck	Cancer Causes & Control 13: 121-129, 2002	0/12	0

* based on detection of T ag

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In the most recent study by Gordon et al. (Oncol Rep 9: 631-634, 2002), fresh frozen tissues from 35 patients were examined by SV40 quantitative PCR.

- 33 tissues were negative for SV40
- In the two positive tissues, SV40 sequences were present in very small amounts, estimated as one copy per >100 cells.

In a comprehensive study, Hubner and Marck (Cancer Causes and Control 13: 121-129, 2002) examined archived mesothelioma tissues from 12 patients using different extraction methods and several sets of primer pairs. They were unable to detect SV40 sequences in any of the tissues. These tissues were previously reported to be positive for SV40 sequences.

Examples of other discrepancies

(from review, Shah, 2000, Rev Med Virol 10: 31-43)

- One study found SV40 in spermatic fluid, another did not.
- Presence of SV40 sequences in leukocytes from normal individuals varied from 0-23%.
- Two laboratories found BKV sequences frequently along with SV40 sequences. Others did not.
- Initially, SV40 sequences were reported from rare cancers such as mesothelioma and pediatric brain tumors. Now they have been reported from a bewildering variety of cancers, including the most common human cancer (bronchopulmonary carcinoma) and the most common brain tumor (glioblastoma).

SV40 sequences in cancer

- Found in patients of all ages, 1-2 years old to 70+ years old
- Found in carcinomas, sarcomas, lymphomas
- Found at different sites: brain, pleura, bone and many others

How does the virus reach all these sites in the infected individuals?

Considerations for Future Studies

(Shah and Rollison, Disease
Markers 17: 159-161, 2000)

- We plan to study cancer patients and controls, so that the “full signature” of SV40 infection (genomic sequences, virus shedding, antibody responses, T cell responses, infections in family members) could be looked for to assess SV40 exposure.
- We will assess SV40 exposure in cases and controls in the context of other known risk factors for the cancer. It is difficult to evaluate the contribution of SV40 exposure in the development of mesothelioma without taking into account exposure to asbestos.