Excerpt from "Microchip-Induced Tumors in Laboratory Rodents and Dogs: A Review of the Literature 1990–2006"

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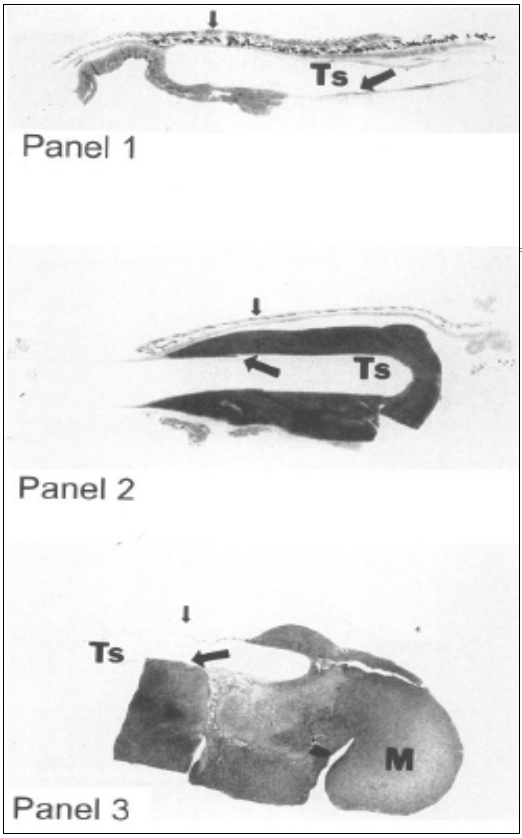
Blanchard et al., 1999

Transponder-induced sarcoma in the heterozygous p53+/- mouse. *Toxicologic Pathology*. 1999;27(5):519--527.

Author(s)	# of Animals	Species	Study Length	Developed Cancer
Blanchard et al., 1999	177	mice	6 months	10.2%



"There was an unequivocal association between the [microchip implant] transponder and sarcoma that was unrelated to drug treatment." (p. 526)

"The presence of the foreign body [microchip transponder] may elicit tissue reactions capable of generating genotoxic byproducts." (p. 526)

FIG. 1.—Subcutaneous transponder sites in transgenic mice in unaffected stage and in various stages of tissue mass development. Panel 1: Transponder site cavity (Ts) prior to mass development. Transponder was located just beneath the skin (small arrow) and surrounded by a typical capsule membrane (large arrow) of condensed connective tissue in which mass (M) development begins. Orientation of the transponder capsule is glass extremity to the left and polypropylene extremity to the right. Panel 2: Mass development is apparent in association with the polypropylene extremity and was often observed to begin at the glass–polypropylene interface. At this stage, early mass development may or may not be macroscopically apparent. Panel 3: Fully developed mass predominantly at the polypropylene extremity. In later stages, the entire site may be involved.

Summary of Study

177 genetically modified mice were implanted with microchips for identification purposes as part of a chemical compound study. After six months, 18 of the mice (10.2%) had developed malignant tumors ("undifferentiated sarcomas") around the microchip. The tumors occurred in both experimental and control animals. The researchers reported an " unequivocal association" between the implants and the cancer.

Study design and key findings

177 transgenic *p53+/-* mice[1] were implanted with microchips as part of a six-month study to investigate the toxicity of various chemical compounds. After six months, 18 of the mice (10.2%) developed malignant tumors ("undifferentiated sarcomas" p. 520) around the microchip. The tumors occurred in both control animals and animals that had received the test compound. The authors wrote that "these masses were not related to test substance administration; they were observed in controls as well as dosed animals." (p. 520)

Of the 177 total mice studied, 56 died before researchers made a link between the microchip and the tumors. The tissue surrounding the implants in the remaining 121 mice was microscopically analyzed.

Researchers discovered that the tumors arose at the microchip's plastic anchoring barb and then expanded to eventually surround the entire microchip. They state: "It appeared that tumor(s) arose in the mesenchymal tissue surrounding the polypropylene component of the transponder, initially involving the barbed area and then in some cases extending completely around the entire transponder site." (p. 523) Further, mass development was often observed to begin at the glass-polypropylene interface. (p. 521, Figure 1 caption, reproduced on previous page.)

The mice used in this study were transgenic p53+/- mice, specially bred to lack part of the tumor suppressor gene known as p53. In normal mice, p53 regulates cell growth and causes potentially cancerous cells to destroy themselves. Missing a part of this gene makes mice more susceptible to cancer from genotoxins, or toxic substances that affect genetic material.

The researchers write that "deletion of a single allele of this tumor suppressor gene in mice appears to be without effect on the development of spontaneous tumors, at least during the first year of life, but it imparts exquisite sensitivity to the mutational and carcinogenic effects of genotoxic chemicals." (p. 524) In other words, p53+/- mice do not develop tumors spontaneously in the absence of genotoxins. When they do develop tumors, it is generally an indication that a genotoxin is present.

Because the glass capsule and polypropylene sheath around the microchip implant are not generally considered to be genotoxins, the mice should not have responded to their presence by developing cancers. Researchers did not expect this outcome, writing: "the observation of transponder implantation site sarcomas in 18/177 (10%) of the animals studied was surprising."

Additional Findings

- "Membrane endothelialization, inflammation, mesenchymal basophilia, dysplasia, and sarcoma were considered unequivocal [unmistakable] responses to the transponder" (p. 523)
- The masses increased in size rapidly. One mass measuring ½" wide in the fifteenth week of the study grew to 2" just ten weeks later. (p. 520)
- The researchers "have subsequently replicated this finding in 2 separate studies with the p53+/- mouse where transponder implantation site sarcomas were also observed." Their article does not indicate whether these studies have been published.

1 These mice are genetically modified to have a higher rate of cancer development when exposed to genotoxicants but to be insensitive to nongenotoxins. The glass and polypropylene components of the BioMedic transponder device are generally assumed to be free from genotoxic materials (mutagenic and/or cytoxic components), so an observation of tumors would not be predicted by this model. (p525)

Study Details

- The study was conducted by Kerry Blanchard and other researchers[2] at the Department of Toxicology and Safety Assessment at Boehringer Ingelheim Pharmaceuticals in Ridgefield, Connecticut, along with John French and Raymond Tennant of the Laboratory of Environmental Carcinogenesis at the National Institute of Environmental Health Sciences in North Carolina.

- Animals used were transgenic p53+/- mice, specially bred to lack part of the tumor suppressor gene known as p53. These mice have an increased susceptibility to cancer from genotoxins (compounds which affect genetic material) but are not known to develop tumors spontaneously in the absence of a carcinogen.

- Microchips used were IMI® implants from BioMedic Data Systems. The microchip is described as encased in a glass capsule and partially encased in a polypropylene sheath.

2 Curt Barthel, Henry Holden, Roger Moretz, Franklin Pack, and Raymond Stoll.