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Stevens L C. The development of transplantable teratocarcinomas from intratesticular grafts of pre- and postimplantation mouse embryos. *Develop. Biol.* **21**:364-82, 1970.
[Jackson Laboratory, Bar Harbor, ME]

Three- to six-day-old mouse embryos were grafted to the testes of adults. They formed growths that resembled spontaneous testicular teratomas. Some contained cells that remained undifferentiated and pluripotent for remarkably long periods of time. Some of these cells continued to proliferate indefinitely and served as stem cells of transplantable teratocarcinomas composed of many kinds of tissues. Teratomas originate from a disorganized population of undifferentiated embryonic cells. For gonadal teratomas, this population is derived from germ cells. For the embryo-derived teratomas discussed here, this population is derived from grafted embryos. [The *SCI*® indicates that this paper has been cited in over 260 publications since 1970.]

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After I obtained my PhD in experimental embryology with Johannes Holtfreter at the University of Rochester in 1952, I went to work with Clarence C. Little, the founder and first director of the Jackson Laboratory. The research of Little involved examining large numbers of strain 129 mice for phenotypic variations that might be heritable. A few months after I arrived in Bar Harbor, I found a mouse with a testicular teratoma. To my knowledge, this was the first testicular teratoma ever observed in the mouse. It soon became apparent that about 1 percent of strain 129 males had these tumors, and since hypotheses concerning the origin of teratomas were controversial, I was eager to do a developmental study of them. Little encouraged me to apply for a grant from the American Cancer Society to begin an investigation of the biology of teratomas. Later, I received a grant from the National Cancer Institute that is still in effect.

We found that certain genetic and environmental influences increased the incidence of teratomas in strain 129 males from about 1 to 10 percent. This made it feasible to examine serial histological sections of neonatal and fetal testes of mice. We could identify clusters of undifferentiated embryonal cells (early teratomas) within the seminiferous tubules as early as 15 days of gestation, and we estimated that they initiated their development at 12 days. We found that teratomas could be experimentally induced by grafting male, but not female, genital ridges from 12-day-old embryos to the testes of adults. The grafts developed into testes, and for some strains, most had teratomas. When we grafted genital ridges from embryos that lacked primordial germ cells, they developed into testes without teratomas. This indicated that gonadal teratomas were derived from germ cells. It seemed possible that we did not obtain teratomas from female primordial germ cells because they had already entered into prophase of the first meiotic division and would not proliferate again until after fertilization. We thought that if we grafted pre- and post-implantation embryos to the testes, they might develop into teratomas. Most grafts did develop into teratomas, and we were surprised to find that some of the cells remained undifferentiated for remarkably long periods of time—some indefinitely as transplantable teratocarcinomas.

I think the reason that this publication has been frequently cited is that many investigators recognized that transplantable teratocarcinomas were a source of large amounts of undifferentiated embryonal cells that could be used for investigations on differentiation.

For a recent review, see reference 1.

1. **Stevens L C.** The origin and development of testicular, ovarian, and embryo-derived teratomas. (Silver L M, Martin G & Strickland S, eds.) *Teratocarcinoma stem cells.* Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, 1983. p. 75-91.