Int. J. Dev. Biol. 37: 17-19 (1993)

Barry Pierce - Why germ cells and germinal tumors?

FRANK DIXON*

Scripps Clinic, La Jolla, California, USA

Factors determining the specific direction of careers in science are most often unplanned and even unrecognized at the time, and this is true for the subject of this Festschrift, Dr. G. Barry Pierce. We all recognize him as a major pathologist-cancer researcher and teacher who has, through a series of well conceived and meticulously conducted experiments, defined the sequence of cellular events responsible for the development of germinal tumors of the testis. But what were the factors that got him started on this path? First, as a houseofficer in the University of Alberta he saw a youngster with a testicular tumor which not only could not be treated effectively but could not even be definitely diagnosed or classified. The failure of then current practice and dogma to explain in a satisfying manner the origin and pathogenesis of this tumor, let alone provide a therapy, was unsettling to Barry. In a search for answers to his questions about this tumor, he came upon a recently published fascicle on «Tumors of the Male Sex Organs» based on a morphologic analysis of over 1,000 testicular tumors found in our military forces during World War II (Dixon and Moore, 1952). This was the second event which guided the course of his career, since the fascicle proposed a morphologically and embryologically based scheme explaining the derivation of germ cell tumors, which piqued his curiosity.

In a desire to learn more about this intriguing group of tumors and perhaps subconsciously to develop his knowledge and skills with embryologic phenomena, he applied for a postdoctoral research fellowship at the newly established Experimental Pathology Department at the University of Pittsburgh, where one of the authors of the germ cell tumor fascicle worked. His experience at the University of Pittsburgh was perhaps the third factor in sealing his scientific fate. Here he saw his discipline, Pathology, practiced in an essentially wet laboratory fashion with morphology as only one and not necessarily *the* major tool of investigations aimed at defining pathogenesis, and this pattern suited him to a T.

I was delighted to have Barry join me in our analysis of germinal tumors, a line of study which he promptly took over and allowed me the role of consultant and pleasantly surprised observer. Not only did he enter an environment where pathology was an experimental laboratory science but he found himself among very competitive and highly successful peers who were working on immunologic problems and, incidentally, laying the foundation for a new hybrid discipline, immunopathology. This challenge of accomplishment by his associates was not wasted on Barry. His innate competitive nature and his will to succeed, which I am sure his friends in later years recognized with no trouble, were called into play. He embarked on a phenomenally successful career as an experimental pathologist beginning in his postdoctoral fellowship years and continuing to the present, and I would bet will continue well beyond the point he has arbitrarily selected as his time of retirement.

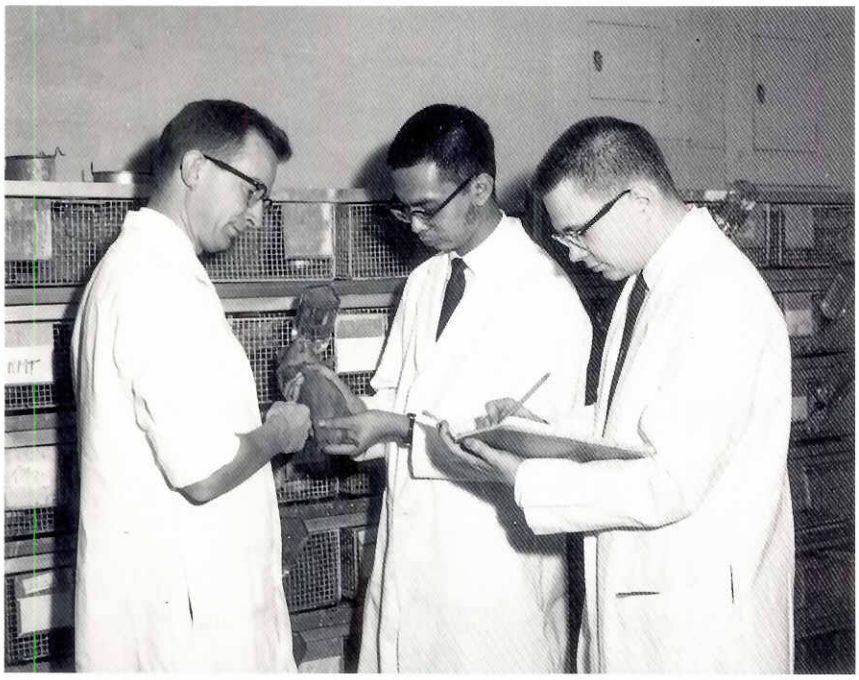
Barry began his studies using human tumors, but in spite of his considerable skill in culturing and maintaining them, it became clear that the supply would not be adequate and predictable enough to fuel a full-blown experimental endeavor. He therefore took advantage of the murine testicular tumors which had recently been described by Roy Stevens and could be produced at will by intratesticular transplants of embryonic genital ridge in adult 129 mice. With a guaranteed supply of tumors with which to experiment, Barry was off, and an uninterrupted stream of reports of insightful experiments, meticulously conducted and critically interpreted, has come from his laboratories in Pittsburgh, Ann Arbor and Denver. That his studies have continued unabated in spite of the many additional intra- and extra-mural responsibilities he has accepted is evidence of his dedication to science and of his effectiveness in and out of the laboratory.

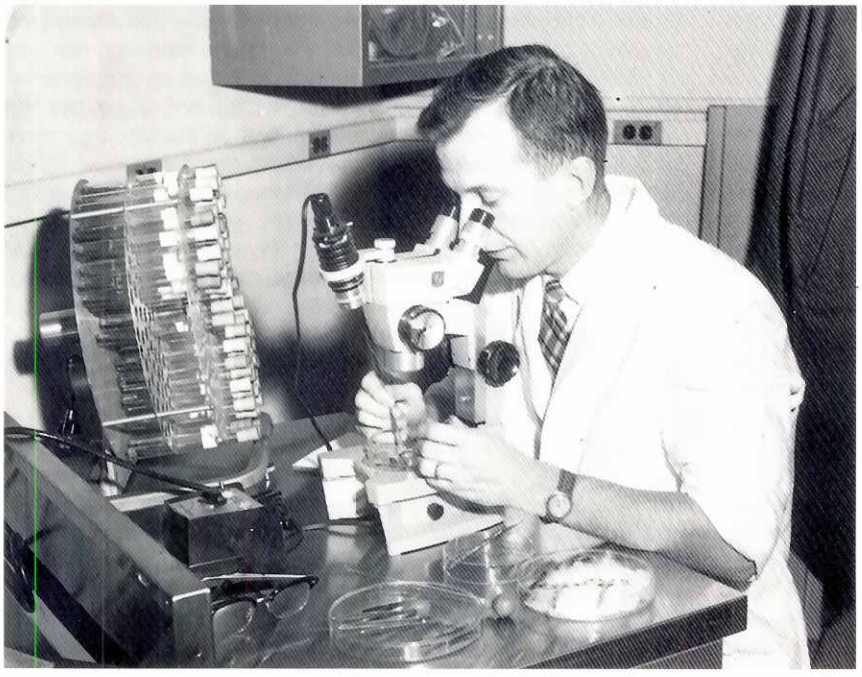
What are the major themes and accomplishments of Barry's experimental work? First, he provided conclusive proof for the proposed scheme of the derivation of testicular tumors from

***Address for reprints**: Scripps Clinic, 1066 N. Torrey Pines Road, La Jolla, CA 92037, USA.

0214-6282/93/$03.00

Printed in Spain





Above. Barry, the teacher, with postdoctoral fellows Ray Mark (center) and Rees Midgley (right) 1958.

Below. Barry, the researcher, examining and dissecting embryoid bodies from an ascites form of murine embryonal carcinoma, 1958.

multipotential germ cells. This had been suggested on the basis of morphologic observations in the aforementioned tumor fascicle. This sequence of postulations based on superb, intuitive morphologic observations (in this case, largely by Robert A. Moore) leading to Barry's experimental verification is in the best tradition of Pathology as it developed from a largely descriptive science to a more experimental one. To me the most impressive jewel in Barry's experimental crown was the simple yet elegant demonstration of a complete teratoid tumor derived from a single multipotential embryonal carcinoma cell (Kleinsmith and Pierce, 1964). To do this he isolated a single embryonal carcinoma cell in the tip of a Pasteur pipette, then transplanted the pipette tip containing the cell into a compatible recipient and observed the resultant teratoid tumor, thereby establishing the origin and pathogenesis of the germ cell-teratoid tumor complex.

A second theme in Barry's research has been an emphasis on the differentiation of malignant embryonal cells toward mature nonmalignant cell types (Pierce, 1983; Pierce *et al.*, 1979, 1982). That the differentiation of some very malignant cells to less or nonmalignant cells is possible is demonstrated by the natural course

of germinal tumors. The ability of normal cells, particularly embryonic normal cells, to reduce or eliminate the malignant potential of neighboring cancer cells, presumably by inducing differentiation, has been one of the objects of Barry's studies. An induced differentiation of cancer cells would, of course, offer a new approach to cancer therapy and recent work in the field of the growth factors gives hope that this conversion may in some tumors be possible.

Whether Barry will recognize the events described here as career determining and whether he will approve of the selection and emphasis I have applied to his research is not certain, but all I can say is that they have been presented by a very intimate observer and admirer of long-standing.

References

DIXON, F.J. and MOORE, R.A. (1952). Tumors of the male sex organs. In *Atlas of Tumor Pathology*, Section VIII-Fascicles 31b and 32. Armed Forces Institute of Pathology, Washington D.C., pp. F32-1-F32-179.

KLEINSMITH, L.J. and PIERCE, G.B. (1964). Multipotentiality of single embronal carcinoma cells. *Cancer Res. 24:* 1544-1551.

PIERCE, G.B., LEWIS, S.H., MILLER, G.J., MORITZ, E. and MILLER, P. (1979). Tumorigenicity of embryonal carcinoma as an assay to study control of malignancy by the murine blastocyst. *Proc. Natl. Acad. Sci. USA 76:* 6649-6651.

PIERCE, G.B., PANTAZIS, C.G., CALDWELL, J.E. and WELLS, R.S. (1982). Specificy of the control of tumor formation by the blastocyst. *Cancer Res. 42:* 1082-1087.

PIERCE, G.B. (1983). The cancer cell and its control by the embryo. Rous-Whipple Award Lecture. *Am. J. Pathol. 113 (1):* 117-124.