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This special issue of The International Journal of Developmental Biology is dedicated to Professor G. Barry Pierce, a pathologist by vocation and a developmental biologist by avocation, who in his many and productive scientific endeavors has explored the no-man's land named by R.A. Willis "the borderland between pathology and embryology".

Preface

Several key words provide the common thread for this issue: ontogeny, proliferation, embryogenesis, transgenesis, programmed cell death, genomic plasticity, stem cells, teratocarcinoma, epithelial-stromal interactions, metastases... Even readers unfamiliar with the field will soon learn that these apparently dissimilar and unrelated topics are neither disparate nor as distinct as may appear at first glance. For example, in tumor models such as teratocarcinoma, neoplastic differentiation parallels differentiation in normal development. After all, many of these neoplasms are, as pointed out by G. Barry Pierce many years ago, nothing but caricatures of normal development. Conversely, the function of alien and potentially lethal genes can be harnessed in transgenic mice, and blatantly malignant cells can be controlled by developmental fields operating within the normal embryo. Within teratocarcinomas, or in vitro, embryonal carcinoma cells are highly malignant, but if injected into the blastocyst they cooperate fully with the normal embryonic cells and become part of the new individual. If the stromal-epithelial interactions are disturbed, abnormal growth and proliferation ensue within both the normal and the «neoplastic» developmental field. Teratogenesis and teratocarcinogenesis seem to have more in common than divergent features. Programmed cell death is a normal feature of ontogeny, but its inhibition is a feature of neoplasia. For individual cells neoplastic transformation is a road to immortality, but individual cell immortality is incompatible with the survival of the organism.

These concepts may seem *intuitively obvious* to the reader; if that is the case, that *obviousness* is a great tribute to Barry Pierce. When he initiated his studies in the early fifties, neoplastic cells did not differentiate: on the contrary, they arose by *dedifferentiation* of fully differentiated «adult» cells; the malignant phenotype was an immutable phenotype which could not be harnessed; all cells in a malignant tumor were malignant... Paradoxically, when scientific concepts become fully accepted, that is, integral parts of the current paradigm, they can be used like coins, without any need to ascribe origin or paternity.

The Editors hope that the issue will be read not only by developmental biologists, but also by scientists working in other fields, especially those interested in experimental oncology. Above all, we hope this issue will reach budding scientists at the inception of their research careers and instill in them a fascination with these topics. Most fervent is our hope that some of the ideas outlined in this volume will fall on fertile ground and inspire new generations of scientists to go farther and deeper into the fields that G. Barry Pierce opened for us more than 35 years ago.

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Ivan Damjanov and Antonio Martínez-Hernández