

# This Week's Citation Classic

Révész L. Detection of antigenic differences in isologous host-tumor systems by pretreatment with heavily irradiated tumor cells. *Cancer Res.* **20**:443-51. 1960. [Institute for Tumor Biology, Karolinska Institute Medical School, Stockholm, Sweden]

Cells damaged lethally by irradiation show no change in either morphology or function, and maintain their specific antigenic character for a prolonged period after radiation exposure and before their final disintegration. Using such cells in transplanted grafts, a simple routine procedure was developed to test a given experimental tumor-host system for the presence or absence of antigenic differences. The paper describes the method and presents several examples for its practical use. [The SC<sup>®</sup> indicates that this paper has been cited over 220 times since 1961.]

L Révész  
Department of Tumor Biology  
Radiobiology Unit  
Karolinska Institute  
S-104 01 Stockholm 60  
Sweden

January 9, 1978

"It is a paradox to find that of all my papers the most cited is that which reports experiments based upon some accidental observations of a phenomenon known for a long time, and of only indirect relevance to my current research. Clearly, this is another example of how futile it is to try to foresee the path of fundamental research, to say nothing of governing it.

"In the mid fifties, I was engaged in experimental work with the purpose of determining the dose-survival relationship in radiation-exposed tumor cell populations. Studies of the *in vivo* proliferation of an irradiated mouse tumor cell-line, and Ehrlich ascites tumor, met with some unforeseen obstacles. After transplantation of the irradiated cells to new hosts it appeared that, in addition to radiation, some reaction of the host organism interfered with cell multiplication. Thus, in many

cases a host resistance developed which completely inhibited tumor growth. The resistance was found to be related to the size of the radiation-killed fraction in the transplanted cell population. The nature of this resistance was subsequently identified with the classical homograft reaction, well-known to operate in systems in which genetically determined iso-antigenic differences exist between the host and the transplanted tumor as in the case with Ehrlich cells. Indeed, in further experiments in which the transplant and the host were always matched genetically, no host resistance to the graft was induced by the presence of irradiated cells.

"The proliferation of antigenic tumors despite a concurrent homograft reaction in an immunogenetically foreign host can be viewed as a race between the development of the host response and the multiplication of tumor cells. Our observation could be interpreted as indicating that this race is influenced in favour of the host by lethally irradiated cells, which lose the ability to reproduce, but remain viable and undamaged in regard to their antigenic character for a prolonged time period after irradiation.

"As a model, our experiments demonstrated the fallacy of genetically non-matched tumor host-systems in therapeutic experiments. However, the findings have also an important positive aspect. Based upon the experience described here, a simple routine procedure can be developed using radiation-killed cells to test a given tumor-host system for the presence or absence of antigenic differences. It is most gratifying to learn from the high citation frequency of the paper which describes the method in detail that the technique has found a wide application."