

Antitumor Immunity

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Prospective

In 1950 Dr. J Englebert Dunphy, then a young attending surgeon at the Department of Surgery, Harvard Medical School, published a working hypothesis titled “Some observations on the natural behavior of cancer in man” in the *New England Journal of Medicine*. In that essay Dr. Dunphy described four cancer cases the outcomes of which seemed unpredictable at the time. Although could not explain what had influenced each of those cases to be what they were, he intended to use them to make an argument that cancer is not always what we think it is: a steadily and irrevocably progressing disease, but has some period of growth rest or even regression amid progress. These rest and regression seem to be caused by the host, not part of the tumor’s own biology. He used the term “local tissue resistance” for that host influence. Today, we call it antitumor immunity and we know a lot more of it than 70 years ago. Yet this revisiting essay is not about how much more we know this “local tissue resistance”, but about how much we have done with this knowledge in terms of making more effective treatments to achieve significantly better clinical outcomes. In that regard, we did very little for the past 70 years. Dr. Dunphy’s intention was clear when he described those cases and raised the issue of unpredictability of cancer behavior naturally or towards clinical interventions. He wanted us to try to understand the mechanisms causing these behaviors behind and to plan battle plans accordingly. That desire to change the situation was again strongly expressed in another essay titled “Changing Concepts in the Surgery of Cancer” in 1953, in which he described the situation that a surgeon dealing with cancer surgery “is seriously handicapped in setting the extent of a procedure by an almost total ignorance of the biological propensities of the lesion he is

attempting to treat.” He further demonstrated his argument by pointing out that “The most radical operation on a seemingly early lesion may be followed by widespread and rapidly progressive metastases and, contrariwise, a palliative resection undertaken with no hope of permanent cure may result in an extraordinarily long period of wellbeing for the patient. Until an accurate appraisal of the growth potentialities of any given tumor can be made, the surgeon must continue to grope in comparative darkness.” 70 years have passed and we are still in darkness when it comes to the outcome of cancer surgery or, in matter of facts, many other cancer therapies. The cancer surgeons today still cannot accurately predict the outcome of almost any cancer surgery with certainty. Despite how much we know about antitumor immunity, the cancer surgeons today still do not consider this factor in his plan of surgery. It is not that today we do not know what can rest tumor and hold them in abeyance for long; it is that we have not used this knowledge to improve outcomes of cancer surgery in specific and cancer therapy in general. Is this knowledge useless for clinical adaption or have we not tried? That is the focus of this essay. In the following sections, we will go through the four cancer cases Dr. Dunphy cited in his original essay and the “biological propensities” as we see behind these cases. Furthermore, we will present four cases in which we try to show that understanding the “biological propensities” behind each cancer case does seem to change the outlook of the battle against cancer. Our emphasis is at elevating our current view of cancer beyond the traditional two-dimensional TNM staging into a three and four dimensional world where each cancer case is viewed with more precision and dealt by individualized strategy with maximal survival benefits.

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