frontiers in IMMUNOLOGY

SPECIALTY GRAND CHALLENGE ARTICLE
published: 11 August 2011
doi: 10.3389/fimmu.2011.00034

Frontiers in Tumor Immunity: Grand Challenge "cancer and immunity: a family drama"

Wolf-Hervé Fridman*[1,2,3,4,5]

[1] Cordeliers Research Centre, Paris, France
[2] Hopital European Georges Pompidou, Paris, France
[3] University Paris Descartes, Paris, France
[4] University Pierre et Marie Curie, Paris, France
[5] INSERM, Paris, France
*Correspondence: herve.fridman@crc.jussieu.fr

The twentieth century has been a time of intense debate on the role of the immune system in controlling cancer initiation, growth, and final victory.

At the beginning of the century, according to the common sense generated by the very recent Pasteur discoveries, physicians and scientists have considered a growing cancer as an internal infection involving a fight with the patient's immune system. They were so convinced of the similarities between cancer and infections that William B. Coley proposed to treat patients with bacterial toxins, hypothesizing that the anti-bacterial immune response would clear the tumor. Although infrequent but undisputable therapeutic successes of this approach, together with epidemiologic studies reporting high incidence of cancer in immunodeficient individuals, yielded to the launching of the theory of immunosurveillance of cancer in the late 1950s. This theory proposed that, as for infectious agents, nascent cancerous cells, although originating from self, bore neoantigens recognized by the host's immune system and are therefore in most cases rejected. Only in immuno-impaired individuals (primary or induced by viruses or chemicals) or when developing in immunoprivileged sites, would cancers grow, become clinically detectable and kill the patient despite the efforts of his immune system, i.e., a family story inside the body, very badly controlled, finishing in a very unhappy ending. Contenders of this theory were however numerous. Most cancers originating in immunodeficient individuals were found to be of viral origin, so that immune surveillance seemed antiviral and not antitumoral, and despite the discovery of tumor-associated antigens in the 1990s, cancer immunotherapy yielded scarce successes. With the exception of Interleukin-2 for the treatment of metastatic renal cell cancer, no immunotherapeutic drugs have been approved. Accordingly, with the recent triumphant march of cancer genomics, and the discovery of targeted chemotherapies, cancer immunology has been consigned to the dark once again.

However, the beginning of the twenty-first century witnessed a renaissance of the field. Basic studies demonstrated that tumors develop more easily and rapidly in immunodeficient animals, even without oncogene activation or chemical promotion. Clinical studies established that, whereas chronic inflammation promotes cancer growth and metastasis, intratumoral Th1/CD8 memory T cell infiltration is a major prognostic factor for disease-free as well as overall survival in cancer patients. Even more practically important, efficient immunotherapies mostly based on the use of monoclonal antibodies targeted to the tumor cells or modulating the immune and stromal status, are being approved, which has changed the management of many cancers. A first therapeutic vaccine, using antigen-pulsed dendritic cells, has become a new treatment modality for metastatic prostatic cancer; others will come. In this regard, it is noteworthy that the efficacy of classical treatments, such as chemotherapies, seems to depend on their capacity to activate an anti-tumor immune reaction.

Even so, major questions have not yet been resolved, among which are: Is an immune reaction efficient because it recognizes cancer cell antigens or because it modifies the tumor microenvironment? How do the cancer cells and the plasticity of their genome influence the immune contexture? What tumor-associated driver molecules should be targeted by immunotherapies? What is the complexity of the tumor-associated immune reaction in terms of immune cell populations and targets, how is it modified during tumor evolution, and how is it in primary sites compared with different metastatic sites? Should all efficient therapies modulate the immune reaction and how?

The era of large libraries of human specimens linked to systems biology and tailored mouse models will allow us to address these questions in an effective manner, and to propose an immunological management of the diseases, taking place in the growing field of targeted therapies based on the cancerous cells but also on the genetics of the patient, as well as the environment of the tumor cells.

Received: 21 July 2011; accepted: 29 July 2011; published online: 11 August 2011.
*Citation: Fridman W-H (2011) Frontiers in Tumor Immunity: Grand Challenge "cancer and immunity: a family drama". Front. Immun. **2**:34. doi: 10.3389/fimmu.2011.00034*
This article was submitted to Frontiers in Tumor Immunity, a specialty of Frontiers in Immunology.