OncoImmunology 1:1, 1-2; January/February 2012; © 2012 Landes Bioscience

OncoImmunology

A new journal at the frontier between oncology and immunology

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Although tumor immunologists have been convincing themselves over the last decades that cancer can be conceived as an immunological problem—a few cells expressing novel antigens proliferate in uncontrolled fashion, in spite of the immune system's attempts to eliminate them—they have been standing alone. Most basic cancer researchers, drug developers and clinical oncologists have been considering neoplasia as a purely cell-autonomous genetic disease and have been ignoring or even neglecting the impact of immunology on tumorigenesis, for multiple reasons.

First, as a complex, multi-step disease, cancer is difficult to comprehend and even more difficult to treat, meaning that most specialists have been advocating reductionism as a strategy to "focus" on oncogenes and tumor suppressor genes as the mechanisms of tumorigenesis and on oncogene addiction (and more recently the non-oncogene addiction) as a therapeutic target. Second, driven by the consideration that cancer drugs must cure human cells, most animal models that have been used to study cancer drugs involve human cancer cell lines or primary tumor explants that are inoculated into severely immunodeficient mice. This means that any contribution of the immune system to anticancer therapy (or its failure) has been systematically overlooked during the development of cancer drugs. Third, in clinical practice, the diagnosis, prognosis or treatment of cancers has not been guided by any kind of immune parameters, including the presence of tumor-infiltrating lymphocytes or the detection of antibodies or T cells specific for tumor antigens. Fourth, many attempts to cure cancer by cytokines, adoptively transferred T cells or therapeutic vaccination have failed (at least as long according to WHO or RECIST criteria), in spite of initial successes reported in animal models, case reports or small clinical trials. Thus, until early 2010, the only FDA-approved anticancer regimens that might be considered as immunotherapies were limited to the toll-like receptor-7 agonist imiquimod for the treatment of basal and squamous cell skin cancer, as well as of genital warts (*Condylomata acuminata*), the cytokines interleukin-2 and interferon-α for the treatment of renal cell carcinoma, and Bacille Calmette-Guérin for the local treatment of superficial bladder cancer.

Strikingly, the last two years have marked a turning point in the field. The FDA has approved two novel immunotherapies for the treatment of cancer, namely sipuleucel-T/PROVENGE®, a dendritic cell-based vaccine against prostatic acid phosphatase for the treatment of advanced prostate cancer (approved in 2010), and ipilimumab/YERVOY®, an antibody that neutralizes the T cell-inhibitory receptor CTLA-4, for the treatment of advanced melanoma (approved in 2011). Recent clinical studies suggest the clinical utility of adoptive T cell transfer and therapeutic vaccinations with gp100 plus interleukin-2 for the treatment of melanoma as well. Ongoing clinical evaluations indicate that many more immunotherapeutic approaches are in the pipeline and are very likely to reach the clinics in forthcoming years.

There are a couple of additional reasons why tumor immunology is becoming an ever more popular area of research and development. First, during recent years, it has become clear that the density, composition, architecture and function of the immune infiltrate determine the prognosis of cancer patients. Moreover, it was discovered in 2010 and 2011 that the immune infiltrate also has predictive value and thus determines the likelihood that conventional anticancer therapies with cytotoxic agents will succeed in reducing tumor mass. These clinical results confirmed the research-based hypothesis that chemotherapy must stimulate an anticancer immune response in order to be successful. Accordingly, there is accumulating evidence that at least some chemotherapeutic agents can stimulate the infiltration of tumor beds by innate and cognate immune effectors. Furthermore, even the first and paradigmatic example of "targeted" cancer therapy, the tyrosine kinase inhibitor imatinib, is much more efficient in controlling the growth of cancer cells in the presence of an intact cellular immune system than in its absence.

In light of the ever-accumulating evidence, the communities of researchers and clinicians, as well as the biotechnological and pharmacological industries, are now accepting a paradigm shift: cancer becomes a life-threatening disease when tumor cells escape from the control of the immune system, and successful therapies rely on the reestablishment of the equilibrium between the tumor and anticancer defense mechanisms. Novel antibodies endowed with enhanced ADCC properties are being

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Submitted: 08/01/11; Accepted: 08/01/11
http://dx.doi.org/10.4161/onci.1.1.17645

generated by the pharmaceutical industry, while numerous biotechnology companies are engaging in the development of innovative cancer vaccines, driven by the conviction that the future standard of care of cancer will involve tailor-made combination therapies that associate immunogenic cytotoxic compounds with immunostimulatory agents and/or therapeutic vaccines.

Hence, the time is ripe for this new journal, *OncoImmunology*, which will publish high-profile articles on all aspects of fundamental and applied tumor immunology. Aided by an Editorial Board of excellent and highly qualified researchers, *OncoImmunology* will publish relevant research articles, monitor important developments in the field, and provide resources to the interested research community. We thank you, readers, patients, physicians and scientists for joining us in this adventure.