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Targets for Immunotherapy in Acute Leukemia

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Acute leukemia was arguably the first cancer for which immunotherapy was effective enough to be adopted as the clinical standard of care [1]. Unfortunately this therapy, allogeneic hematopoietic stem cell transplantation (allo-HSCT), is associated with considerable morbidity and mortality therefore limiting use to only the highest risk cancers in younger patients. The recent developments of effective chimeric antigen receptor T cell therapy have generated considerable excitement in the area of leukemia immunotherapy (reviewed elsewhere [2, 3]) unfortunately clinical utility will be limited by the availability of appropriate cell surface targets. In this special issue of *Current Drug Targets*, experts at the interface between immunotherapy and hematological malignancies discuss recent advances and future opportunities in this exciting and fast moving area of research.

One of the most intellectually appealing aspects of immunotherapy for acute leukemia is the theoretical potential to specifically target the malignant leukemic clone while avoiding damage to the normal host. Goswami [4] discusses potential antigens for acute myeloid leukemia with the focus on targets that would not require sacrifice of normal hematopoiesis due to on-target but off-tumor effects. Cruz and Bollard review the exciting progress from their group and others demonstrating that it is now possible to generate in the clinical laboratory T lymphocyte cell products with cancer antigen specificity [5]. This important development frees future adoptive cellular therapy from the current constraint that targeted antigens must be extracellular.

Humility is perhaps not the first descriptor that comes to mind when considering cancer immunologists, but some dose may be an asset when considering that the most effective cancer immunotherapies to date have been those least elegantly targeted. In cases such as allo-HSCT any human opinion on the best leukemia antigen to specifically direct therapy towards is superfluous. This is also the case for the new generation of immunomodulatory and immune checkpoint agents, beautifully reviewed here by Zeidner and Foster [6] and Knaus and colleagues [7]. These drugs are already proven clinically effective in other cancers and represent highly promising candidates in acute leukemia [8]. Finally, and most provocatively, Krakow and colleagues discuss the intriguing possibility that allo-reactive cell therapy without substantial engraftment (including microchimerism) may represent a high accessible, affordable and effective form of cancer immunotherapy [9].

Of course a brief special issue such as this cannot fully cover the full scope of acute leukemia immunology. In particular important topics such as the role of the tumor microenvironment, vaccine therapy, natural killer cells and immune modulation in allo-HSCT were not included in this issue but have been reviewed elsewhere. After decades of

unmet promises and unwarranted hype cancer immunotherapy has finally reached a stage where it can provide true clinical benefit for patients. This issue hopes to provide the reader with insight into how cancer immunotherapy may be investigated and ultimately integrated into the care of our patients with acute leukemia.

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