Antigen specific active immunotherapy: Quo vadis?

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The concept of using a patient's own immune system to fight a tumour is very attractive. The successful manipulation of the immune system in any disease setting is a first step in this direction. Over the past 10 years there has been a revolution in our understanding and therapeutic approach to inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease or psoriasis. Blocking single cytokines or interfering with cell surface molecules on T cells have a dramatic impact on the clinical outcome of these chronic inflammatory diseases [1].

Have these therapeutic successes advanced our ability to modulate the immune system with the aim to fight cancer? One of the strongest arguments that cellular effectors of the immune system are able to fight cancer is the well known Graft versus Leukemia effect [2]. It has been also demonstrated that infusion of soluble effectors of the immune system, ie antibodies are able to destroy cancer cells [3]. These examples provide a sound basis for the view that effectors of the immune system are able to fight cancer.

Adamina and Oertli review the last decade regarding antigen specific active immunotherapy (ASAI), which started with the discovery of tumour antigen specific antigens with special emphasis on melanoma [4]. They provide an overview of the technologies used and the progress made during this time period. They also discuss shortcomings of current immunotherapy approaches and potential ways to improve those. ASAI and cancer vaccination aim to induce a protective immune response against cancer by injecting tumour antigens plus adjuvant. Adoptive immunotherapy relies on the passive infusion of immune effectors such as T cells or antibodies. The molecular understanding and approach of ASAI has made considerable progress in the last ten years [5]. While the general approach in the 1970's and 1980's was to inject sometimes ill-defined tumour cell preparations into patients and hoping for a therapeutic response, the molecular definition of tumour antigens has opened new ways of tumour immunotherapy in the 1990's and the current century. This development combined with better ways of monitoring a patient's immune response during ASAI [6] has provided a basis for the scientific assessment of ASAI. It has been convincingly demonstrated that ASAI is able to induce tumour antigen specific immune responses in cancer patients. However, apart from isolated clinical responses in early pilot trials, large phase III trials have yet to prove the clinical efficacy of ASAI. One area where ASAI might be successful is the adjuvant setting, when all detectable tumour is resected [7]. Apart from these developments there are also obstacles on the road for successful tumour immunotherapy. ASAI depends on a complex interplay of variables including dose, route of administration, immunization schedule, choice of tumour antigen and adjuvant. Furthermore, immunological endpoints might not always correlate with clinical endpoints [8].

In conclusion, the potential of ASAI is far from being fully exploited. Steps have been taken in the right direction and will hopefully lead to improved therapeutic approaches for patients suffering from cancer.

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References

1 Feldmann M, Brennan FM, Paleolog E, Cope A, Taylor P, et al. Anti-TNFalpha therapy of rheumatoid arthritis: what can we learn about chronic disease? Novartis Found Symp 2004;256:53–69.
2 Bleakley M, Riddell SR. Molecules and mechanisms of the graft-versus-leukaemia effect. Nat Rev Cancer 2004;4:371–80.
3 Rastetter W, Molina A, White CA. Rituximab: expanding role in therapy for lymphomas and autoimmune diseases. Annu Rev Med 2004;55:477–503.
4 Adamina A, Oertli D. Antigen specific active immunotherapy: lessons from the first decade. Swiss Med Wkly 2005;135:212–21.
5 Jager E, Jager D, Knuth A. Antigen-specific immunotherapy and cancer vaccines. Int J Cancer 2003;106:817–20.
6 Romero P, Cerottini JC, Speiser DE. Monitoring tumor antigen specific T-cell responses in cancer patients and phase I clinical trials of peptide-based vaccination. Cancer Immunol Immunother 2004;53:249–55.
7 Jocham D, Richter A, Hoffmann L, Iwig K, Fahlenkamp D, et al. Adjuvant autologous renal tumour cell vaccine and risk of tumour progression in patients with renal-cell carcinoma after radical nephrectomy: phase III, randomised controlled trial. Lancet 2004;363:594–9.
8 Marincola FM, Wang E, Herlyn M, Seliger B, Ferrone S. Tumors as elusive targets of T-cell-based active immunotherapy. Trends Immunol 2003;24:335–42.

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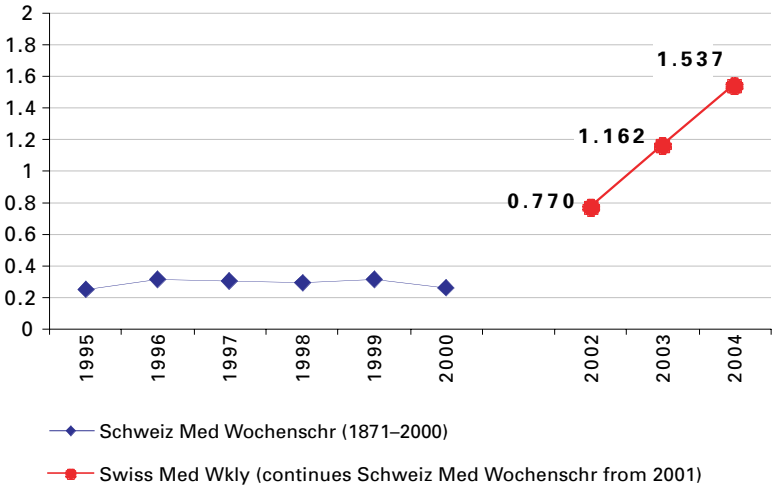

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