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Tumour associated antigens which act as biomarkers of survival and targets for immunotherapy in acute myeloid leukaemia

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We have used a number of techniques to identify tumour antigens recognized by the immune system of acute myeloid leukaemia (AML) patients including RT-PCR, SEREX, protein and cDNA arrays. We identified synovial sarcoma X breakpoint 2-interacting protein (SSX2IP) as a biomarker for survival. We analyzed 312 presentation AML samples and segregated AML patients based on above- and below-median levels of expression of SSX2IP. Analysis of Kaplan-Meier curves showed a significant association between elevated SSX2IP expression and improved survival times in AML patients who lacked detectable cytogenetic abnormalities (log-rank test, $n=180$; $P=0.007$). We have also identified the cancer-testis antigen PASD1 through the immunoscreening of a testes cDNA library with pooled AML patient sera. We identified a number of algorithm-selected naturally occurring 9 amino acid peptides which could bind HLA-A*0201 however these peptides failed to show detectable MHC binding in T2 assays. We modified one of the two anchor residues and showed these analogue peptides had enhanced binding, with decreased off-rates, in T2 assays. T cells from patients and normal donors responded to analogue peptide-loaded antigen presenting cells by secreting IFN γ . For clinical application, a DNA fusion gene vaccine encoding Pa14 was designed and tested in "humanized" mice. Splenocytes from vaccinated mice showed in vitro cytotoxicity against tumor cells, either exogenously loaded with the corresponding wild type peptide (Pw8) or expressing endogenously processed PASD1 protein. We show for the first time that a DNA vaccine encoding an altered PASD1 epitope can induce CTL able to target the natural peptide expressed by human tumor cells.

Biography

Barbara Guinn completed her PhD in Medicine in 1995 from University of Wales College of Medicine, Cardiff. Her Postdoctoral studies were performed at the University of Toronto. She is an Associate Professor at the University of Bedfordshire and Academic Director for Undergraduate Life Science. She is also the Editor-in-Chief of Biomarkers in Cancer, Senior Editor of Vaccines and Vaccinations, and has published more than 70 manuscripts in peer review journals. In addition she has served as a reviewer on an ad hoc basis for more than 35 journals and more than 10 national and international funding bodies.

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