Barbara Guinn, J Blood Disord Transfus 2013, 4:5
http://dx.doi.org/10.4172/2155-9864.S1.004

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference on
Hematology & Blood Disorders
September 23-25, 2013 DoubleTree by Hilton Hotel Raleigh-Durham Airport at RTP, NC, USA

Utilisation of pMHC arrays to identify tumour antigen specific T-cell populations in leukaemia

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Peptide major histocompatibility complex (pMHC) arrays, also known as tetramer arrays, were developed to identify "untouched" populations of $CD8^+$ T cells in the peripheral blood of cancer patients. The technique is able to analyse multiple T cell populations using small numbers of $CD8^+$ T cells (~1.2x106 cells/array) and pMHC (1ng per spot) spotted onto polyacrylamide gels. The pMHC array can simultaneously analyse a large number of T cell populations without haplotype restriction. We negatively isolated $CD8^+$ T cells from the peripheral blood of leukaemia patients. T cells were lipophillically dyed with DiD fluorescent tracer and incubated with arrays printed with pMHCs from more than 50 tumour-associated antigen and viral epitopes (including HLA-A*0201/CMV and Flu controls). Positive scoring of T cell populations were only made when T cells were consistently bound to 3 of 6 of the same pMHC spots in two distinct regions on the array.

To date we have analyzed 33 leukaemia patients (25 AML, 3 ALL, and 5 CML) and 18 normal donors. Although normal donor T cells recognized Flu and CMV epitopes, no binding to tumour antigen epitopes were found. In contrast we found that of the 12 patients who had tumour antigen specific-T cell populations eight of these had T cells which recognized PASD1 epitopes.

We have developed a robust method for the simultaneous analysis of T cell populations in leukaemia patients, the use of which can indicate a short-list of tumour antigen specific T cell populations for further investigation of T cell function, such as ELISpot and CTL assays, minimizing reagent and sample use.

Biography

Barbara Guinn completed her Ph.D. in Medicine from University of Wales College of Medicine in Cardiff in 1995. She undertook postdoctoral fellowships at the University of Toronto, Canada and has established her own research groups at King's College London, University of Southampton and most recently as an Associate Professor at the University of Bedfordshire in England. She has published more than 60 peer reviewed papers and is Editor-in-Chief of Biomarkers in Cancer. Her research focuses on the identification of novel antigens in solid and haematological malignancies, development of vaccines for immunotherapy and the study of T cell responses in patients during treatment.

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