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Poster Session V
Immunology, vaccination and host defences

HUMAN MEMORY T CELLS MORE AVIDLY RESPOND TO STAPHYLOCOCCCUS AUREUS IN PATIENTS RECOVERING FROM BLOODSTREAM INFECTION

A. Brown[1], T.R. Rogers[2], R. McLoughlin[1]

[1]Biochemistry & Immunology, Trinity College Dublin, Dublin, Ireland ; [2]Clinical Microbiology, Trinity College Dublin, Dublin, Ireland

Objectives:

Little is known about the normal human immune response to infection with *Staphylococcus aureus*. Exposure to this commensal organism may lead to the generation of specific humoral and cellular responses to some of its many polysaccharide and protein antigens. Anti-staphylococcal antibodies are present in the majority of the normal population but only appear to be protective against the rare staphylococcal toxic shock syndrome. To date, all completed anti-*S.aureus* vaccine trials that have centred on the generation of protective antibodies have failed, despite having shown promise in pre-clinical animal models. It is likely that generating humoral immunity alone may not be sufficient to confer protection against invasive *S.aureus* infection in humans.

Until now no study has been undertaken to profile the repertoire of T cells expanded as a consequence of *S.aureus* exposure in humans, nor to examine whether these T cell subsets can in fact specifically respond to *S.aureus* antigens at all. A clinical study was established to characterise *S.aureus* antigen-specific T cell subsets present in peripheral blood of adult patients without apparent or known immunodeficiency recently bacteraemic with *S.aureus* or *E.coli* as well as healthy volunteers. Future T cell targeted vaccine design must firstly identify which cells are most important in recovery from natural infection, and secondly which bacterial antigens are the most potent T cell activators in humans. This is the first study in humans aiming to answer these questions.

Methods:

Peripheral blood mononuclear cells (PBMCs) were isolated on mean of day 7 post-bacteraemia and stained with CFSE before being cultured with heat-killed laboratory and clinical strains of *S.aureus* (1µg/ml) for 10 days. Cells were then stained for extracellular markers (CD3, CD4, CD8, CD45RO) and intracellular cytokines (IFNy, IL-17A, IL-10) and processed for flow cytometric analysis on a BD FACS-LSRFortessa®.

Results:

Mean age in *S. aureus* bacteraemia (SAB) patients was 55 years (SD=27), and in *E.coli* bacteraemia (ECB) patients was 66 (SD=17, p=0.38). Eighty-one percent (n=9) of SAB patients recruited had complicated disease. Recovery from SAB is associated with a greater expansion in lymphocytes over the initial 7 days than in ECB (0.9 vs 0.2 cells x 10^9/L increase, p=0.09). CD4+ T cells isolated from *S.aureus* bacteraemic patients demonstrate significantly increased levels of antigen-specific proliferation when cultured in vitro with heat-killed *S.aureus* as compared to T cells isolated from *E.coli* bacteraemic patients. The majority of proliferating cells are CD45RO+, suggesting that they are circulating *S.aureus*-specific memory T cells expanded as a consequence of the recent exposure to the organism. These expanding cells exhibit a Th1-predominant phenotype – secreting IFNγ in response to bacterial antigen.

Conclusions:

Antigen-specific Th1 memory cells seem primed to *S. aureus* during recovery from bloodstream infection. This finding could be used in intelligent design of T cell-targeted anti-*S. aureus* vaccines.