T Cell Memory Response to Pneumococcal Protein Antigens in an Area of High Pneumococcal Carriage and Disease

Marianne W. Mureithi,1,2,a Adam Finn,3 Martin O. Ota,1 Qibo Zhang,2,a Victoria Davenport,2,a Timothy J. Mitchell,3 Neil A. Williams,2 Richard A. Adegbola,1 and Robert S. Heyderman2,4

1Bacterial Diseases Programme, Medical Research Council Laboratories, Banjul, Gambia; 2Department of Cellular and Molecular Medicine, School of Medical Sciences, University of Bristol, Bristol, and 3Division of Infection & Immunity, University of Glasgow, Glasgow, United Kingdom; 4Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, Malawi

Background. Streptococcus pneumoniae is a leading cause of vaccine-preventable disease worldwide. Pneumococcal protein antigens are currently under study as components of potential vaccines that offer protection against multiple serotypes. We have therefore characterized T cell pneumococcal immunity acquired through asymptomatic carriage.

Methods. Peripheral blood mononuclear cells from 40 healthy Gambian adults were stimulated with supernatants derived from S. pneumoniae strain (D39), 2 isogenic mutant strains lacking either pneumolysin or choline binding protein A, and recombinant pneumolysin. Immune responses were measured by cellular proliferation and by interleukin-10 (IL-10) and interferon-γ (IFN-γ) enzyme-linked immunosorbent spot and bioplex cytokine assays. Nasopharyngeal swabs were cultured to determine carriage rates.

Results. S. pneumoniae nasopharyngeal carriage was detected in 60% of individuals. Both effector and resting (or central) CD4+ T cell memory were frequently present to a range of pneumococcal antigens. However, the level of the effector memory response did not relate to current nasopharyngeal carriage. Pneumolysin was not immunodominant in these T cell responses but induced a distinct proinflammatory profile (high IFN-γ, IL-12[p40], and IL-17 levels and low IL-10 and IL-13 levels).

Conclusions. In this population, T cell–mediated immunological memory potentially capable of pathogen clearance and immune surveillance is common but is not associated with the absolute interruption of pneumococcal carriage. How this naturally acquired immune memory influences pneumococcal vaccine efficacy remains to be determined.

Invasive bacterial diseases caused by pathogens that normally colonize the upper respiratory tract are most common in young children, elderly persons, and immunocompromised individuals [1]. An estimated 1.6 million deaths associated with pneumococcal infection occur each year, and they largely involve children, rather than healthy adults, and predominantly occur in resource-poor countries [2]. The relative infrequency of Streptococcus pneumoniae–associated cases of pneumonia, meningitis, and sepsis among healthy adults, even in these settings where the childhood incidence is high, may be due to the progressive acquisition of immune memory through multiple nasopharyngeal colonization events that commence early in life [3].

Classically, serum antibodies to pneumococcal capsular polysaccharide and, possibly, noncapsular protein antigens have been thought to provide protection against disease [4]. However, more recently it has been