

Title: COMPLEMENT-MEDIATED ALTERATION OF DENDRITIC CELL FUNCTION

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Complement protein C3 is a central component in the complement cascade. Cleavage of C3 liberates a number of effector molecules that interact with their cognate receptors to stimulate phagocytosis, cell activation and inflammation. In addition, C3 is of strategic importance for the development of adaptive immunity. The immunological development and immune responses have been studied in a C3 deficient patient. The patient exhibited strong defects in adaptive immune responses whereby switched memory CD19+IgD-CD27+ B cells were vastly reduced in peripheral blood and long-term Ab responses were not detected following vaccination. Further, peripheral lymphocytes displayed a decreased ability to stimulate alloreactive responses indicating that the antigen presenting capacity of the patient's cells was affected. Defects in maturation development of dendritic cells (DCs) were also observed with decreased CD1a expression and IL-12p70 secretion. CD1a-expressing DCs have similarities to the CD8 alpha DC subset in mouse which can polarize naive CD4+ T cells to Th1 phenotype and can cross prime CD8+ cytotoxic T cells. These cells express complement receptors and their expression changes with LPS-induced maturation. We are in the process to examine their antigen processing capacity in the presence or absence of C3.