A17 SECONDARILY NECROTIC CELL-DERIVED MATERIAL (SNEC) CAUSES SYSTEMIC INFLAMMATION IN SLE BY EXPOSING AUTOANTIGENS FOR IMMUNE COMPLEX FORMATION

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Background and objectives Systemic lupus erythematosus (SLE) is a multifactorial genetically predisposed disease resulting from inflammatory responses of the immune system against several autoantigens. Considering actual evidence, the onset of autoimmune manifestations is triggered by the interplay between environmental factors and several major complex intrinsic defects. Deficiencies in the recognition and engulfment of apoptotic cells have been reported in patients with SLE. If dying cells are not promptly cleared, accumulate, undergo secondary necrosis, and expose nuclear autoantigens. The goal of this work is to analyse whether the remnants of apoptotic cells are involved in the induction of inflammatory responses in SLE.

Materials and methods Secondarily necrotic cell (SNEC) were generated by treatment of dead human lymphocytes with serum DNase-I and C1q. We employed fluorescence microscopy, FACS, and an ex vivo phagocytosis assays to demonstrate the availability of autoantigens to cells of the innate immune system.

Results SNEC binds several dead and dying cells ligands, and are readily recognised by lupus autoantibodies. Autoantibodies recognising DNA in the surface of nuclear remnants are able to opsonise them and to foster its uptake by non-professional blood borne phagocytes. We observed a significantly secretion of inflammatory cytokines by the phagocytes which were cultured with SLE plasma containing AAb. Phagocytosis of SNEC and the subsequent production of inflammatory cytokines were strongly influenced by the presence of DNA in the target particle.

ConclusionsLupus autoantigens are exposed on the surface of SNEC and available to assemble immune complexes. The clearance of cellular remnants that are not properly removed from the organism is targeted to innate phagocytes by lupus autoatibodies causing systemic inflammation in some patients with SLE.