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POSTER ABSTRACT

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The clearance of dying cells is impaired in some patients with Systemic Lupus Erythematosus (SLE)

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Impaired clearance of apoptotic cell material has been implicated in the pathogenesis of Systemic Lupus Erythematosus (SLE), since nuclear autoantigens are released when the apoptotic cells enter the stage of secondary necrosis. SLE is characterized by the presence of various autoantibodies, particularly against nuclear antigens. In human SLE decreased levels of serum DNase I activities as well as deficiencies in components of the classical complement pathway are well established to predispose to the disease. We investigated the fate of apoptotic cells in the germinal centers (GC) of patients with SLE and analyzed the role of serum factors which could be responsible for the clearance of human chromatin.

The numbers of tingible body macrophages, usually containing engulfed apoptotic nuclei, were significantly reduced in GC in a subgroup of patients with SLE. Furthermore, free apoptotic cells accumulated in the GC of the lymph nodes of some SLE-patients. In contrast to all controls, TUNEL positive apoptotic material was observed to be attached to the surfaces of follicular dendritic cells (FDC). Regarding the degradation of human chromatin we found that C1q and DNaseI do co-operate in the clearance of chromatin from dying cells. Reconstitution of C1q depleted serum with C1q strongly increased its capability to degrade necrotic cell-derived chromatin. Although C1q itself displayed no DNase activity, it strongly augments the activity of the serum DNaseI. Though an excess of DNaseI alone powerfully degraded chromatin from necrotic cells, an efficient uptake of the degraded material could only be observed in the presence of C1q. Sera from SLE patients with a low antibody dependent complement activity showed a strongly reduced degradation of necrotic cells compared to sera from healthy controls.

Our findings show that apoptotic cells are not properly cleared from the GC in a subgroup of SLE patients. We conclude that apoptotic cells-derived autoantigens bound to FDC may provide a survival signal for autoreactive B cells thereby overriding an important initial control mechanism of B cell tolerance. Furthermore, C1q or DNaseI deficiencies may precipitate human autoimmunity.