The present invention provides methods and compositions for treating immune complex associated diseases (ICAD), such as SLE, rheumatoid arthritis, and hepatitis-C related immune complex disease (e.g., cryoglobulinemia) in a subject having an ICAD or at risk for developing ICAD. The invention is based upon the surprising finding that chromatin-containing immune complexes activate autoreactive B cells and dendritic cells by a dual receptor engagement process which, in both cell types, involves a Toll-like receptor (TLR). The methods of treating ICAD comprise administering a compound to an individual in need thereof that either 1) inhibits formation of the immune complex either by preventing formation and/or binding to the TLR, or 2) interferes with binding of an autoantigen-containing immune complex (or the antigenic component thereof) to the TLR, or 3) inhibits signaling pathways initiated by dual engagement of BCR and TLR (in B cells) or FcR and TLR (in dendritic cells) via immune complexed or uncomplexed autoantigens.

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