P010 Stimulation of inflammatory cytokines, CC-chemokines, DC maturation and adjuvant function by the 18 kDa HSP70 peptide binding domain

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Microbial HSP70 stimulates inflammatory cytokines, CC-chemokines and induces maturation of DC. The structure of HSP70 consists of three functionally distinct domains: the 44 kDa N-terminal ATPase fragment followed by an 18 kDa peptide-binding domain and a 10 kDa C-terminal portion. In an attempt to identify the stimulatory domains of HSP70, we generated three fragments of HSP70; the N-terminal 44kD ATPase portion (HSP70 1-358), the C-terminal 28kDa portion (HSP70 359-610) and the 18 kDa peptide-binding domain (HSP70 359-494). The data suggest that stimulation of human DC with HSP70 is mediated by the C-terminal fragments (HSP70 359-610 and HSP70 359-494) which elicit maturation of DC, as demonstrated by up-regulation of CD83, CCR7 CD86 and HLA class II, and production of the cytokines IL-12 and CC-chemokines. The N-terminal ATPase portion failed to induce expression of DC markers or stimulate any of these cytokines. Immunisation with peptide-bound C-terminal fragment (HSP70 359-610) in mice induced higher serum IgG2 and IgG3 antibodiest than the native HSP70-bound peptide. This study suggest that the peptide binding domain is responsible for HSP70 stimulating innate immunity and the adjuvant function.