

Didecameric keyhole limpet hemocyanin is potent in promoting antigen cross-presentation and inducing antigen-specific cytotoxic T cell activation

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Activation of antigen-specific cytotoxic T cells is an essential component of the cellular immune responses that must be induced for therapeutic vaccines against cancers to be effective. Antigen cross-presentation is required for the activation of tumor antigen-specific cytotoxic T cells. Here we report that keyhole limpet hemocyanin (KLH) in its didecameric form is a potent promoter of antigen cross-presentation and the subsequent induction of antigen-specific cytotoxic T cell activation. KLH is a well-established immune stimulant, hapten carrier and vaccine adjuvant with a 50-year record of safety in humans. The KLH protein is extensively glycosylated, existing in its native form as an 8 MDa cylindrical didecamer of 400 KDa subunits. Using ovalbumin as a model antigen, a murine immature dendritic cell line and a murine cytotoxic T cell hybridoma cell line that can be activated specifically by ovalbumin antigen presented by the MHCI molecules on dendritic cells, we found that KLH didecamers promoted antigen cross-presentation and induced antigen-specific cytotoxic T cell activation. In marked contrast, KLH dimers failed to elicit these activities. We also found that KLH didecamers that had lost specific glycosyl moieties during purification or storage lost their ability to promote antigen cross-presentation and could not induce antigen-specific cytotoxic T cell activation. Analyses with endocytosis inhibitors suggest that exposure to intact KLH didecamers may change the pathways of dendritic cell antigen uptake, thereby promoting antigen cross-presentation. Our data thus suggest that intact and fully glycosylated KLH didecamers can serve as a safe and effective adjuvant for vaccines against cancers.

Biography

Shuguang Bi completed his Ph.D in biochemistry from Georgetown University in 2004. He Angeles and University has been doing research on immunology and cancer vaccine in University of California at Los of California at Santa Barbara ever since graduation. He has published more than a dozen papers in reputed journals, including PNAS, JBC and Glycobiology.

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