

239i Analysis of Endocytic Sorting on Regulation of Exogenous Antigen Presentation

Hong Shen and W. Mark Saltzman

Antigen presentation plays an essential role in the induction of effective immunity against invading pathogens and in the maintenance of tolerance towards self-antigens (autoimmunity). The classical immunological paradigm of antigen presentation is that exogenous antigen is presented on Major Class Histocompatibility Complex (MHC) Class II pathway while endogenous antigen is presented on MHC Class I pathway. Recent evidence has shown that this apparent dichotomy does not hold true for most of professional antigen presenting cells. In those cells, exogenous antigen can also be presented on MHC Class I pathway, termed as cross-presentation. Functionally, cross-presentation has been recognized to be crucial for generating immune responses against tumor cells or some viral infections and controlling autoimmunity. Cell biologically, the mechanism is of great interest because it appears to involve overcoming a normally impenetrable topology barrier. Several questions need to be addressed: does cross-presentation use the endocytic pathway as MHC Class II pathway? how do the endocytic pathway and the classical class I pathway converge? how much overlap is there between the class I and class II antigen presentation? The goal of this work is to use a mathematical model of endosomal sorting to address these questions and to understand cellular mechanisms of exogenous antigen presentation.