

A4 Antigen processing in the endocytic compartment

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Proteases perform two key roles in the class II MHC antigen processing pathway. They initiate removal of the invariant chain chaperone for class II MHC and they generate peptides from foreign and self proteins for eventual capture and display to T cells. How a balance is achieved between generation of suitable peptides versus their complete destruction in an aggressive proteolytic environment, is not known. Nor is it known in most cases which proteases are actually involved in antigen processing. Our recent studies have identified asparagine endopeptidase (AEP or legumain) as an enzyme that contributes to both productive and destructive antigen processing in the class II MHC pathway. New studies will be presented which show that AEP is also involved in invariant chain processing. Other new work shows that limited AEP processing of the tetanus toxin antigen is sufficient to generate a suitable substrate for class II MHC binding and presentation even when low doses of physiologically captured antigen are involved. These results, which emphasise MHC binding as an early event, begin to explain how T cell epitopes can escape destruction in the lysosomal environment to supply the immune system with the peptidic information it needs to make appropriate responses.