



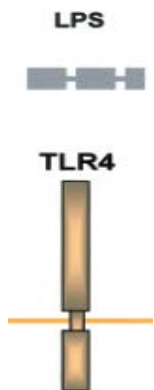
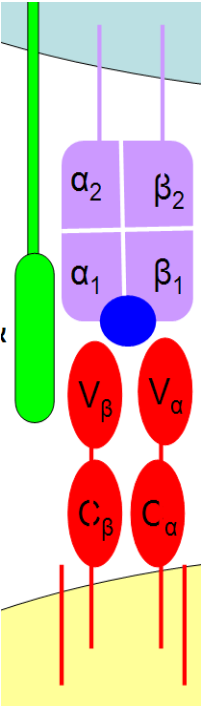
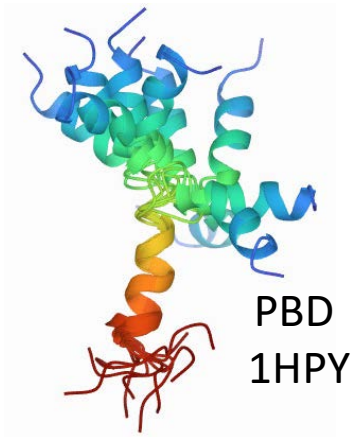
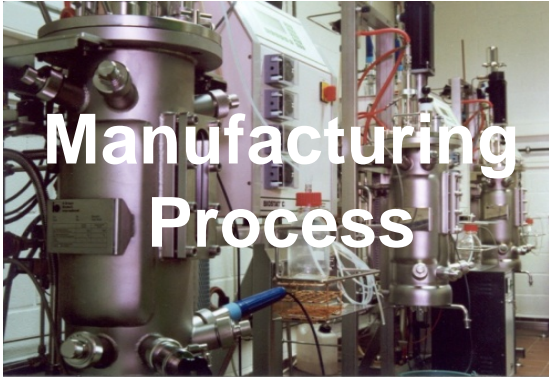
Closing: Non-clinical Immunogenicity Assessment of Generic Peptide Products

Center for Drug Evaluation and Research, U.S. FDA

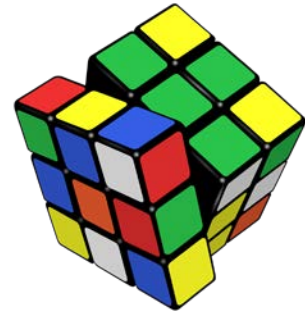
January 26, 2021

Steven Kozlowski, Director OBP in OPQ, CDER

Pathways



A Puzzle Over Decades



- Genetic control over immune responses
 - An Immune Response (Ir) Gene
 - Linkage to graft rejection associated loci (MHC)

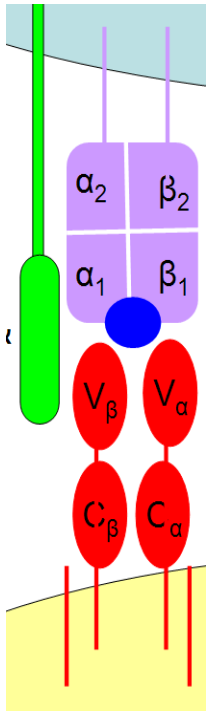
Histocompatibility-Linked Immune Response Genes

A new class of genes that controls the formation of specific immune responses has been identified.

1970

Baruj Benacerraf and Hugh O. McDevitt

- Initially thought to be a T-cell Receptor gene located between unrelated histocompatibility markers



A Puzzle Over Decades

- MHC Restriction: Immune cell & Target (or APC)

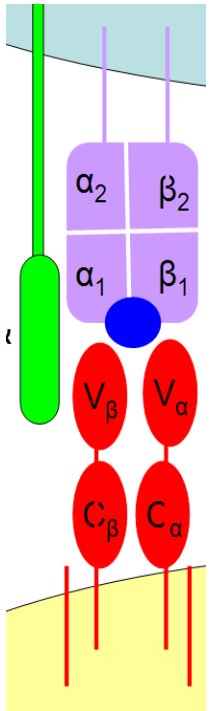
Brief Definitive Report

1975

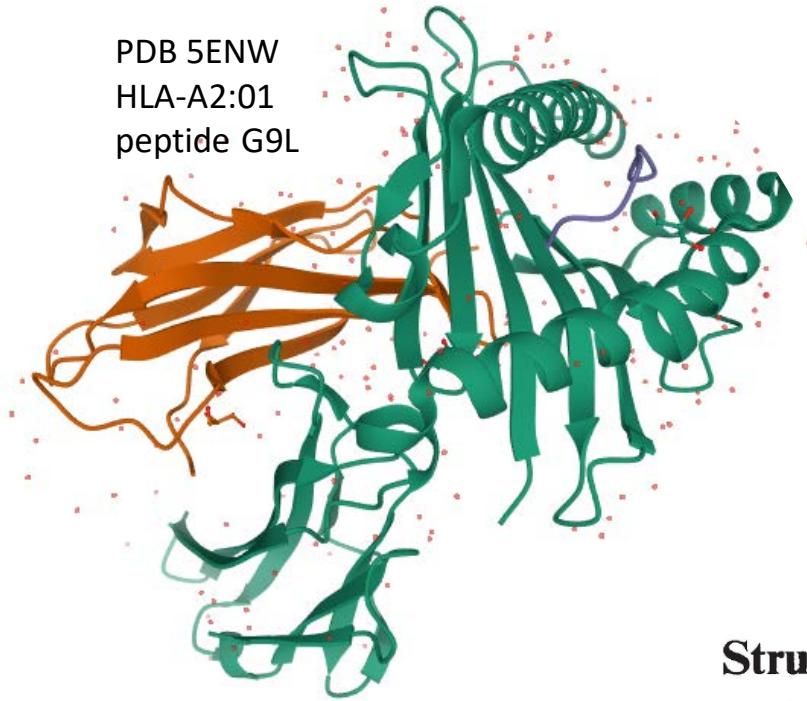
*H-2 COMPATIBILITY IS REQUIRED FOR T-CELL-MEDIATED
LYSIS OF TARGET CELLS INFECTED WITH LYMPHOCYTIC
CHORIOMENINGITIS VIRUS*

By PETER C. DOHERTY AND ROLF M. ZINKERNAGEL

- MHC on target cell matters
- Immunoprecipitation, serology, monoclonal antibodies to MHC provide evidence the genetic linkage is identity
- Does MHC bind antigen?



PDB 5ENW
HLA-A2:01
peptide G9L



Binding of immunogenic peptides to Ia histocompatibility molecules

Bruce P. Babbitt*, Paul M. Allen*, Gary Matsueda†, Edgar Haber† & Emil R. Unanue*

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* Washington University School of Medicine, St Louis, Missouri 63110, USA

† Cardiac Unit, Massachusetts General Hospital, Boston, Massachusetts, 02114, USA

Structure of the human class I histocompatibility antigen, HLA-A2

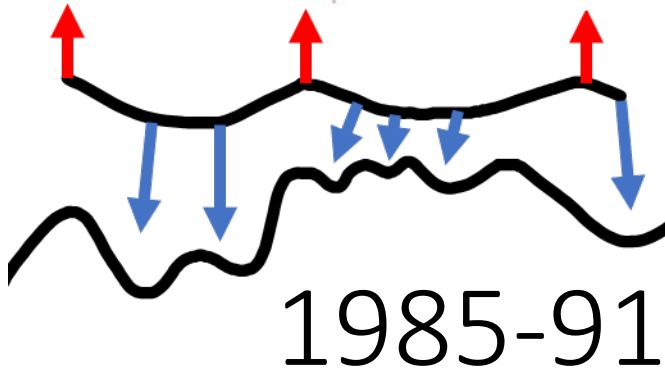
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Ag Presentation
Danger Signals
T-cell Receptor

ARTICLES

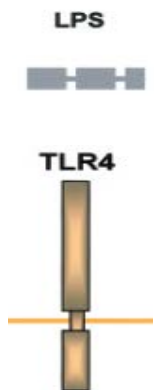
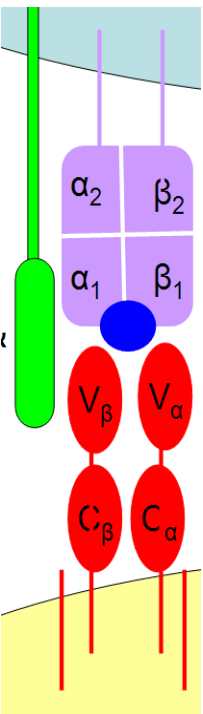
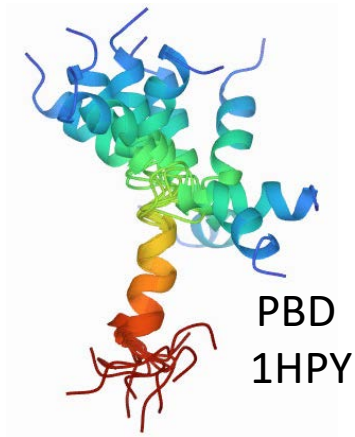
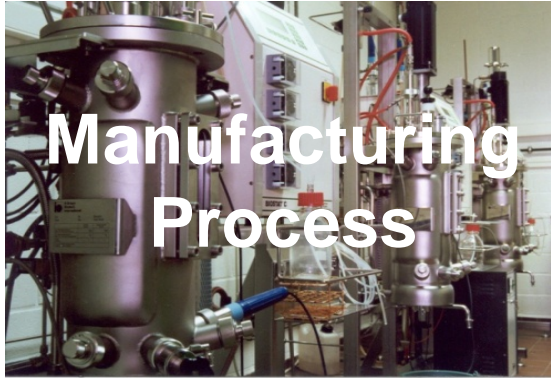
Allele-specific motifs revealed by sequencing of self-peptides eluted from MHC molecules

Kirsten Falk, Olaf Rötzschke, Stefan Stevanović*, Günther Jung* & Hans-Georg Rammensee†

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Pathways



Goals

- Discuss regulatory concerns and considerations regarding the use of non-clinical assays for immunogenicity assessment of generic peptides
- Foster communication regarding technical challenges with validating or performing assays to assess immunogenicity risk and help establish best practices.
- Explore future research directions that facilitate the performance of sensitive and reproducible assays to assess the immunogenicity risk of impurities in generic peptide products



Thank You!