

Potent Immunity Achieved by Targeted, Sequential Administration of Recombinant DNA Vectors and Anchor-Modified Epitope Peptides

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➤ *Diabetes*

- ✦ *Late stage development*

➤ *Oncology*

- ✦ *Early stage development*



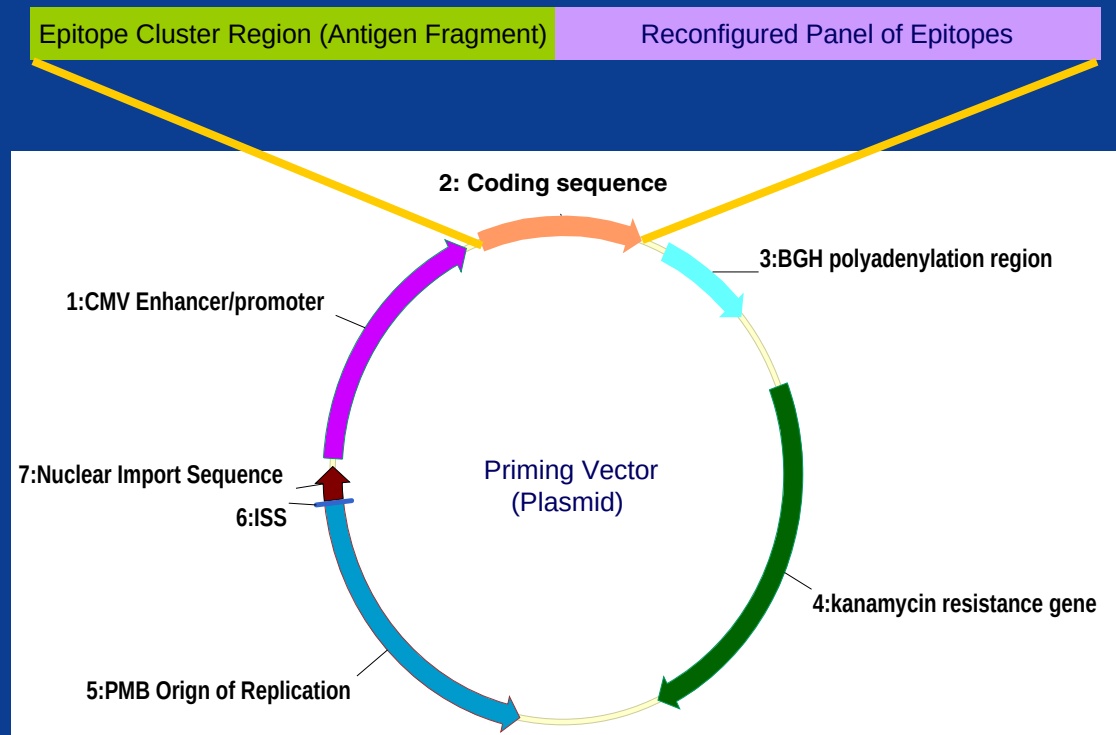
Plasmid Vectors: a Typical Case of Yin & Yang

Features

- Co-expression of Tc and Th epitopes
- CpG motifs

Response

- T1 immune profile
- Limited magnitude



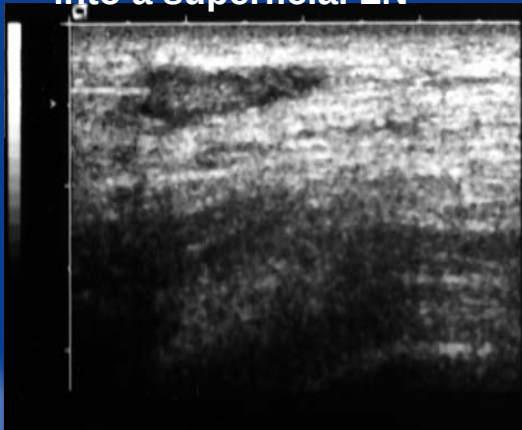


Targeted Intra-Lymph Node Delivery

Imaging the inguinal lymph node

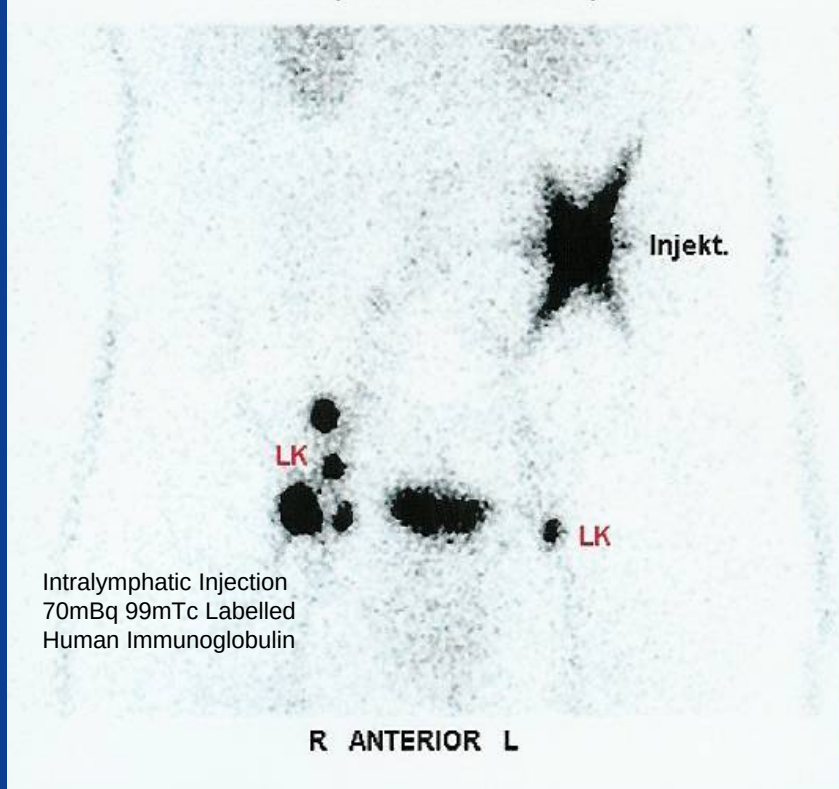


Insertion of a needle into a superficial LN



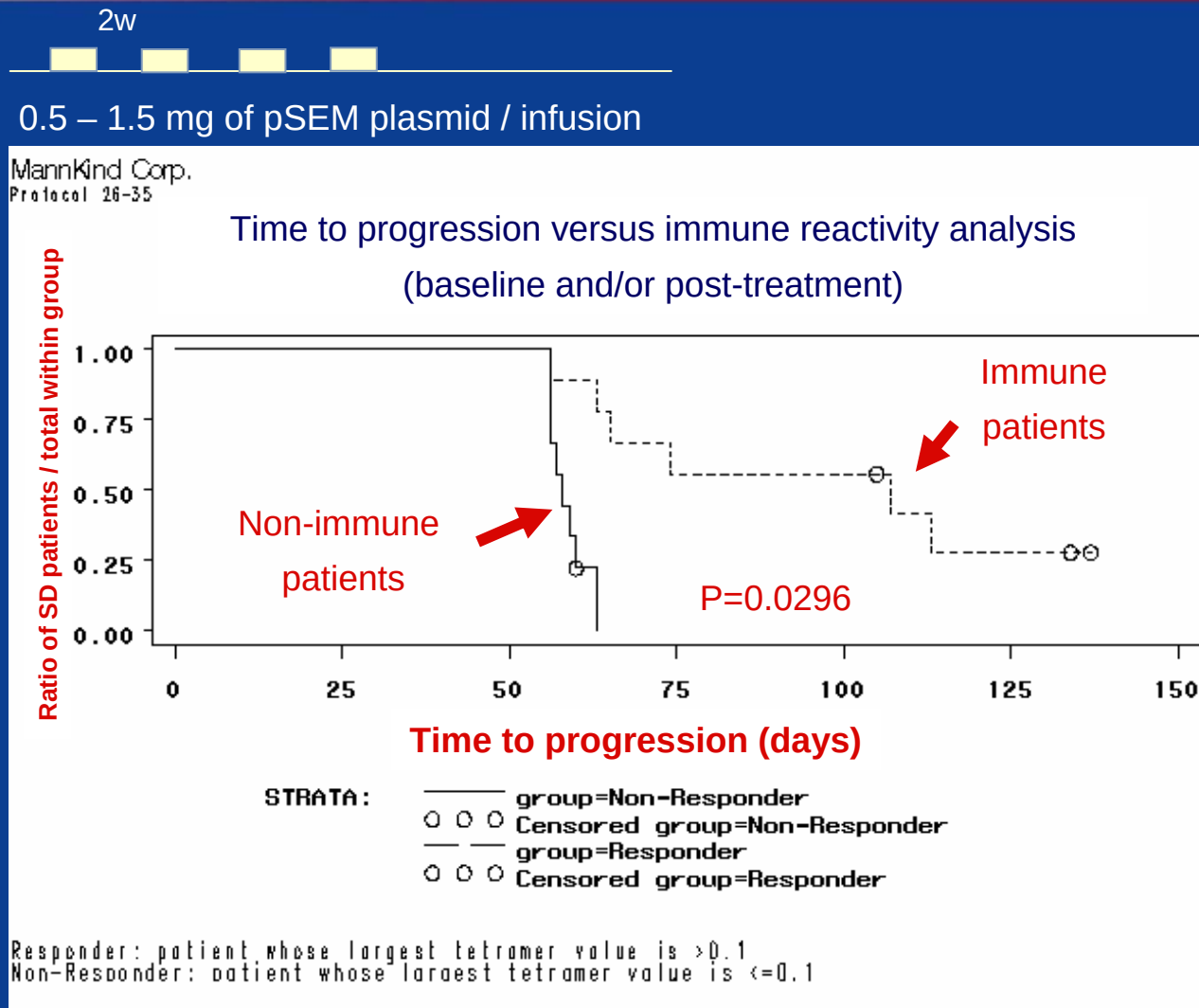
Imaging of draining lymph nodes subsequent to administration of radio-labeled tracer

70 MBq 99mTc-HIG bds 4h p.i.





Immune Reactivity to a Tumor Associated Antigen Correlates with the Clinical Outlook



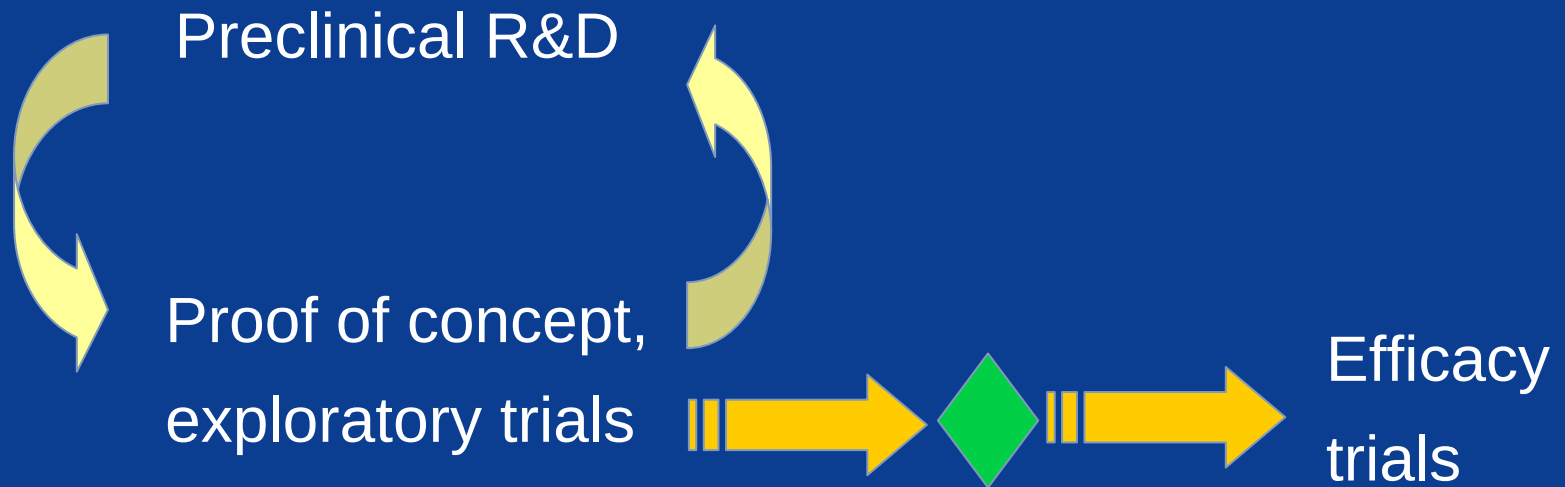


Two Mutually Exclusive Possibilities

- TAA immunity is mechanistically relevant
 - ✦ The immunization methodology needs improvement
- TAA immunity is largely an epiphenomenon

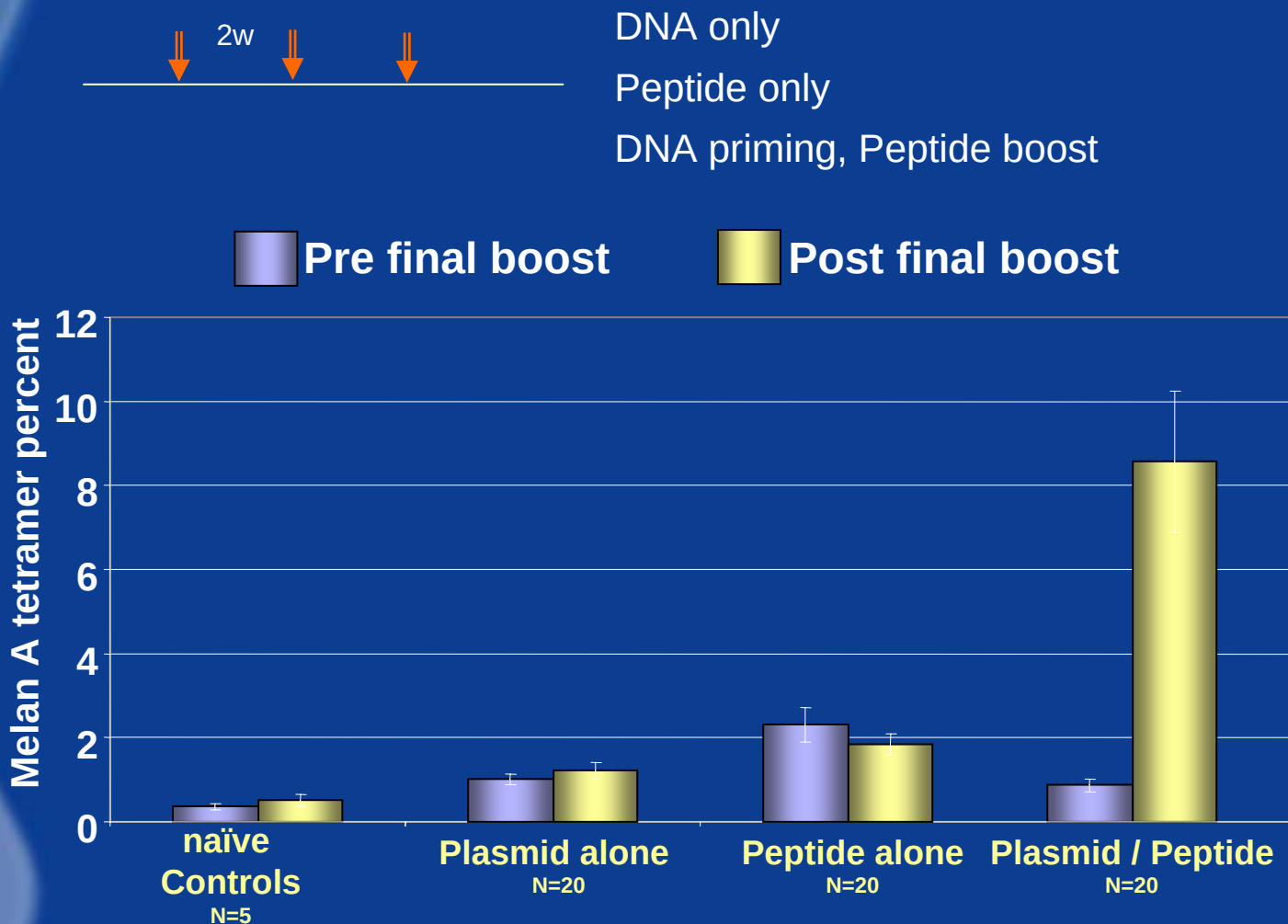


Optimization of Active Immunotherapeutic Strategies in Development



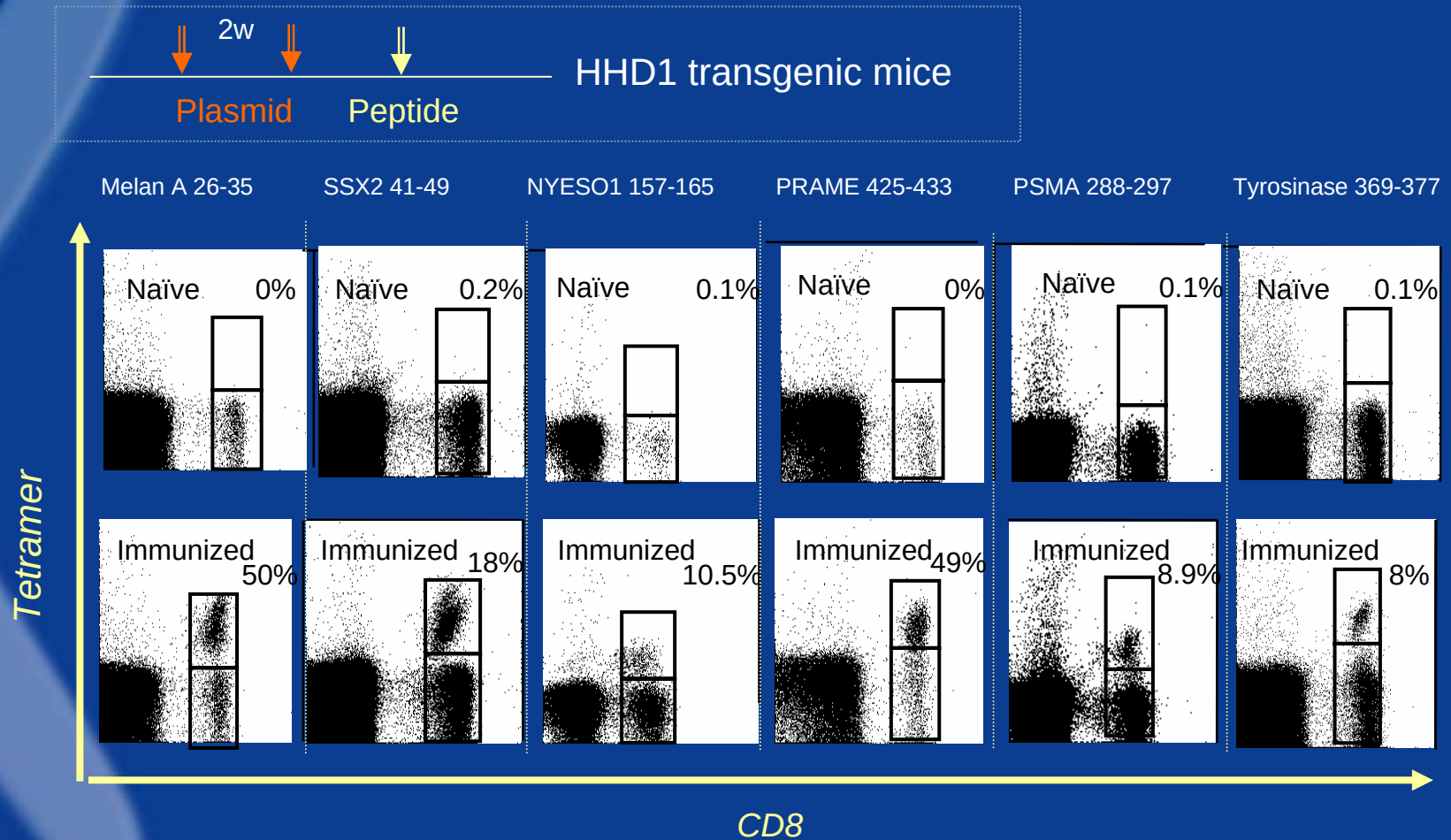


Building on the Immune Response Initiated by Plasmid DNA: Preclinical Data





Robust Expansion of T Cell Immunity against Self or Non-Self Epitopes by Targeted, Lymph Node Delivery of Peptide Analogues



A Novel Immunotherapeutic Approach: Features

➤ ***Multi-component***

- ✦ Plasmids and peptide analogues
- ✦ Peptides are anchor-modified

➤ ***Multivalent***

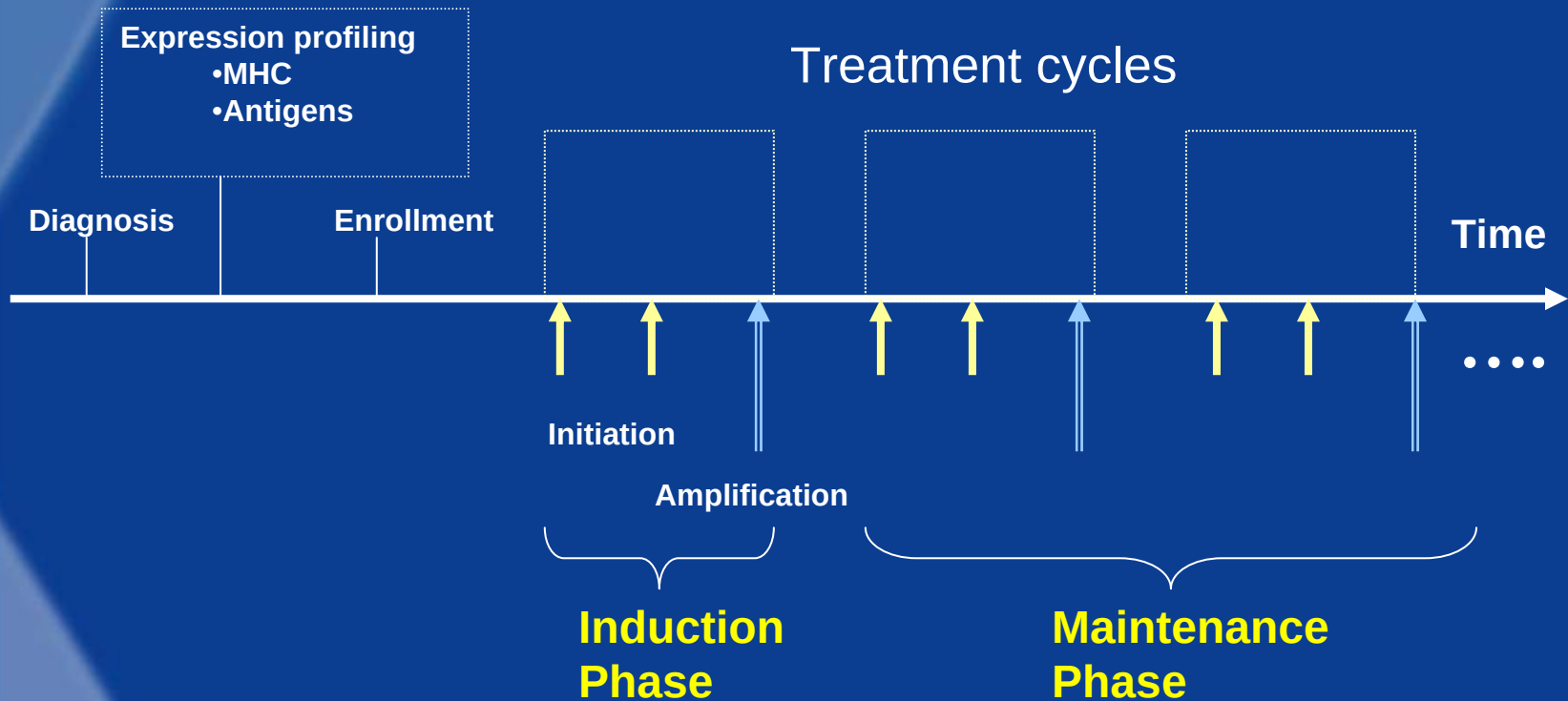
- ✦ Co-targets
 - Cancer cells
 - Neovasculature

➤ ***Targeted Approach***

- ✦ Lymph node delivery
- ✦ 'Theranostic' strategy



Prospective Immunization Protocol

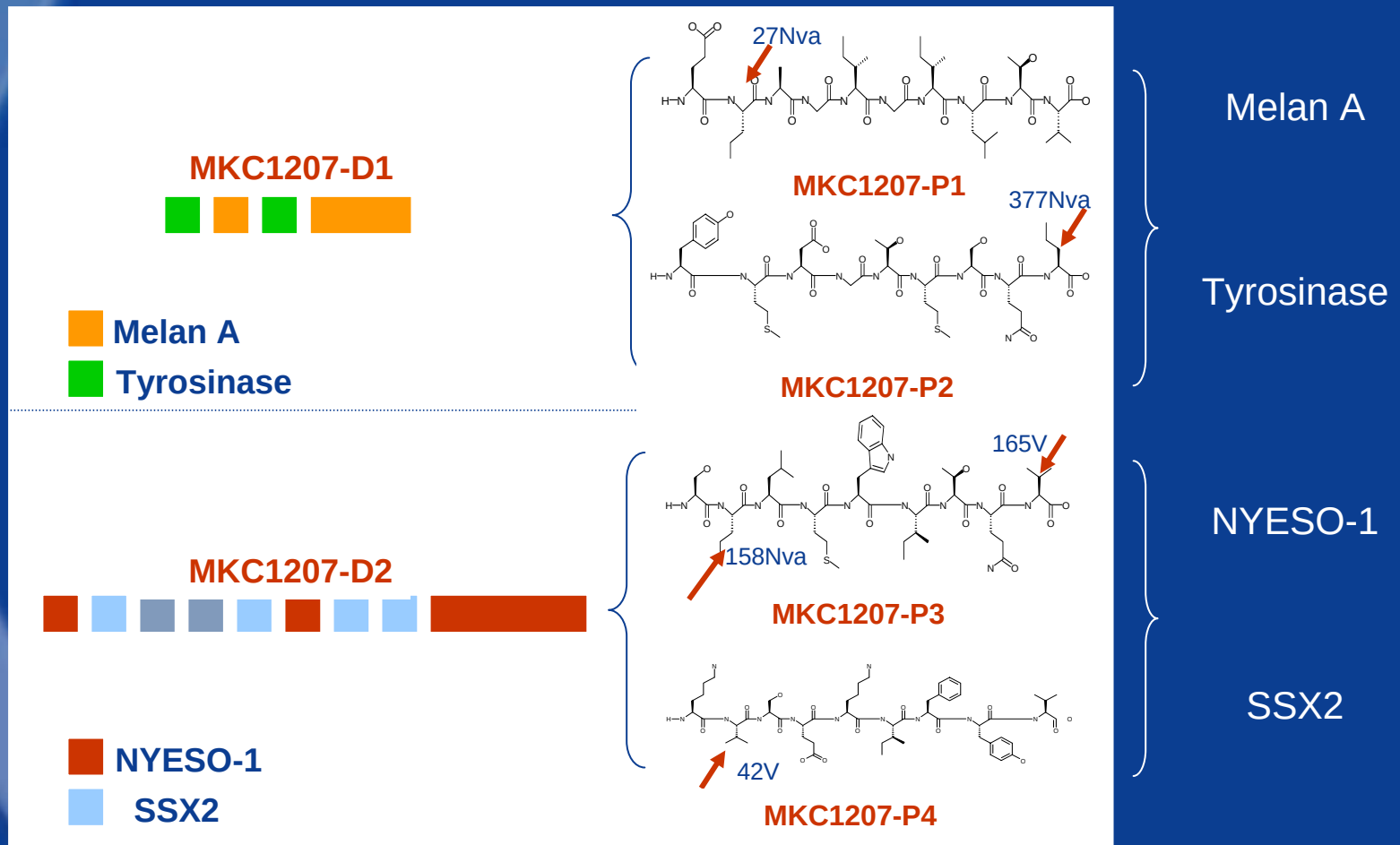


A Multivalent Immunotherapeutic Candidate for Melanoma

Plasmids (expressed portion)

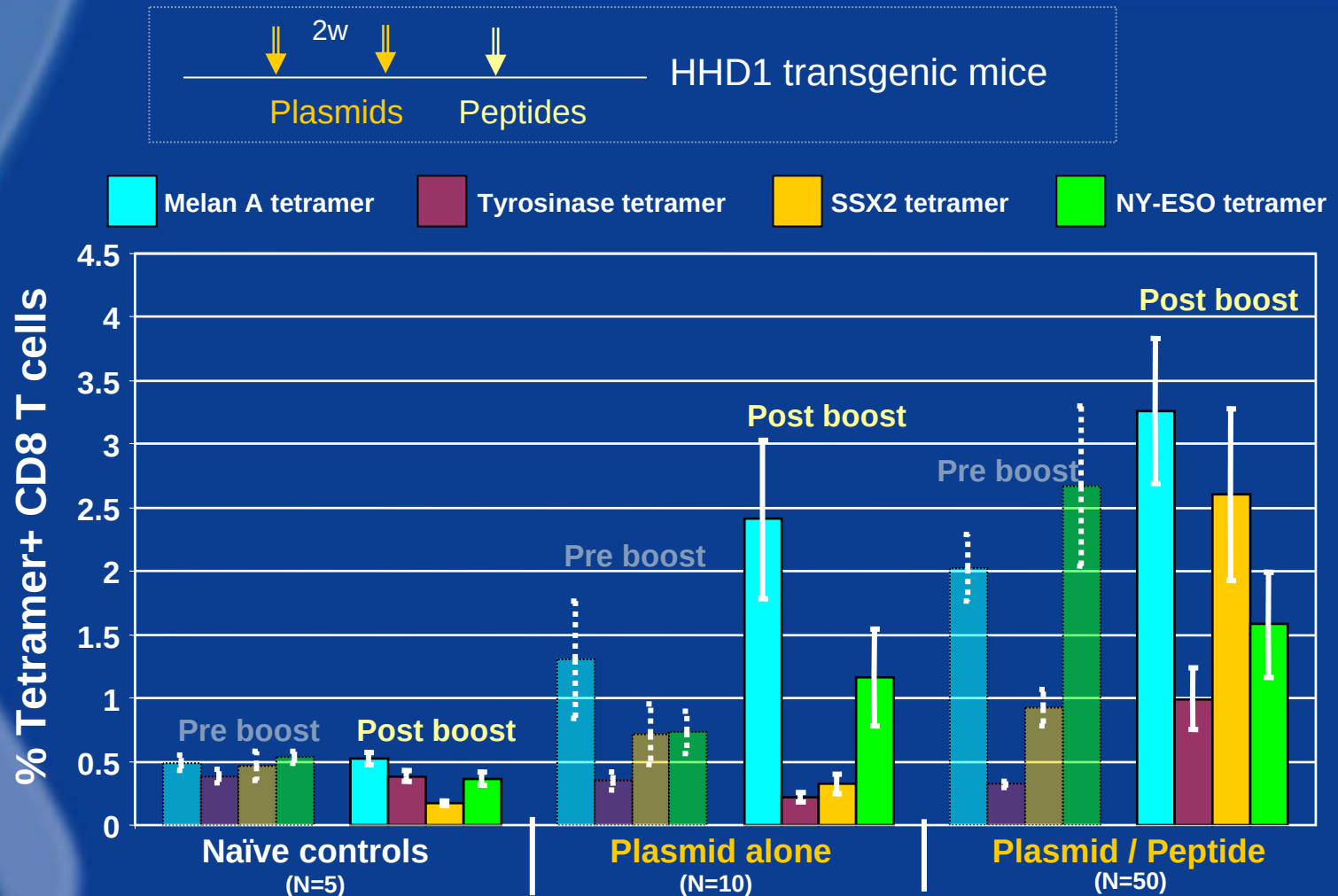
Peptides

Targets





A Multivalent Immunotherapeutic Candidate for Melanoma

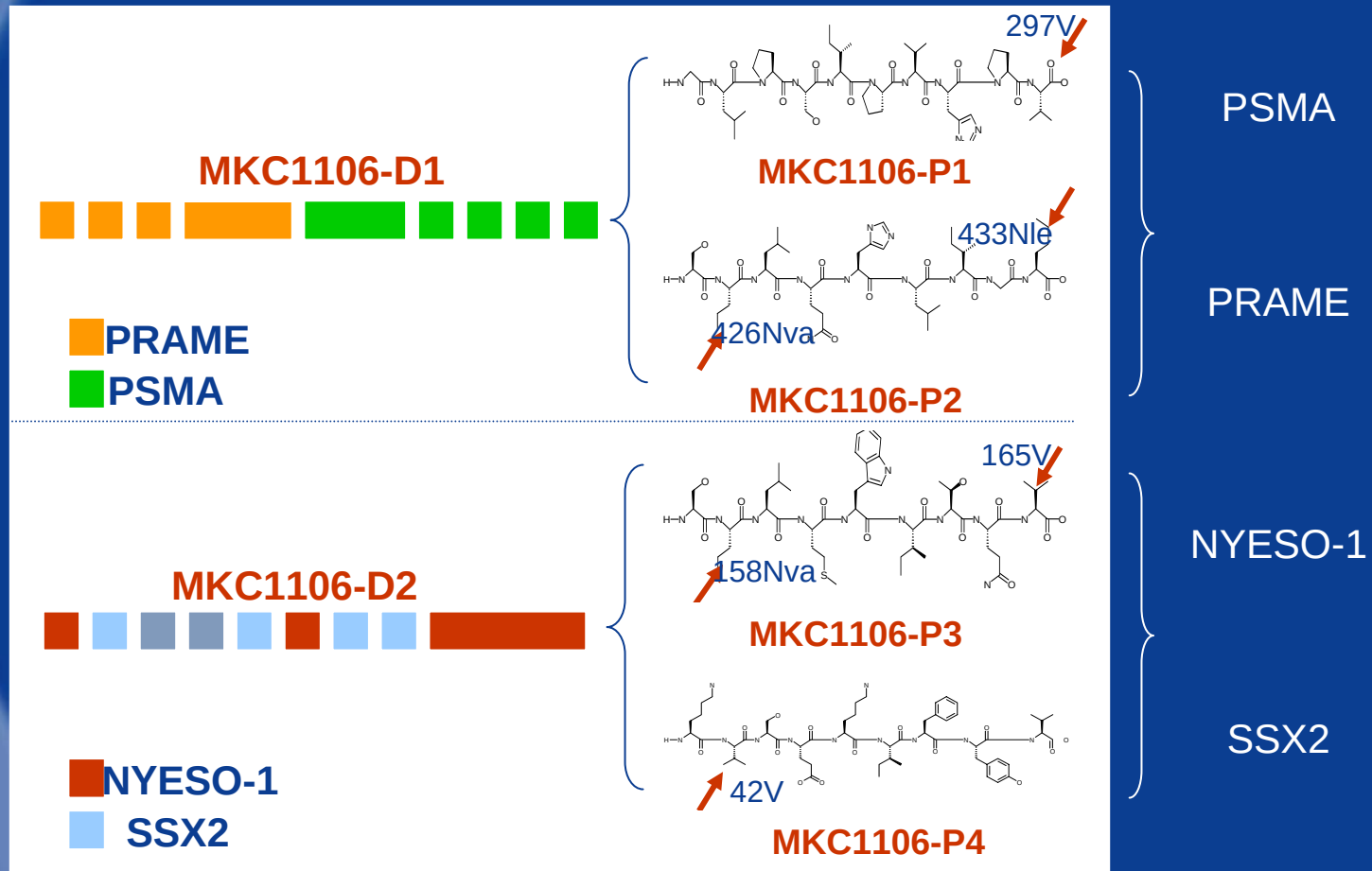


A Multivalent Immunotherapeutic Candidate for Ovarian Carcinoma

Plasmids (expressed portion)

Peptides

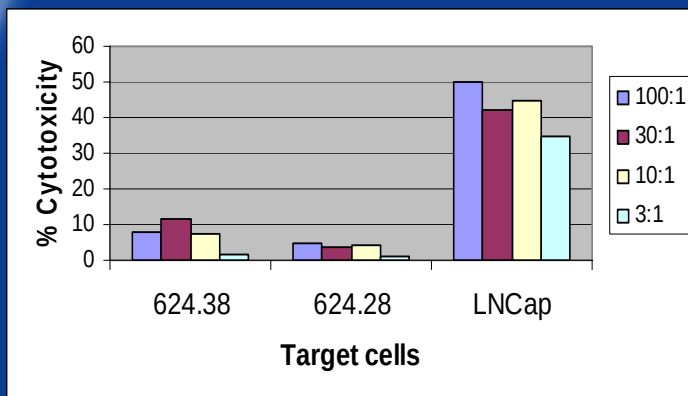
Targets



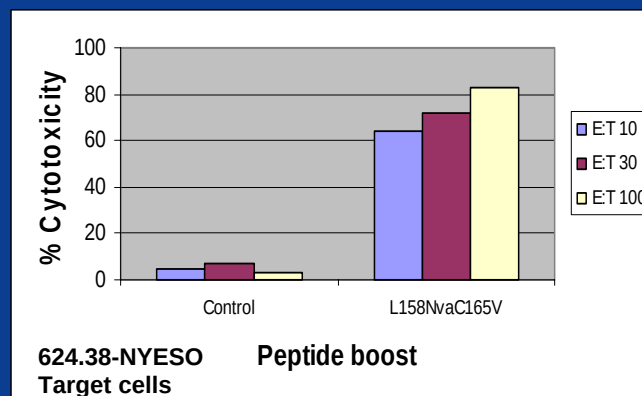


A Multivalent Immunotherapeutic Candidate for Ovarian Carcinoma

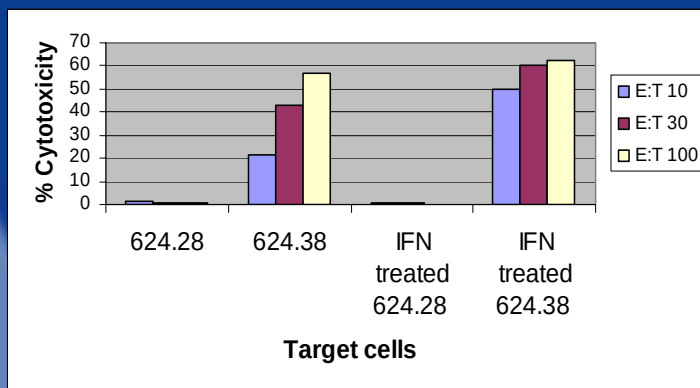
PSMA



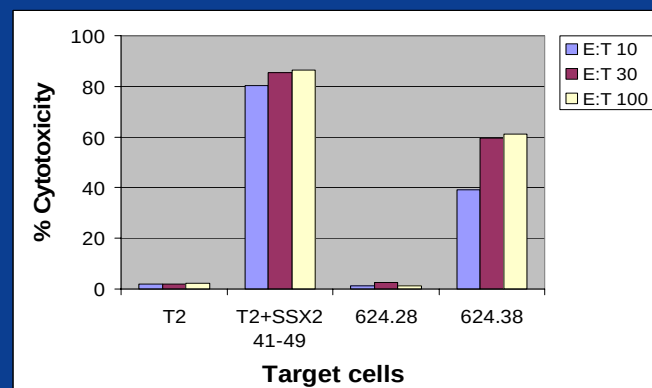
NYSEO-1



PRAME



SSX2





Directions

- Preclinical development
- Proof of principle in exploratory trials
 - ✦ Safety, immunity, relationship with clinical outcome
- Optimization
 - Composition
 - Combinatorial approach
 - ◆ Approved therapeutics
 - ◆ Novel therapeutic candidates
- Efficacy trials



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