Vaccines that Induce Broadly Neutralizing Antibodies against Human Papillomaviruses

Project #2

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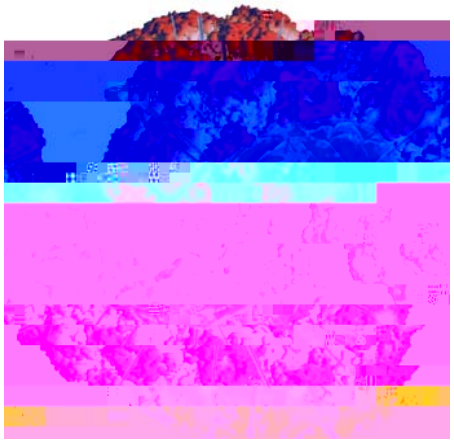
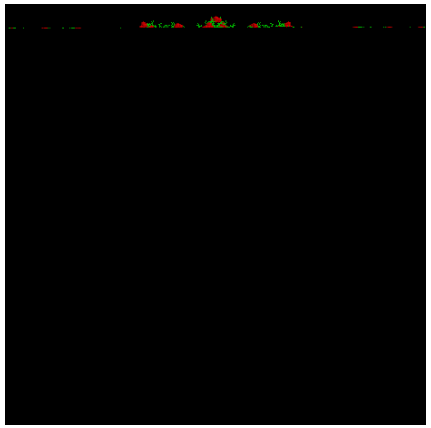


Project # 2 Background Rationale
Virusπlike Particles: Flexible Platforms for Vaccine Development



Virus like Particles (VLPs) are composed of viral coat proteins that, when overexpressed, spontaneously self assemble into particles that are indistinguishable from infectious virus

- VLPs can be derived from diverse virus types as **highly effective vaccines** against the virus from which they are derived
- The dense, repetitive structure of VLPs confers **high immunogenicity**
- VLPs can also be used a platforms for display of **heterologous antigens**
- VLP display is so immunogenic it effectively targets **self antigens**
- We have used this strategy to induce high titer antibody responses against a wide variety of targets, including:

Displaying heterologous antigens on VLPs

Using VLPs derived from bacteriophage (MS2, Qß, and PP7), we have developed a suite of technologies targeting diverse pathogens and self antigen targets

1)Chemical Conjugation of target antigens to the surface of preformed Qß VLPs.

TNF alpha (J Clinical Invest 2002)

Amyloid beta (BMC Neuroscience 2004, Vaccine 2006, J Neur Pharm 2010)

CCR5 (J Virol 2004, Vaccine 2009)

2)Genetic Insertion of target peptides onto the surface of MS2 and PP7 VLPs

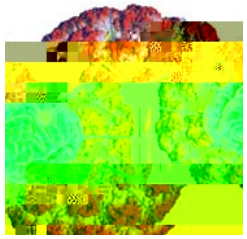
CCR5 (J Mol Biol 2008)

HPV L2 (unpublished data)

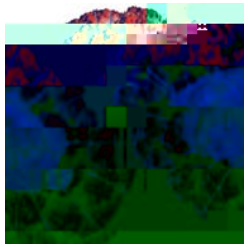
3)Affinity Selection of specific VLPs from a library of VLPs that display random peptides (i.e. phage display on VLPs).

HIV gp41 (funding from the Gates Foundation)

Anthrax Protective Antigen (unpublished data)



Project #2 Aims



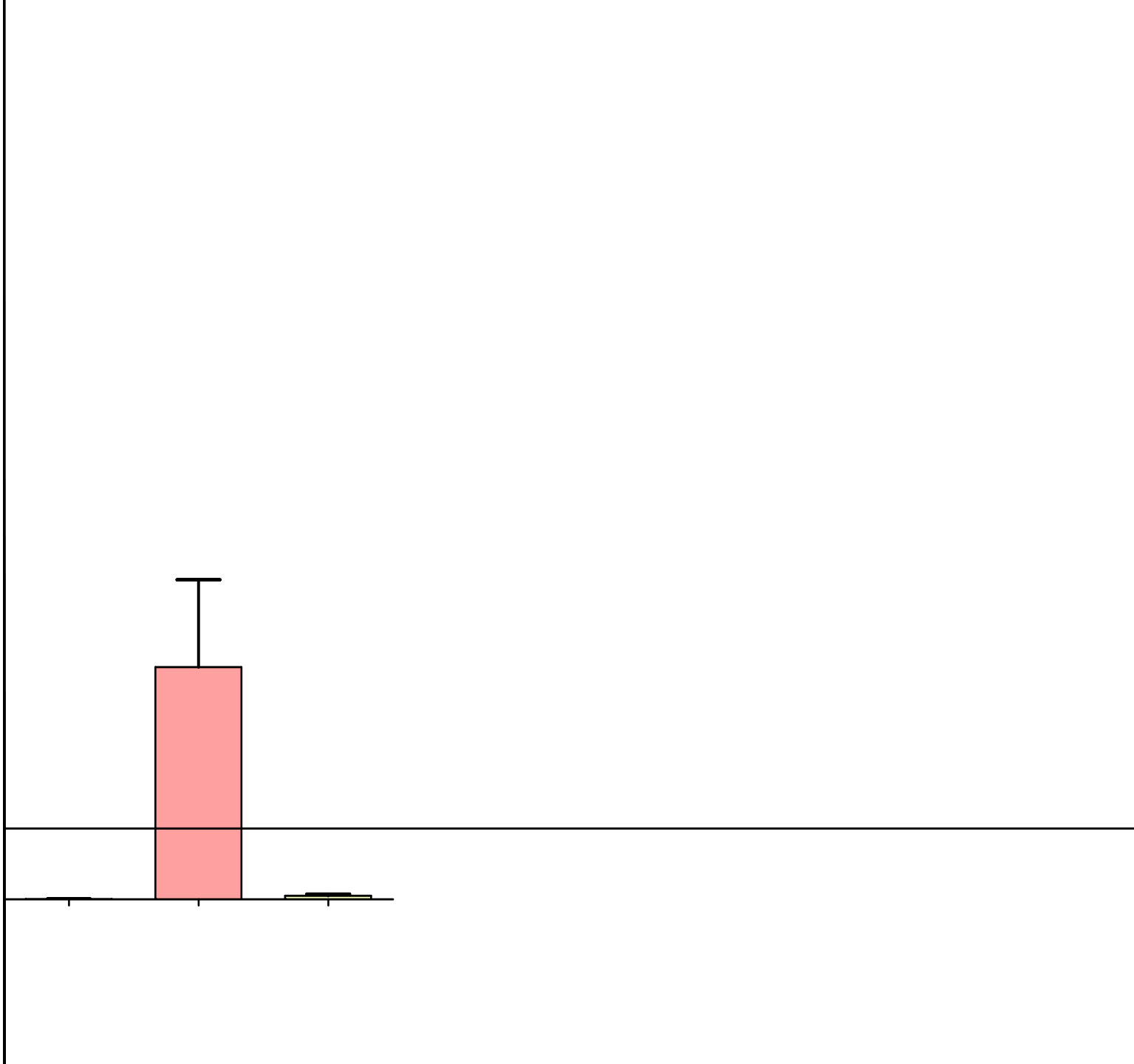
CENTRAL HYPOTHESIS: Current HPV vaccines only provide protection against 2 of at least 15 carcinogenic HPV genotypes. HPV L2 minor capsid protein contains inter-typic cross neutralizing epitopes for which immunogenicity can be enhanced using VLP-display technology

AIM 1: Rational design of peptide displaying VLP based vaccines targeting L2 neutralizing epitopes

AIM 2: Identification of novel candidate vaccines by genetic display of L2 epitopes on VLPs

AIM 3: Induction of mucosal and systemic immune responses against HPV vaccines – evaluation of aerosol delivery systems

Results Project #2
PP7 VLPs displaying a 16 aa epitope derived from HPV 16 L2



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