

Antibody Standards Derived from Trans-chrosomic Bovine

Presentation prepared by LCDR Nicholas J Martin, PhD for discussion at
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Background

- The Naval Medical Research Center (NMRC) has established a cooperative research and development agreement with Sanford Applied Biosciences (SAB) to develop antibody standards and therapeutics for viral diseases
 - SAB developed a large animal (bovine) trans-chromosomal (Tc) platform to produce fully human antibodies
 - These cattle have the entire human immunoglobulin (Ig) heavy (H) and light (L) chain loci
 - Animals are capable of producing 30-60 L of plasma (150-300 g purified human immunoglobulin) each month

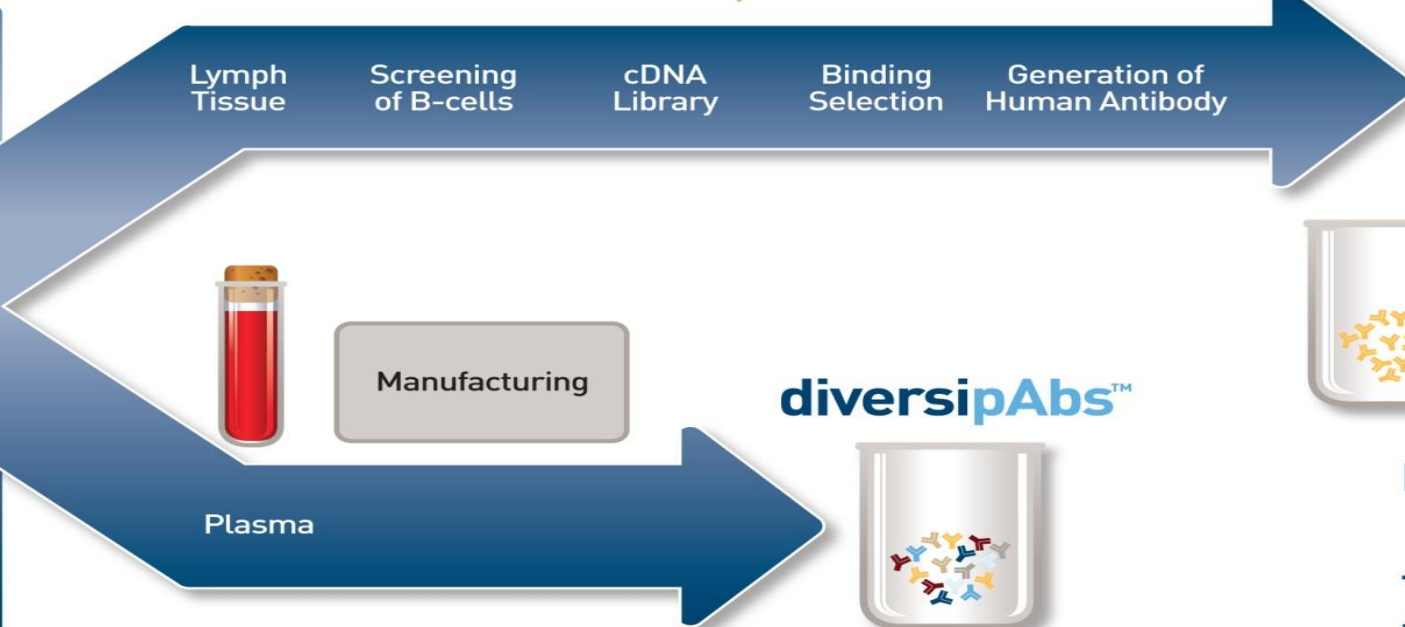
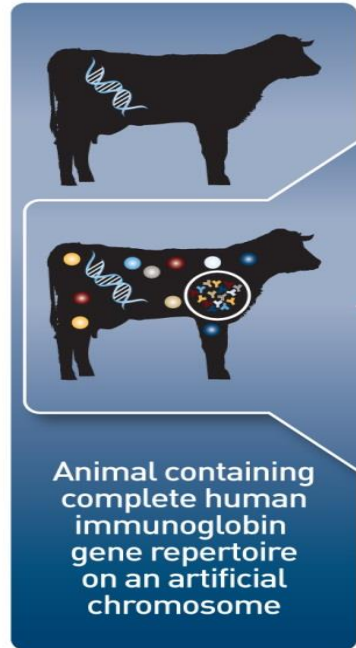


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Antibody Diversity is the key to successfully treating human disease



diversitAb™ platform



diversipAbs™



Polyclonals

diversimAbs™

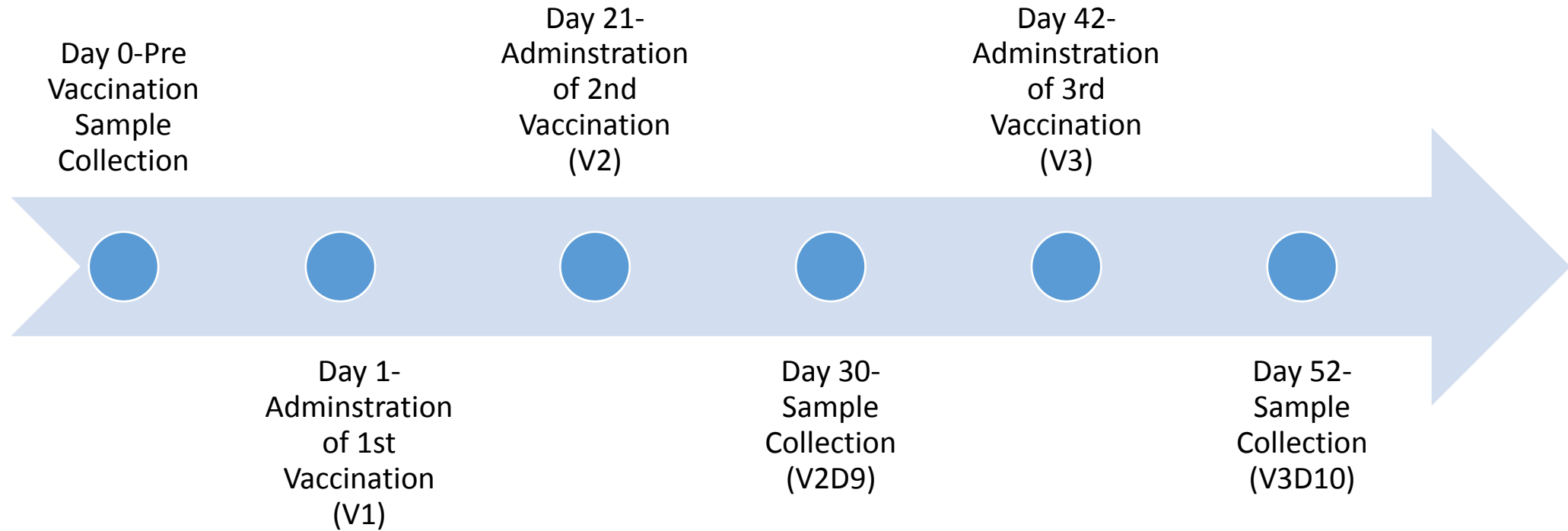


Monoclonals

Oligoclonals

The best system to make fully HUMAN polyclonal and monoclonal antibodies

Vaccination

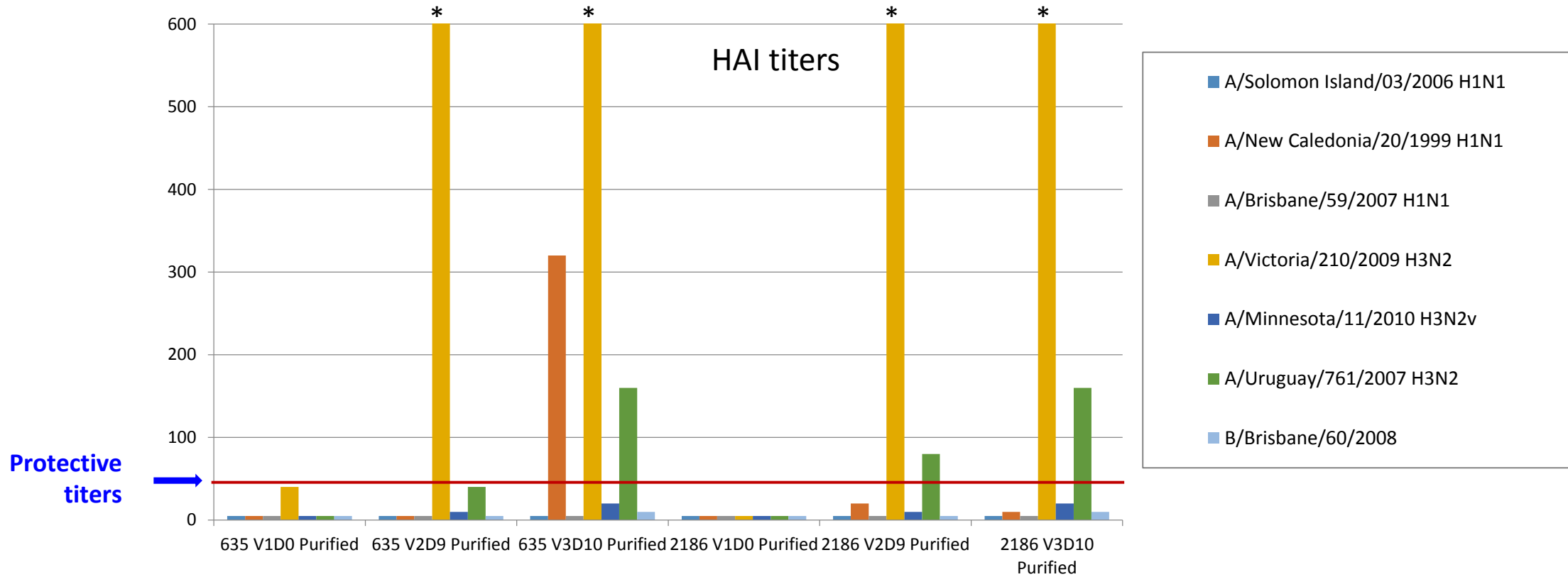


Results

	Day	H1N1	H3N2	Influenza B
Animal 635	0	ND	ND	ND
Animal 635	30	2560	320	640
Animal 635	52	1810	1280	2560
Animal 2186	0	ND	ND	ND
Animal 2186	30	5120	1280	1280
Animal 2186	52	1810	2560	5120
Animal 635 Purified IG	0	ND	ND	ND
Animal 635 Purified IG	30	2560	160	320
Animal 635 Purified IG	52	3620	2560	2560
Animal 2186 Purified IG	0	ND	ND	ND
Animal 2186 Purified IG	30	5120	640	640
Animal 2186 Purified IG	52	1280	1280	1280



Tc animals generated cross reactive antibodies against flu viruses not in seasonal vaccine



* Titers $\geq 1,200$



Conclusions

- The HAI results demonstrate the Tc-bovine produced high titers in response to the administered vaccine
 - MN assays were performed for a single time point resulting in 2-day MN titers of >5,000 against A/California/7/2009
- The high HAI and MN results, coupled with the ability of each animal to produce 30 - 60 L plasma/month could be leveraged to generate control plasma in 30-60 days



Future Work

- Additional work is planned to evaluate Ab generation following administration of inactivated virus and virus like particles (VLPs)
 - Leverages NMRC's experience with virus inactivation and SAB's Tc-bovine platform
 - Current/future efforts include evaluating immune responses against the following viruses:
 - Dengue types 1 – 4
 - MERS-CoV
 - Filovirus VLPs





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