Advice from AVRWG on Adevovirus Vectors

On January 30, 2007 a one-day Workshop was convened with DAIDS' AIDS Vaccine Working Group (AVRWG) to review adenovirus (Ad)-based HIV vaccine research currently funded by the NIH and assess the need for DAIDS' further funding in this area. The most advanced Ad-based HIV vaccines utilize Ad5 serotype as the vector, with Merck's vaccine in Phase IIb clinical trials and VRC's vaccine gearing up toward Phase IIb trials. To overcome the potential problem of pre-existing Ad5 immunity dampening immune responses to the current rAd5-based HIV vaccines, many investigators have developed alternative strategies. The majority of the currently funded approaches at the preclinical stage are based on rare human and chimpanzee serotypes or novel adenoviral chimeras to be used as priming or boosting agents for the Ad5-based vaccines or as alternatives to Ad5.

The first presentation by the HVTN (HIV Vaccine Trial Network) highlighted ongoing and planned Phase IIB clinical studies with the Merck and VRC rAd5 HIV vaccines. Subsequently the two lead companies funded through NIAID, Crucell and GenVec, presented the companies' perspectives on development of the adenovirus platform technology emphasizing approaches to their respective vaccines. The remainder of the workshop focused on current approaches to using alternative adenovirus serotypes (human and chimpanzee), chimeric hexon/fibers, and replicating adenoviruses by individual investigators. The attached Table highlights key information from the different presentations.

Finally, AVRWG members provided feedback on the following points raised by DAIDS:

1. Is future funding for the development of alternative serotype/novel Ad-based vaccines: sufficient, insufficient, or should be limited?
2. What support is appropriate for further development of alternative serotype/novel Ad-based approaches that already exist?

The overall consensus was that DAIDS provides sufficient funding for alternative serotypes/novel Ad-based approaches, and should consider limiting future funding to those situations in which the PI was able to demonstrate significant improvements over the existing approaches. Based on this recommendation, DAIDS will include language in future vaccine development Program Announcements and RFPs/BAAs that discourage applicants from seeking funding for rAd-based vector approaches unless such improvements are demonstrated. AVRWG also recommended that DAIDS should continue to fund the alternative serotypes/novel Ad-based approaches currently under development.

Adenovirus-Vectored HIV Vaccines

Adenovirus Vector	HIV inserts	Developer/Manufacturer/ Cell Substrate	Phase of Development
Ad5 serotype	3 separate vectors: Gag, Pol, Nef (clade B)	Merck (PER.C6)	Phase II/IIB studies
Ad5 serotype	4 separate vectors: clade B Gag/Pol, clade A Env, clade B Env, clade C Env	VRC/GenVec (293)	Phase II/IIB studies
Ad6 serotype	3 separate vectors: Gag, Pol, Nef (clade B)	Merck	Phase I studies
Ad35 serotype	clade A Env	VRC/GenVec (293)	IND 2Q 07
Ad5 ΔCAR, Ad5ΔRGD	N/A, reporter genes	VRC/GenVec (293)	in development
Ad35/Ad5-fiber shaft/knob	N/A, reporter genes	VRC/GenVec (293)	in development
Ad41 serotype	clade A Env	VRC/GenVec (293)	in development
Ad35	Gag/RT-IN/Nef and Env(clade C)	IAVI/Transgene (Crucell, HER96)	IND/EU target 3-4Q 07, PI target 2Q 08
Ad C7 (non-human primate Ad)	Gag/RT-IN/Nef and Env(clade C)	IAVI/GSK/Cobra (Crucell, HER96)	in development
Ad26 serotype	clade A Env	Barouch (Harvard)/Crucell (HER96)	4Q 07
Ad5HVR48 (hexon chimera)	clade A Env	Barouch (Harvard)/Crucell (HER96)	1Q 07
Ad C6 and C7 (non-human primate Ad)	clade B Gag/Pol/Nef, possibly Env	Ertl (Wistar)/Molecular Medicine (293)	in early development
Ad4 serotype-replication competent	clade C Env	Robert-Guroff (NCI)/NIAID/TBD	in development