



TUBERCULOSIS VACCINE CANDIDATES – 2009

Stop TB Partnership Working Group on New TB Vaccines

According to the Global Plan to Stop TB, 2006-2015, “Encouraging and consistent scientific results from the laboratory and from early field trials indicate that the introduction of new, effective TB vaccines will be an essential component of any strategy to eliminate tuberculosis (TB) by 2050. New TB vaccines to prevent childhood and adult forms of tuberculosis, to reduce tuberculosis in persons co-infected with HIV, and to shorten drug treatment regimens will fundamentally alter our approach to TB control.”

A number of the new generation of TB vaccines may work best using a heterologous prime-boost strategy to complement the immune response induced by the current BCG. This “prime-boost” strategy could include administration of BCG or a new recombinant live replacement vaccine as the “prime”, followed by a “booster” inoculation with a different vaccine to infants and young children before they are exposed to TB (pre-exposure), as a separate booster to young adults, either before they are exposed or who may have already been exposed to TB (post-infection) or as an adjunct to chemotherapy (immunotherapy).

TB vaccines under development could work in several ways:

- Prevent infection
- Prevent primary disease
- Prevent latent infection
- Prevent reactivation of latent infection
- Shorten the course and improve the response to chemotherapy

The [2009 Pipeline of Tuberculosis Vaccine Candidates](#) is highlighted in the following **Table** of Tuberculosis Vaccine Candidates currently under development and presented in the following categories:

Candidates in Clinical Trials-2009 (Section I): TB vaccine candidates that are in clinical studies as of 2009. Vaccines that have been in earlier clinical studies but are not currently being actively pursued as candidates are listed as “In Active”.

Candidates in Advanced Preclinical Studies & GMP-2009 (Section II): TB vaccine candidates that are not yet in clinical trials, but as of 2009 have been manufactured under Good Manufacturing Practice (GMP) for clinical use and have undergone some preclinical testing that meets regulatory standards.

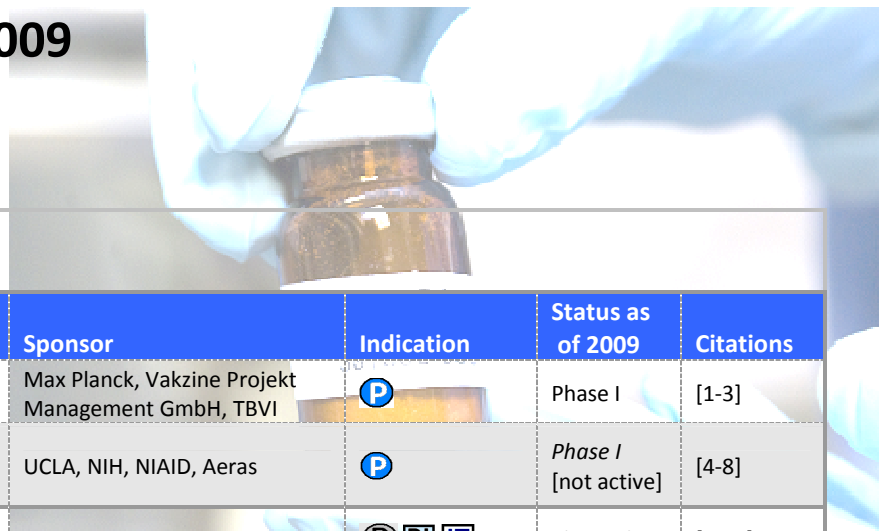
Next Generation Candidates-2009 (Section III): TB vaccines candidates that are in the research and development stage with some preclinical testing performed to show that they may contain protective antigens.

Vaccine candidates are further divided into specific Vaccine Types: Recombinant Live; Viral Vected; Recombinant Protein or Other and a brief description is provided. The Table lists vaccines intended to be used as a Prime (P) or Booster (B) vaccine, as a Post-infection vaccine (PI) or in immunotherapy (IT).

The information contained here was provided by the vaccine developers, unless otherwise indicated (noted by asterisk in Table).

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SECTION I: Candidates in Clinical Trials - 2009						
Type of Vaccine	Products	Product description	Sponsor	Indication	Status as of 2009	Citations
Recombinant Live	VPM 1002	<i>rBCG Prague strain expressing listeriolysin and carries a urease deletion mutation</i>	Max Planck, Vakzine Projekt Management GmbH, TBVI	P	Phase I	[1-3]
	rBCG30	<i>rBCG Tice strain expressing 30 kDa Mtb antigen 85B; phase I completed in U.S..</i>	UCLA, NIH, NIAID, Aeras	P	Phase I [not active]	[4-8]
Viral Vectedored	Oxford MVA85A / AERAS-485	<i>Modified vaccinia Ankara vector expressing Mtb antigen 85A</i>	OETC, Aeras	B PI IT	Phase IIb	[9-13]
	Crucell Ad35/ AERAS-402	<i>Replication-deficient adenovirus 35 vector expressing Mtb antigens 85A, 85B, TB10.4</i>	Crucell, Aeras	B	Phase II	[14-17]
	AdAg85A	<i>Replication-deficient adenovirus 5 vector expressing Mtb antigen 85A</i>	McMaster University	P B	Phase I	[18-22]
Recombinant Protein	Hybrid-I+IC-31	<i>Adjuvanted recombinant protein composed of Mtb antigens 85B and ESAT-6</i>	SSI, TBVI, Intercell	P B PI	Phase IIa	[23-26]
	Hybrid-I+CAF01	<i>Adjuvanted recombinant protein composed of Mtb antigens 85B and ESAT-6</i>	SSI	P B PI	Phase I	–
	M72	<i>Recombinant protein composed of a fusion of Mtb antigens Rv1196 and Rv0125 & adjuvant</i>	GSK, Aeras	B PI	Phase II	[27-29]
	HyVac 4/AERAS-404	<i>Adjuvanted recombinant protein composed of a fusion of Mtb antigens 85B and TB10.4</i>	SSI, Sanofi-Pasteur, Aeras, Intercell	B	Phase I	[30, 31]
Other	RUTI	<i>Fragmented Mtb cells</i>	Archivel Farma, S.I.; Badalona, Spain	B PI IT	Phase I	[32-36]
	<i>M. vaccae</i>	<i>Inactivated whole cell non-TB mycobacterium; phase III in BCG-primed HIV+ population completed; reformulation pending</i>	NIH, Aeras, Immodulon	B PI IT	Phase III	[37-41]
	<i>M. smegmatis</i> *	<i>Whole cell extract; phase I completed in China</i>	*communicated by the Wuhan Inst. of Biol.Products	B PI IT	Phase I [not active]	–

P Prime, B Boost, PI Post-infection, IT Immunotherapy






























SECTION II: Candidates in Preclinical Studies & GMP- 2009





Type of Vaccine	Products	Product description	Sponsor	Indication	Citations
Recombinant Live	AERAS-rBCG	<i>rBCG Danish 1331 strain expressing perfringolysin and at least three Mtb antigens or with ΔsecA2-DNIsodA modification (dominant-negative interfering SodA mutant)</i>	Aeras	P	[14, 16, 42]
	Mtb [ΔlysA ΔpanCD ΔsecA2]	<i>Non-replicating, Mtb strain auxotrophic for lysine and pantothenate; attenuated for secA2</i>	Albert Einstein School of Medicine	P	[43, 44]
	MTBVAC01 [ΔphoP, Δfad D26]	<i>Live vaccine based on attenuation of Mtb by inactivation of phoP and fad D26 genes</i>	University of Zaragoza, Institute Pasteur, TBVI	P	[45-49]
Recombinant Protein	HBHA	<i>Naturally methylated 21-kDa purified protein from M.bovis BCG</i>	Institute Pasteur of Lille, INSERM	P B PI IT	[50-54]
	Hybrid 56	<i>Adjuvanted recombinant protein composed of Mtb antigens 85B, ESAT-6 and Rv2660</i>	SSI, Aeras, Intercell	P B PI	–
Other	HG85 A/B	<i>Chimeric DNA vaccines—Ag85A/Ag85B</i>	Shanghai H&G Biotech	B IT	[55-59]

SECTION III: Next Generation Candidates – 2009





Type of Vaccine	Products	Product description	Sponsor	Indication	Citations
Recombinant Live	HG856-BCG	<i>rBCG overexpressing chimeric ESAT-6/Ag85A DNA fusion protein</i>	Shanghai H&G Biotech	B PI IT	–
	paBCG	<i>BCG with reduced activity of anti-apoptotic microbial enzymes including SodA, GlnA1, thioredoxin, and thioredoxin reductase</i>	Vanderbilt University with exclusive license to Aeras	P	[60]
	rBCG(mdtB)30	<i>rBCG with limited replication overexpressing the 30 kDa Mtb Antigen 85B</i>	UCLA, NIH, NIAID	P	[61]
	rBCG T+B rM. smegmatis T+B	<i>rBCG and rM. smegmatis expressing multiple T and B epitopes of Mtb</i>	Finlay Institute, Universiti Sains Malaysia	P B PI	[62-64]
	rBCG TB-Malaria	<i>Expresses multiple epitopes of Mtb fused to malarial epitopes and antigens</i>	Universiti Sains Malaysia	P B PI	[65]
	<i>Streptomyces</i> live vector	<i>Recombinant streptomyces expressing multiple T and B epitopes from M.tb</i>	Finlay Institute, Institute of Pharmacy and Food, Cuba	P B PI IT	[63, 64, 66]

P Prime, **B** Boost, **PI** Post-infection, **IT** Immunotherapy

Recombinant Protein	Ac ₂ SGL Diacylated Sulfoglycolipid *	<i>Mycobacterial lipids with Ac₂SGL, a novel glycolipid antigen</i>	Institut de Pharmacologie et Biologie Structurale du CNRS	   	[67]
	HspC TB *	<i>Heat shock HspC protein antigen complexes</i>	ImmunoBiology Ltd.		[68, 69]
	ID83 and ID93 in GLA-SE adjuvant	<i>Subunit fusion protein composed of 3 Mtb antigens (ID83) or 4 Mtb antigens (ID93)</i>	Infectious Disease Research Institute	  	[70, 71]
	r30	<i>30kDa Mtb Ag85B protein purified from rM. smegmatis</i>	UCLA, NIH, NIAID	 	[72-76]
	R32Kda * (recombinant 85A)	<i>Purified recombinant 85A protein from BCG</i>	Bhagawan Mahavir Medical Research Center		–
Other	AERAS-Capsid	<i>Shigella-delivered recombinant double-stranded RNA nucleocapsid</i>	Aeras	 	[16]
	HG856A	<i>Chimeric DNA vaccines—ESAT-6/Ag85A; Ag85A/Ag85B</i>	Shanghai H&G Biotech	 	[77]
	HG856-SeV	<i>Recombinant Sendai virus overexpressing chimeric ESAT-6/Ag85A protein</i>	Shanghai H&G Biotech		–
	Hsp DNA vaccine *	<i>Codon-optimized heat shock protein from M. leprae, a CpG island</i>	Cardiff University, Sequella		[78-81]
	HVJ-Envelope/HSP65 DNA+IL-12 DNA	<i>Combination of DNA vaccines expressing mycobacterial heat-shock protein 65 & IL-12</i>	Osaka University	  	[82-86]
	Liporale-BCG	<i>Live attenuated BCG Danish Strain in a novel lipid adjuvant and delivery system for an oral vaccine</i>	Immune Solutions Ltd.	 	[87-91]
	NasL3/AM85B conjugate	<i>Nasal vaccine with man-capped Arabinomannan oligosaccharide conjugated to Ag85B in Eurocine L3TM adjuvant</i>	Karolinska Institute		[92-96]
	NasL3/HtkBCG (BCG adjuvant)	<i>Intra-nasal heat-killed whole BCG Copenhagen strain in Eurocine L3TM adjuvant</i>	Karolinska Institute	  	[97-99]
	TBVax	<i>T cell epitope-based DNA-prime/peptide boost vaccine</i>	EpiVax , Inc.	 	[100-102]
	PS- conjugate *	<i>Subunit Mtb polysaccharide protein conjugate</i>	Albert Einstein School of Medicine		–

 Prime,  Boost,  Post-infection,  Immunotherapy

Key:

-  Prime
-  Boost
-  Candidate is indicated post-infection
-  Candidate is indicated for immunotherapy

BCG – Bacille Calmette-Guérin

IL – Interleukin

GMP – Good Manufacturing Practices Manufacturing

GSK – GlaxoSmithKline Biologicals

M. bovis – *Mycobacterium bovis*

Mtb – *Mycobacterium tuberculosis*

NIAID– National Institute of Allergy and Infectious Diseases

NIH – National Institutes of Health

OETC – Oxford-Emergent Tuberculosis Consortium, Ltd.

SSI – Statum Serum Institute

TBVI – Tuberculosis Vaccine Initiative

UCLA – University of California Los Angeles

* No new information received from vaccine sponsor in 2009.

The aim of the **Stop TB Working Group on New Vaccines** is to bring together the wide range of international groups with an interest in TB vaccine development, acting as a "broker" to promote synergy and to accelerate identification and introduction of the most effective vaccination strategy. This is achieved by representation of national and international public health organisms, major funding organizations, TB endemic countries, commercial and non-profit institutions involved in TB vaccine development, as well as experts in regulatory issues associated with vaccine development.



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