



TUBERCULOSIS VACCINE CANDIDATES – 2010

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

In the following table, tuberculosis vaccine candidates are presented in three categories:

Candidates Tested in Clinical Trials (Section I): TB vaccine candidates that are in clinical studies in 2010. Certain candidates that have been in clinical studies but are not currently in clinical trials are listed as 'completed.'

Candidates in Preclinical Studies & GMP-2010 (Section II): TB vaccine candidates that as of 2010 are not yet in clinical trials, but have been manufactured under good manufacturing practice (GMP) for clinical use and have undergone some preclinical testing that meets regulatory standards.

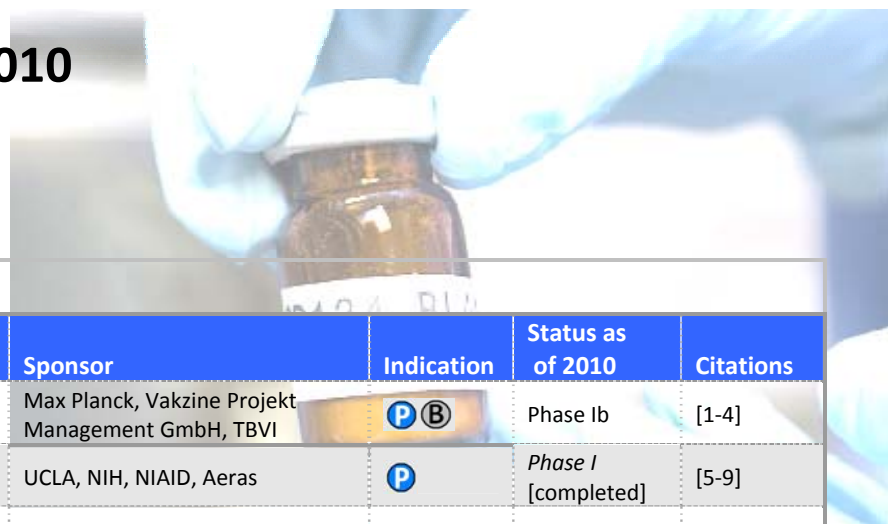
Next Generation Candidates-2010 (Section III): TB vaccine candidates that are in the research and development stage with some preclinical testing performed to show that they may confer protection.

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 and updated by the vaccine developers unless otherwise indicated. In cases where an update regarding a previously listed vaccine candidate was not received in 2010, the 2009 listing was retained.

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SECTION I: Candidates Tested in Clinical Trials						
Type of Vaccine	Products	Product description	Sponsor	Indication	Status as of 2010	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 B	Phase Ib	[1-4]
	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 [completed]	[5-9]
	AERAS-422	<i>Recombinant BCG expressing mutated PfoA and overexpressing antigens 85A, 85B, and Rv3407</i>	Aeras	P	Phase I	[10-12]
Viral Vectored	Oxford MVA85A / AERAS-485	<i>Modified vaccinia Ankara vector expressing Mtb antigen 85A</i>	Oxford Emergent Tuberculosis Consortium (OETC), Aeras	B PI IT	Phase IIb	[13-17]
	AERAS-402/ Crucell Ad35	<i>Replication-deficient adenovirus 35 vector expressing Mtb antigens 85A, 85B, TB10.4</i>	Crucell, Aeras	B	Phase IIb	[10-11, 18-20]
	AdAg85A	<i>Replication-deficient adenovirus 5 vector expressing Mtb antigen 85A</i>	McMaster University	P B	Phase I	[21-25]
Recombinant Protein	M72 + AS01	<i>Recombinant protein composed of a fusion of Mtb antigens Rv1196 and Rv0125 & adjuvant AS01</i>	GSK, Aeras	B PI	Phase II	[26-29]
	Hybrid-I+IC31	<i>Adjuvanted recombinant protein composed of Mtb antigens 85B and ESAT-6</i>	Statens Serum Institute (SSI), TBVI, EDCTP, Intercell	P B PI	Phase I	[30-34]
	Hybrid-I+CAF01	<i>Adjuvanted recombinant protein composed of Mtb antigens 85B and ESAT-6</i>	SSI	P B PI	Phase I	–
	HyVac 4/AERAS-404, +IC31	<i>Adjuvanted recombinant protein composed of a fusion of Mtb antigens 85B and TB10.4</i>	SSI, Sanofi-Pasteur, Aeras, Intercell	B	Phase I	[35-37]
Whole Cell, Inactivated or Disrupted	<i>M. vaccae</i>	<i>Inactivated whole cell non-TB mycobacterium; phase III in BCG-primed HIV+ population completed; reformulation pending</i>	NIH, Immodulon	B PI IT	Phase III [completed]	[38-42]
	<i>Mw [M. indicus pranii (MIP)]</i>	<i>Whole cell saprophytic non-TB mycobacterium</i>	Department of Biotechnology (Ministry of Science & Technology, Government of India), M/s. Cadila Pharmaceuticals Ltd.	IT	Phase III	[43-45]

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

	RUTI	Fragmented <i>Mtb</i> cells	Archivel Farma, S.I.	B PI IT	Phase II	[46-50]
	<i>M. smegmatis</i> ^a	Whole cell extract; phase I completed in China	–	B PI IT	Phase I [completed]	–

SECTION II: Candidates in Preclinical Studies & GMP- 2010

Type of Vaccine	Products	Product description	Sponsor	Indication	Citations
Recombinant Live	Mtb [Δ lysA Δ panCD Δ secA2]	Non-replicating, <i>Mtb</i> strain auxotrophic for lysine and pantothenate; attenuated for secA2	Albert Einstein College of Medicine	P	[51-52]
	MTBVAC [Δ phoP, Δ fad D26]	Live vaccine based on attenuation of <i>Mtb</i> by stable inactivation by deletion of phoP and fad D26 genes	University of Zaragoza, Institute Pasteur, BIOFABRI, TBVI	P	[53-57]
Recombinant Protein	HBHA	Naturally methylated 21-kDa purified protein from <i>M.bovis</i> BCG	Institute Pasteur of Lille, INSERM, TBVI	P B PI IT	[58-62]
	Hybrid 56 + IC31	Adjuvanted recombinant protein composed of <i>Mtb</i> antigens 85B, ESAT-6 and Rv2660	SSI, Aeras, Intercell	P B PI	–
Other	HG85 A/B	Chimeric DNA vaccines—Ag85A/Ag85B	Shanghai H&G Biotech	B IT	[63-67]
	Spray-dried BCG ^b	Live attenuated BCG Danish Strain spray-dried for nasal administration	MEND	P	[68]

SECTION III: Next Generation Candidates – 2010

Type of Vaccine	Products	Product description	Sponsor	Indication	Citations
Recombinant Live	HG856-BCG	rBCG overexpressing chimeric ESAT-6/Ag85A DNA fusion protein	Shanghai Public Health Clinical Center	B PI IT	[63-65, 69-70]
	IKEPLUS <i>M. smegmatis</i> with ESX-3 deletion/complementation	Live <i>M. smegmatis</i> with deletion of ESX-3 encoding locus and complementation with <i>Mtb</i> locus	Albert Einstein College of Medicine, Aeras	B	–
	paBCG	BCG with reduced activity of anti-apoptotic microbial enzymes including SodA, GlnA1, thioredoxin, and thioredoxin reductase	Vanderbilt University	P	[71]

^a Candidate information communicated by the Wuhan Institute of Biological Products.





^b Candidate information communicated by TBVI.

	Proapoptotic rBCG	<i>Recombinant BCG expressing mutated PfoA and including mutations shown at AECOM to induce macrophage apoptosis</i>	Aeras, Albert Einstein College of Medicine	P	–
	rBCG(mbtB)30	<i>rBCG with limited replication overexpressing the 30 kDa Mtb Antigen 85B</i>	UCLA, NIH, NIAID	P	[72]
	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	[73-75]
	rBCG TB-Malaria	<i>Expresses multiple epitopes of Mtb fused to malarial epitopes and antigens</i>	Universiti Sains Malaysia	P B PI	[76]
	rBCG38	<i>rBCG Tice strain overexpress the 38 kDa protein</i>	Universidad Nacional Autónoma de México	P B	[77-80]
	rBCGMex38	<i>rBCG Mexico strain overexpress the 38 kDa protein</i>	Universidad Nacional Autónoma de Mexico	P B	[79, 81]
	rBCG overexpressing L,D-Transpeptidase	<i>Recombinant M. bovis BCG overexpressing an Mtb L,D-Transpeptidase</i>	Johns Hopkins University	P	[82]
	Replication deficient rBCG	<i>Recombinant BCG expressing PfoA and classical, latency, and resuscitation antigens in live, non-replicating background</i>	Aeras	P	–
	rM.microti30 rM.microti38	<i>rM.microti strain overexpress the 30 or 38kDa protein</i>	Universidad Nacional Autónoma de Mexico	P	[78, 83]
	<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	[74-75, 84]
Recombinant Protein	ID93 in GLA-SE adjuvant	<i>Subunit fusion protein composed of 4 Mtb antigens</i>	Infectious Disease Research Institute	B PI IT	[85-86]
	Latency fusion proteins	<i>Recombinant fusion proteins composed of antigens 85A-85B-Rv3407, Rv3407-Rv1733c-Rv2626c, Rv0867c-Rv-1884-Rv2389c</i>	Aeras	B	–
	r30	<i>30kDa Mtb Ag85B protein purified from rM. Smegmatis</i>	UCLA, NIH, NIAID	B PI	[87-91]
	R32Kda (recombinant 85A)	<i>Purified recombinant 85A protein from BCG</i>	Bhagawan Mahavir Medical Research Center, LEPRa Society-Blue Peter Research Centre	B PI IT	[92-95]
Viral Vectored	Recombinant LCMV	<i>Recombinant lymphocytic choriomeningitis virus expressing Ag85A, Ag85B, or Ag85B-ESAT6</i>	University of Geneva	P B PI IT	–
	pND vector	<i>pND 14 vector with tpa factor expressing esat6, cfp10, hspx, Ag85A, Ag85B, or Ag85c</i>	HEC-Pakistan	P PI	–

Other	Ac ₂ SGL Diacylated Sulfoglycolipid	<i>Mycobacterial lipids with Ac₂SGL, a novel glycolipid antigen</i>	Institut de Pharmacologie et Biologie Structurale du CNRS	P B PI IT	[96]
	HG856A	<i>Chimeric DNA vaccines—ESAT-6/Ag85A; Ag85A/Ag85B</i>	Shanghai H&G Biotech	B IT	[97]
	HG856-SeV	<i>Recombinant Sendai virus overexpressing chimeric ESAT-6/Ag85A protein</i>	Shanghai H&G Biotech	B	–
	Hsp DNA vaccine	<i>Codon-optimized heat shock protein from M. leprae, a CpG island</i>	Cardiff University, Sequella	B	[98-101]
	HVJ-Envelope/HSP65 DNA+IL-12 DNA	<i>Combination of DNA vaccines expressing mycobacterial heat-shock protein 65 & IL-12</i>	Osaka University	B PI IT	[102-106]
	Liporale-BCG	<i>Live attenuated BCG Danish Strain in a novel lipid adjuvant and delivery system for an oral vaccine</i>	Immune Solutions Ltd.	P B	[107-111]
	Mycobacterial liposomes and proteosomes	<i>Liposomes from M. smegmatis and proteo-liposomes from BCG and M. smegmatis</i>	Finlay Institute Universiti Sains Malaysia	P B PI IT	–
	NasL3/AM85B conjugate	<i>Nasal vaccine with man-capped Arabinomannan oligosaccharide conjugated to Ag85B in Eurocine L3TM adjuvant</i>	Karolinska Institute	B	[112-116]
	NasL3/HtkBCG (BCG adjuvant)	<i>Intra-nasal heat-killed whole BCG Copenhagen strain in Eurocine L3TM adjuvant</i>	Karolinska Institute	P B PI	[117-119]
	PS- conjugate	<i>Subunit Mtb polysaccharide protein conjugate</i>	Albert Einstein College of Medicine	B	–
	pUMVC6/7 DNA ^c	<i>DNA vaccine plasmid vectors pUMVC6 or pUMVC7 expressing Rv3872, Rv3873, Rv3874, Rv3875 or Rv3619c</i>	Kuwait University	P	[120]
	Recombinant B/HPIV	<i>Recombinant B/HPIV vector encoding fusion of antigens 85A-85B-Rv3407, Rv3407-Rv1733c-Rv2626c, Rv0867c-Rv-1884-Rv2389c</i>	NIH, Aeras	B	–
	T-BioVax	<i>Heat shock HspC protein antigen complexes</i>	ImmunoBiology Ltd.	B	[121-122]
	TBVax	<i>T cell epitope-based DNA-prime/peptide boost vaccine</i>	EpiVax , Inc.	B PI	[123-125]

^c Candidate information acquired from published literature.

Key:

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

BCG – Bacille Calmette-Guérin

IL – Interleukin

GMP – Good Manufacturing Practices

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

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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