The field of tuberculosis (TB) vaccine development is a dynamic area of vaccinology. Recently, several vaccine candidates have entered clinical trials for the first time—more than 80 years since the introduction of BCG—the first (live vaccine) against the disease.

The pathogenesis and immune response against Mycobacterium tuberculosis, the causative agent for the disease, is still not fully understood and this is reflected in the wide array of experimental strategies that are used for the development of new generation TB vaccines. Research and development on TB vaccines span from basic research up to clinical studies.

The objective of this book is to depict this diverse and sometimes controversial approaches of TB vaccine development. This book is not intended to provide a comprehensive review of all the efforts that are being pursued by various researchers working in this field but to give readers an insight into some of the multiple challenges of the field—covering areas in epidemiology, immunology, bioinformatics, technology platforms as well as ethical, regulatory and clinical aspects, among others.

The authors of the different chapters represent among the international leaders in tuberculosis vaccine development and in other relevant fields. As such, the editors have not attempted to unify their arguments and hypotheses on their respective subjects. Rather, the editors have left the personal views contained in the respective chapters to reflect the way this challenging field is evolving. In essence, the “art” of scientific reservations are left to the imagination and skills of each author.

Artistic images from renowned artists are included to visualise the affliction of tuberculosis on those affected by it—and help broaden the message of the book beyond the technical scope. The book thus represents the need for all parties to work together to combat this scourge.

This book is an example of an altruistic collaboration between scientists and artists of different parts of the world working together to provide an update on the Art & Science of Tuberculosis Vaccine Development.

Norazmi Mohd Nor is a Professor of Molecular Immunology at the School of Health Sciences, Universiti Sains Malaysia. Norazmi has been working on tuberculosis vaccine development since 2008 in collaboration with his co-editor, Armando Acosta and Maria Sarmiento. He started his work in this area using the recombinant BCG platform and is now exploring other potential strategies for boosting BCG, particularly aimed at infant vaccination. Norazmi has other research interests in vaccine development and molecular immunology.

Armando Acosta and Maria E Sarmiento are Professors of Immunology and Physiology respectively working at Finlay Institute. They have been working on tuberculosis vaccine development since 1991. They started their work in exploring the role of specific antibodies in the protection against mycobacteria. They are currently working on projects related with tuberculosis vaccine and diagnostic development in collaboration with their co-editor Norazmi Mohd Nor.
The Art & Science of Tuberculosis Vaccine Development
The Art & Science of Tuberculosis Vaccine Development
‘Introduction of new effective TB vaccines will be an essential component of any strategy to eliminate TB by 2050. New TB vaccines to prevent childhood and adult forms of TB, to reduce TB in person co-infected with HIV and to shorten drug treatment regimens will fundamentally alter our approach to TB control.’


Paths – Lisbet Fernández
Installation on a traffic circle
30 sculptures/terracotta

‘If you have built castles in the air, your work need not be lost; that is where they should be. Now put the foundations under them.’

Walden; or Life in the Woods (Essay)
– Henry David Thoreau
Lisbet Fernández paints big format portraits with children as her central subject.

The Myto Gallery exhibited her collection entitled ‘Con los ojos abiertos’, which brings together her latest works, consisting of five life-size pieces about children, made of clay and located in different contexts.

She participated in the exhibition ‘Escultura Transeúnte’ (Street Sculpture), organized by CODEMA in 2005 and in the exhibition ‘Doble Blanco’, collateral to the 9th Havana Biennale, together with artists Alain Pino, Iván and Yoán Capote.
The Editors indicate in the title of the book, that creative tuberculosis (TB) vaccine research is in the realm of science as well as art. This aspect is further emphasized by attaching one artwork to each of the chapters. My perception of this approach is, that the art images perhaps reflect the challenges felt by the scientists when endeavouring to invent and develop effective means for alleviating the suffering which TB still imposes on mankind. Reference to art may also imply, that researchers need to complement rational scientific design and interpretation with some degree of intuitive guesswork. Moreover, the inspiration for the presented art images might reflect the human impact of this devastating disease on the mainly socio-economically underprivileged individuals and populations of the world. Integrating art to a book, appears to be uniquely original for a monograph of any scientific discipline. Hence, the Editors deserve to be praised not only for adopting this format, but also for attracting artists who felt inspired by the associations with TB and for suitably matching their images with the respective scientific chapters.

Despite extensive research efforts and major advances, current knowledge of the fundamental mechanisms of host resistance against TB retains a number of gaps and paradoxes. In such circumstances, the procedures currently used for controlling the disease are still failing to reduce its enormous impact on global health. Hence, it is pertinent to quote Maurice Lefford, who wrote in 1974, that ‘much as one might wish otherwise, the drop in the prevalence in TB is not attributable to the undoubted scientific contributions (pasteurization of milk, immunization, chemotherapy), but was a consequence of improved socio-economic conditions’. The continued validity of this statement is apparent from the striking disparity in TB prevalence between countries and also between communities within the same country, with disparate levels of marginalization and poverty. Taking this into account, the research strategies aimed at TB control
need to take into consideration their scope for implementation to populations living in poor socio-economic conditions. One may quote as a striking example of this problem the case of chemotherapy of TB, which is extremely successful under controlled trial conditions, but suffering from poor compliance—due to the need for protracted (at least six months) treatment—in poor countries with the highest disease incidence. The complexity of the socio-economic, geographical, and environmental aspects are being discussed in this book by Graham AW Rook (Chapter 28), pointing out how environmental mycobacteria cause resistance to TB and may wipe off any additional protection following vaccination. He also elaborates how elevated levels of Th2 cytokines (mainly IL-4 and TGF-β), due to helminthic infections and a high bacterial infection load in overcrowded accommodation, may affect resistance to natural infection and perhaps also to vaccination. Hence, he poses the question whether ‘we might need to consider different types of vaccine for different populations and environments’.

Vaccination against infectious diseases has been credited with the highest merits for achieving their global elimination in an efficient and cost-effective manner. Therefore, vaccine development has attracted a predominant share of current funding for TB research from both governmental and charitable sources. While the emphasis is on moving novel TB vaccines and regimens (e.g. prime-boost) to the stage of evaluation in human trials, our understanding of the immunobiology of TB retained a number of unresolved paradoxes. These can be listed as follows: a) It is generally assumed that protection against TB is mediated by IFNγ, produced predominantly by Th1 lymphocytes; however, patients with active TB have abundant IFNγ production and recombinant IFNγ has not been therapeutic; b) Natural infection and all vaccine-imparted host resistance drives the dividing tubercle bacilli (MTB) into latency, from which they have the capacity to reactivate at a later stage. In contrast, vaccines which had been successful in eradicating other infectious diseases (e.g. smallpox, polio) impart sterile immunity; c) About 95 per cent of the human population is naturally resistant to reactivated dormant infection and therefore vaccination needs to target the 5 per cent susceptible individuals. However, the stimuli which lead to reactivation in otherwise healthy young individuals (the bulk of adult TB), and the mechanisms of their action, remain virtually unknown.

Slow advance in the knowledge about the above-listed fundamental issues makes it difficult to design the structure, delivery, and potency testing for the intended ‘better than BCG’ novel vaccines. The lack of satisfactory knowledge may have led the editors of this book to relegate TB vaccine development in the title to the realms of both ‘art’ and science. The reference to art may imply that the researchers in this field needed to engage a certain deal of guesswork in addition to rational scientific design. While intuitive judgement is beneficial for exploratory
research, and has led to a number of major discoveries, its use for translating projects to evaluation in human trials is of further ethical concern. The tendency to move fast is understandable, however, as a reflection of the endeavours to meet targets for improving TB control, set by the Global Plan to Stop TB 2006–2015 (Chapter 1). Although this chapter was able to quote exactly what is the gap in the funding (US$2.5 billion) to achieve the TB control measures, it seems to be beyond reach to make promises for an effective prophylactic vaccine with any degree of confidence. On the whole, the chapter has given a clearer explanation of the notion of ‘sustainable development’ for TB control than to the notion of ‘sustainable science’. Nevertheless, it is gratifying that priority funding and due attention to the importance of the regulatory requirements (Chapter 24) have succeeded in moving this field to a number of currently ongoing clinical trials.

This book contains updated chapters from the participants of the ‘International Workshop on Tuberculosis Vaccines’ in Varadero, Cuba in 2007 and chapters from other authors, complementary to the general theme. Chapter 9 on the history of BCG vaccination highlighted a number of intriguing aspects. One of them is that revaccination with BCG in human trials showed no benefits or was at least not consistent. This outcome is of concern especially when considering that the ‘BCG prime/subunit boost’ vaccination strategy is currently one of the favoured strategies for improved vaccination. As the latter concept was supported by results in experimental animal models, there is a need for confirmation from human trials that boosting improves protection. There is a striking contrast between the original protracted period of attenuation (combined with safety testing) of BCG and the fascinating range of new variant strains of BCG and a remarkable list of new attenuated strains of MTB, generated by genetic manipulation (Chapter 13). Thus, BCG has been improved by the introduction of cytokine genes (IL-2, GM-CSF or IFN-γ, IL-18), or by the insertion of RD1 coded and other antigens. Enhanced CD8 responses were stimulated by a variant BCG—secreting listeriolysin in an acidified environment—achieved by defective urease production. A number of auxotroph mutants of MTB, for example, defective in pantothenate synthesis, were shown to be highly attenuated but not more protective than BCG. Superior protection was reported following the deletion of transcription factors (e.g. PhoP) or by the inactivation of the secA2 gene, resulting in increased apoptosis of macrophages.

DNA vaccines (Chapter 15) have been reviewed from the point of view of both basic immunology and practical vaccination, mostly from the 2006–8 period, when the number of publications doubled to a total of almost 500 papers. Further advances were achieved in transfection and expression efficacy by electroporation or cationic lipid adjuvants and by using plasmids with optimized codon usage. Immunogenicity has been increased by the co-administration of plasmids encoding co-stimulatory molecules (CD80/CD86) or adjuvant cytokines (GM-CSF or IL-
The authors consider the best option is to combine DNA coding for a fusion protein or poly-epitope with BCG, although the sequence in which they are best to be applied is a matter of debate. ‘Therapeutic’ DNA vaccination following MTB infection produced contradictory results, but promising experimental data were obtained using DNA vaccines as an adjunct to chemotherapy. Despite the expansion of research in mice, guinea pigs, and non-human primates, DNA vaccines have not advanced into clinical trials so far.

Considering the strong tropism of TB for the lungs, better understanding of the organ-specific mechanisms of protection are highly topical (Chapter 16). Alveolar macrophages appear to be the first and most predominant to be infected, while ineffective (to the pathogen's advantage) in activating naïve T cells. That role falls to dendritic cells, acting locally, rather than following migration to draining lymph nodes. Homing of immune effector cells to the lungs is necessary for effective protection against the aerosol infection. Therefore, intranasal (i.n.) vaccination could in principle have an advantage over sub- or intra-cutaneous vaccine delivery. It appears that i.n. vaccination effectively stimulates particularly the airway luminal CD8 T cells more persistently than parenteral immunization. However, operational limitations on efficient antigen delivery and concerns about safety against excessive inflammatory reactions in the lungs (1) remains unresolved. Overall, i.n. vaccination is favoured as a booster route following BCG priming. Both protein and DNA boosting were tried using a number of adjuvants (DDA/MPL, DD/ISCOMs, LTK63 or ASO2A). Perhaps the favoured i.n. delivery has been the use of replication-defective viral vectors (mostly modified Vaccinia virus-MVA and replication-deficient human type 5 adenovirus-Ad5). They possess natural tropism to the respiratory mucosal epithelium and thus can induce high levels of transgene product, although pre-existing antibody levels against and their production following vaccination are a notable limitation.

Therapeutic vaccination, presented in Chapter 19, deals with the immunization of healthy PPD+ve, BCG non-vaccinated individuals (i.e. with latent TB infection) by polyantigenic extract (RUTI) in conjunction with isoniazide chemoprophylaxis. This combined chemo- and immunotherapy, targeting dividing and persisting bacilli respectively, aims to eliminate or reduce the rate at which they can reactivate into active disease. This is an important objective for the global control of TB, considering that one-third of the world’s population harbours MTB in an asymptomatic, latent form, which retains a lifelong risk of future disease. Cardona supports the rationale for the combined therapy by his ‘dynamic hypothesis’, envisaging constant endogenous reactivation and reinfection by tubercle bacilli. He argues that dormant MTB pass from foamy macrophages in the periphery of lung granulomas into the lung alveoli and then by alveolar fluid into the upper bronchi and, after being swallowed,
the stomach. His hypothesis is contrary to the more established concept that reactivation originates from secondary foci of the lungs to which they are haematogenically disseminated during the early stages of TB infection.

Control of TB in cattle is governed by statutory obligations and, due to the failure of existing measures, vaccine development is supported as a priority in the UK. Chapter 20 reviews the progress made in the formulation of vaccine candidates and in the necessary testing of protective efficacy as well as for distinguishing between vaccinated and infected cattle. As for humans, the strategies mostly involved improving on BCG by prime-boost regimens, rather than replacing it. Using the same or similar antigen subunits, either in DNA or protein formulation it has been beneficial, that potency could be tested by naturally transmitted challenge. Consequently, important advances have been made in the testing of potency, using a range of cytokine based assays, which seem to deserve to be translated to corresponding studies in humans.

This book highlights the fundamental immunobiology of vaccination against TB and the rationale for the favoured regimens of delivery of the novel genetically constructed subunit vaccines. It is accepted knowledge that T cell immunity can sustain MTB organisms in their latent phase in about 95 per cent of infected humans. The unresolved question remains, however. Why does this protection fail in about 5 per cent of the infected population? Both genetic factors and some special ‘reactivation environment’ probably play a role. Without understanding the mechanisms which operate in the minority of reactivation susceptible subjects, vaccination is being developed on the basis of evaluation of protection in the population as a whole. Hence there is a possibility, that the vaccine can miss out on correcting some critical defects affecting the prospective disease-vulnerable subjects.

Future research needs to focus on immunological markers in latently infected subjects, which are predictive of reactivation risk. Such markers could possibly be found in HIV-infected subjects. Testing of cultured ELISPOT responses (central memory) for IFNγ, IL-17, and TNFα (protection markers) and IL-4 and FoxP3 (failure markers) production could be better than the ex vivo assay. The phenotype of the protective T cell population, expected to be CD45RO/CD62L and corresponding RT-PCR analysis, could also be performed. Encouraging results of vaccine potency testing were reported in cattle, segregated into ‘protected’ and ‘failure’ groups on the basis of the outcome following virulent challenge (Chapter 20). An alternative exploratory approach could be to measure the capacity for relapse of MTB growth from latently infected macrophages, induced by incubation in the presence of hydrocortisone or anti-TNF.

To conclude, the list of current research activities in the short- and medium-term future—supported by the Global Plan to Stop TB 2006–2015—has been summarized in Chapter 26. The strategies fall into three categories, aimed
at: 1) uninfected newborns by a vaccine which leads to sterile immunity (i.e. fundamentally different from BCG), thus abolishing the risk of reactivation; 2) all latently infected individuals by a vaccine, diminishing their reactivation rate; and, 3) potentially immunocompromised (e.g. HIV infected or TNFα treated) individuals, combining chemo- and immunotherapy. In this latter instance, passive vaccination may also be considered (2).

Juraj Ivanyi

References


We can allow the TB epidemic to become more lethal or we can act now to prevent the death and suffering caused by the disease.

Kuala Kangsar from the Perak River 2002 – Mansor Ghazalli
Water Colour
(36 x 30 cm)

‘For the sake of goodness and love, man shall let death have no sovereignty over his thoughts’

_The Magic Mountain_ (Novel) – Thomas Mann
Mansor Ghazalli

Mansor Ghazalli was considered by many as one of the top water colour artist in Malaysia. His paintings are displayed in most major art galleries in Malaysia, and during his lifetime, has participated in many exhibitions all around the world. He paints out of love for art, and less for fame and monetary returns. Experts have considered his work a well-kept secret amongst art lovers and collectors.
Recently in 2009, the world was very much focused on the outbreak of the ‘swine flu’ in Mexico and elsewhere. While it has nothing to do with tuberculosis per se, it does illustrate how vulnerable a situation can be when an epidemic occurs.

Under those circumstances, what can be better than to have readily accessible the most updated book at hand so as to facilitate a more informed decision-making. This is one of the main aims of the book—to act as a comprehensive reference source for the various TB-related organizations and institutions globally. The book is also relevant to students and scientists who are involved in TB vaccine development.

Indeed, herein lies the unique feature of this book: it recognizes the contributions from other non-science disciplines, and as far as possible attempts to integrate them together. It is hoped that this will make the message related to the control of the disease comprehensive and far reaching.

Lastly, I would like to take this opportunity to thank and congratulate all the contributors and editors, as well as the publisher for making the book possible. In particular, I would like to thank Dr Concepcion Campa, Director of Finlay Institute in Havana, for her encouragement to closely collaborating with the Universiti Sains Malaysia in initiating this invaluable project.

Dzulkifli Abdul Razak
Tuberculosis is a devastating disease whose control needs the interaction, collaboration, and integration at the international level of all concerned. One of the key factors in the control of TB is the development of an efficacious vaccine.

This book has as its main objective the dissemination of knowledge related to the development of new vaccines against TB and to include the more recent advances in the different aspects connected to this topic.

The authors of the different chapters represent a group of the more important authorities in this field who generously joined this project, giving their effort, knowledge, experience, and valuable time.

The illustrations in the book represent the work of artists from different parts of the world committed to the fight against TB. They amplify the scope, message, and impact of the book, incorporating in a symbolic way the interaction between scientists and artists in the pursuit of an altruistic common goal.

This book is a non-profit initiative and will be freely distributed to research institutions, universities and organizations involved with the control of TB and the development of new vaccines against this disease.

This book is a promising example that international collaboration is possible in the fight against diseases.

Dr Concepción Campa
Art is as old as the human species. There are as many artistic legacies as humans have ways of expressing their aspirations and needs. The relationship between art and science is not unconnected to this fact—it is as ancient as humankind. Many are the scientists and researchers who, more or less successfully, have made their way into the world of art; and on their canvases an equal or greater number of artists have dealt with subjects related to advances in the field of science, or have suffered from a disease.

Although it may seem a paradox, epidemics and the most debilitating diseases have always had their artistic counterparts. Numerous scientific works resorted to visual images to illustrate medical procedures, as well as plant and animal species that contribute to their cure, or on the contrary, cause them. Whether they are originals or reproductions, these works today are not only a source of knowledge for researchers, but also visual identity references of the most important cultures and artistic styles of humanity; for example, drawings made by the Italian Renaissance artists enhanced the understanding of the human body and its vital functions to achieve works of art that are identifiable with the modern ideal of human beauty.

This artistic interest is also presented in this book; the result of prolonged and conscientious investigation with respect to the scourge of TB in our contemporary societies; its scientific character does not disengage it from those visual art expressions, as a way of complementing its essential scientific contents. The particular manner in which art makes one see and conceptualize the most dissimilar aspects of the objective and subjective reality, turns it into an active and perpetual persuasion factor and, therefore, into an aid of any behaviour or research directed towards human physical and spiritual improvement.

The editors of this scientific endeavour have understood the perpetual yet current conditions of this affliction and have appealed to a number of artists
in the most varied visual expressions (photography, fine arts, engraving, digital art, etc.) with the highly commendable purpose of giving the opportunity to the artists to join the fight against TB. Touching through their artworks and visions, different aspects of the human and social problems associated with TB adds aesthetic value to this book. It is a social advocacy effort—not exempt from beauty—based on the most representative visual codes of today’s art. The new, more or less realistic and symbolic figuration, expressionism and minimalism, are some of the codes used here as visual introductory sections to the chapters of the text. In its conception and shaping, the artists have resorted to both traditional and experimental techniques. The same has happened with the materials used—from canvas through photographic film and even X-ray photographic plates. With these plates, very novel results have been achieved from an aesthetical point of view, especially due to its technological link with medical activity, which contributes additional conceptual relevance to the artistic representations. Lastly, the harmonious and inclusive character of the book’s design should be emphasized. Also, in agreement with the aesthetic and communicational values of the art selected for each chapter, the cover and back cover designs reflect the optimism of any effort directed towards physical and, consequently, spiritual improvement of our species and the world we inhabit by resorting to a universal visual metaphor—the tree as a human lung.

We have no doubt that such visual depictions will favour better comprehension and attention to the battle, still being waged day-by-day, by science against TB and other diseases. Art at the service of science, as in other times, makes the need for a healthy species more imperative. In this case, subjectivity and objectivity complement each other, to provide testimony and warn about a reality that is not, and can never be, a topic unrelated to the most committed art of our times, because it affects human health.

Jorge R Bermúdez
This non-profit project is made possible by the great contributions from scientists and artists from around the world to address the scourge of TB. We are indeed privileged to be working with world renowned personalities in the arts and sciences, and are humbled by their dedication, generosity and patience. Their precious time and effort in ensuring the success of this project signify their readiness to contribute to a major problem of the world that primarily affects the underprivileged in underdeveloped nations. We hope their sincere contribution will make a difference to how we view and combat this disease.

We are also aware that many others are willing to contribute to this project but are unable to do so due to time constraints. We hope this project will pave the way for future ‘editions’ of the book which will have additional contributions from other scientists and artists. It is also our intention to make each edition of the book freely available online.

We would like to recognize the support provided by Universiti Sains Malaysia and Finlay Institute to this project. We acknowledge the financial support of Universiti Sains Malaysia, and the excellent support and guidance of Penerbit USM. We are very grateful to the team at Oxford Fajar Sdn Bhd for their patience, professionalism, and enthusiasm for the publication of the book. Thanks are also due to all of our colleagues, friends, and relatives who encouraged and helped us in different ways for the realization of this project.

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<td>Ag85B</td>
<td>30kDa protein</td>
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<tr>
<td>AIDS</td>
<td>acquired immune deficiency syndrome</td>
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<td>BCG</td>
<td>Bacillus Calmette-Guerin / Bacille de Calmette et Guérin</td>
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<td>BSL3</td>
<td>Biosafety Level 3</td>
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<tr>
<td>CAB</td>
<td>community advisory board</td>
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<td>CBER</td>
<td>Center for Biologics Evaluation and Research</td>
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<td>CFP</td>
<td>culture-filtrate proteins</td>
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<td>CFU</td>
<td>colony-forming unit</td>
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<td>CGMP</td>
<td>current good manufacturing practice</td>
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<td>CIOMS</td>
<td>Council for International Organizations of Medical Sciences</td>
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<td>CMI</td>
<td>cell-mediated immune mechanism</td>
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<td>CMO</td>
<td>Contract Manufacturing Organization</td>
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<td>CMV</td>
<td>Cytomegalovirus</td>
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<td>COG</td>
<td>cluster of orthologous groups</td>
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<td>CST</td>
<td>clonal selection theory</td>
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<td>CTD</td>
<td>common technical document</td>
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<td>CTL</td>
<td>cytotoxic T lymphocyte</td>
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<td>DAT</td>
<td>diacyltrehaloses</td>
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<td>DDA</td>
<td>dimethyl dioctadecylammonium bromide</td>
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<td>DIVA</td>
<td>differentiate infected from vaccinated animals</td>
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<td>DOTS</td>
<td>directly observed treatment/therapy short course</td>
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<td>eCTD</td>
<td>electronic common technical document</td>
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<td>ELISA</td>
<td>enzyme-linked immunosorbent assay</td>
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<td>Abbreviation</td>
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<td>ELISPOT</td>
<td>enzyme-linked immunosorbent spot</td>
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<td>EMEA</td>
<td>European Medicines Agency</td>
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<td>EPI</td>
<td>expanded programme on immunization</td>
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<td>ESAT</td>
<td>Early Secreted Antigen Target</td>
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<td>ESX</td>
<td>ESAT-6 gene clusters</td>
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<td>EU</td>
<td>the European Union</td>
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<td>EuPh</td>
<td>European Pharmacopoeia</td>
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<td>FCMTB</td>
<td>fragmented cells of MTB</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FIA</td>
<td>Freund's incomplete adjuvant</td>
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<td>FM</td>
<td>foamy macrophages</td>
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<td>GM-CSF</td>
<td>granulocyte-macrophage colony-stimulating factor</td>
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<tr>
<td>GMO</td>
<td>genetically modified organism</td>
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<td>HBHA</td>
<td>Heparin Binding Hemagglutinin Adhesin</td>
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<td>HEW</td>
<td>Department of Health, Education, and Welfare</td>
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<td>HIV</td>
<td>human immunodeficiency virus</td>
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<td>HSP60</td>
<td>60 kDa heat shock protein</td>
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<td>IACUC</td>
<td>Institutional Animal Care and Use Committee</td>
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<td>IDU</td>
<td>intravenous drug users</td>
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<td>IL-4</td>
<td>interleukin-4 receptor</td>
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<td>ILI</td>
<td>intracellular lipid inclusions</td>
</tr>
<tr>
<td>INH</td>
<td>Isonicotinic Acid Hydrazide or isoniazid</td>
</tr>
<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
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<tr>
<td>IU</td>
<td>international units</td>
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<td>IVIG</td>
<td>intravenous immunoglobulin</td>
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<tr>
<td>LAM</td>
<td>lipoarabinomannan</td>
</tr>
<tr>
<td>LB</td>
<td>lipid bodies</td>
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<tr>
<td>mAbs</td>
<td>monoclonal antibodies</td>
</tr>
<tr>
<td>ManLAM</td>
<td>Mannose-capped Lipoarabinommanan</td>
</tr>
<tr>
<td>mce</td>
<td>mammalian cell entry</td>
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<tr>
<td>MDG</td>
<td>Millennium Development Goals</td>
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<tr>
<td>MDR</td>
<td>multidrug-resistant</td>
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<tr>
<td>MDR-TB</td>
<td>multidrug-resistant TB</td>
</tr>
<tr>
<td>MeSH</td>
<td>Medical Subject Headings</td>
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<tr>
<td>MHC</td>
<td>major histocompatibility complex</td>
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**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>MIRU</td>
<td>Mycobacterial Interspersed Repetitive Unit</td>
</tr>
<tr>
<td>MTB</td>
<td><em>Mycobacterium tuberculosis</em></td>
</tr>
<tr>
<td>MTBC</td>
<td>MTB complex</td>
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<tr>
<td>MVA</td>
<td>Modified Vaccinia Ankara</td>
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<tr>
<td>NBAC</td>
<td>National Bioethics Advisory Commission</td>
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<tr>
<td>PAT</td>
<td>polyacyltrealoses</td>
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<tr>
<td>PBMC</td>
<td>peripheral blood mononuclear cell</td>
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<tr>
<td>PE</td>
<td>Pro-Glu</td>
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<tr>
<td>PGRS</td>
<td>polymorphic glycine rich sequences</td>
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<td>PKS</td>
<td>polyketide synthases</td>
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<tr>
<td>PMTCT</td>
<td>Prevention of Mother to Child Transmission programme</td>
</tr>
<tr>
<td>PPD</td>
<td>purified protein derivative</td>
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<tr>
<td>proC</td>
<td>proline</td>
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<td>rpf</td>
<td>resuscitation promoting factors</td>
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<tr>
<td>SATVI</td>
<td>South African TB Vaccine Initiative</td>
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<tr>
<td>SCID</td>
<td>severe combined immunodeficiency</td>
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<tr>
<td>SL</td>
<td>sulpholipids</td>
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<tr>
<td>SNP</td>
<td>single nucleotide polymorphism</td>
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<td>SOM</td>
<td>Self Organizing Maps</td>
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<td>SOP</td>
<td>standard operating procedure</td>
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<tr>
<td>STCF</td>
<td>short term culture filtrate</td>
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<tr>
<td>TB</td>
<td>tuberculosis</td>
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<tr>
<td>TCS</td>
<td>PhoP/R two-component system</td>
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<tr>
<td>TGF-β</td>
<td>transforming growth factor beta</td>
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<td>TLR</td>
<td>toll-like receptors</td>
</tr>
<tr>
<td>TPA</td>
<td>tissue plasminogen activator</td>
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<tr>
<td>TRC</td>
<td>Tuberculosis Research Centre</td>
</tr>
<tr>
<td>trpD</td>
<td>tryptophan</td>
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<tr>
<td>TST</td>
<td>Tuberculin Skin Tests</td>
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<tr>
<td>UNAIDS</td>
<td>Joint United Nations Programme on HIV/AIDS</td>
</tr>
<tr>
<td>USM</td>
<td>Universiti Sains Malaysia</td>
</tr>
<tr>
<td>VCAM-1</td>
<td>vascular cell adhesion molecule-1</td>
</tr>
<tr>
<td>VSV</td>
<td>vesicular stomatitis virus</td>
</tr>
</tbody>
</table>
Abbreviations

WHO  World Health Organization
WMA  World Medical Association
XDR  extensively drug resistant
XDR-TB  extensively drug-resistant TB
‘TB has been with us for too long…’

Dr Lee Jong-wook

The Deep – Alain Pino
Plexiglas and aluminium
(Variable dimensions)

‘When he woke up, the dinosaur was still there’

The Dinosaur (Short story) – Augusto Monterroso
Alain Pino studied at the Professional School of Art and at the Higher Institute of Art, both in Havana. He also attended the Workshop in the BAC in Boston.

He has held solo exhibitions and participated in group exhibitions since 1994. These exhibitions were held in Argentina, Belgium, Canada, Costa Rica, Cuba, France, Germany, Italy, Malaysia, Spain, and the United States.

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