Department of Immunology

Director: Stefan H. E. Kaufmann

1. Introduction

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Our research continues to focus on the crosstalk between *Mycobacterium tuberculosis* (Mtb) and its mammalian host. This includes:

(i) basic investigations into both host and pathogen;
(ii) targeted research towards better intervention measures;
(iii) translation from preclinical into clinical studies;
(iv) reverse-translation of clinical findings into basic research.

Tuberculosis (TB) remains a health threat of global dimension which affects Sub-Saharan Africa, China and India most severely [1]. At the same time, TB is a highly interesting target for basic research since it reflects the outcome of a long-standing coevolutionary process between pathogen and host. An estimated 2 billion individuals are infected with Mtb, of whom ca. 90-95% will carry the pathogen lifelong without developing active TB (Figure 1) [1-3]. These individuals with so-called latent TB infection (LTBI) harbor dormant Mtb bacilli with low metabolic and replicative activity, which are controlled by an ongoing immune response [4]. In 5–10% of LTBI cases, active TB disease develops within the first 2 years but also occasionally at later times of life. It is becoming increasingly clear that LTBI and TB are not distinct entities but form a continuum. Accordingly, protection and pathology in TB are the outcome of a complex and highly dynamic crosstalk between Mtb and the immune system.

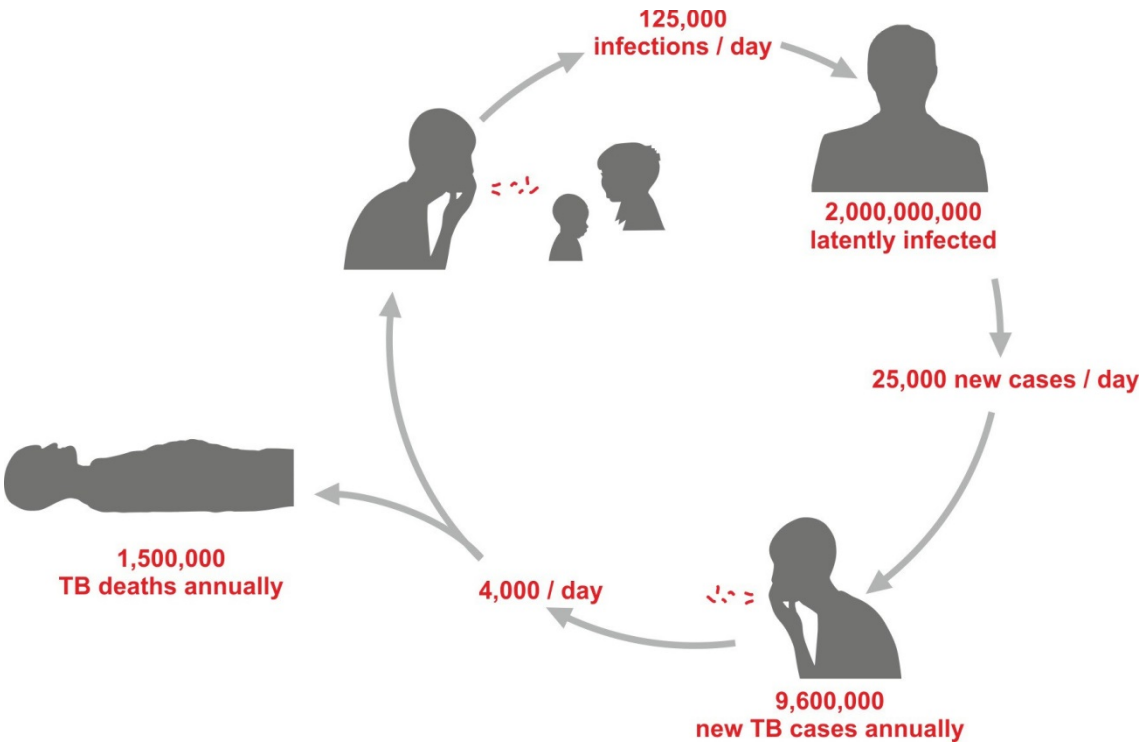

Figure 1- Epidemiology of TB (adapted from Kaufmann, Immunity 2010: Fig. 1, p. 568).

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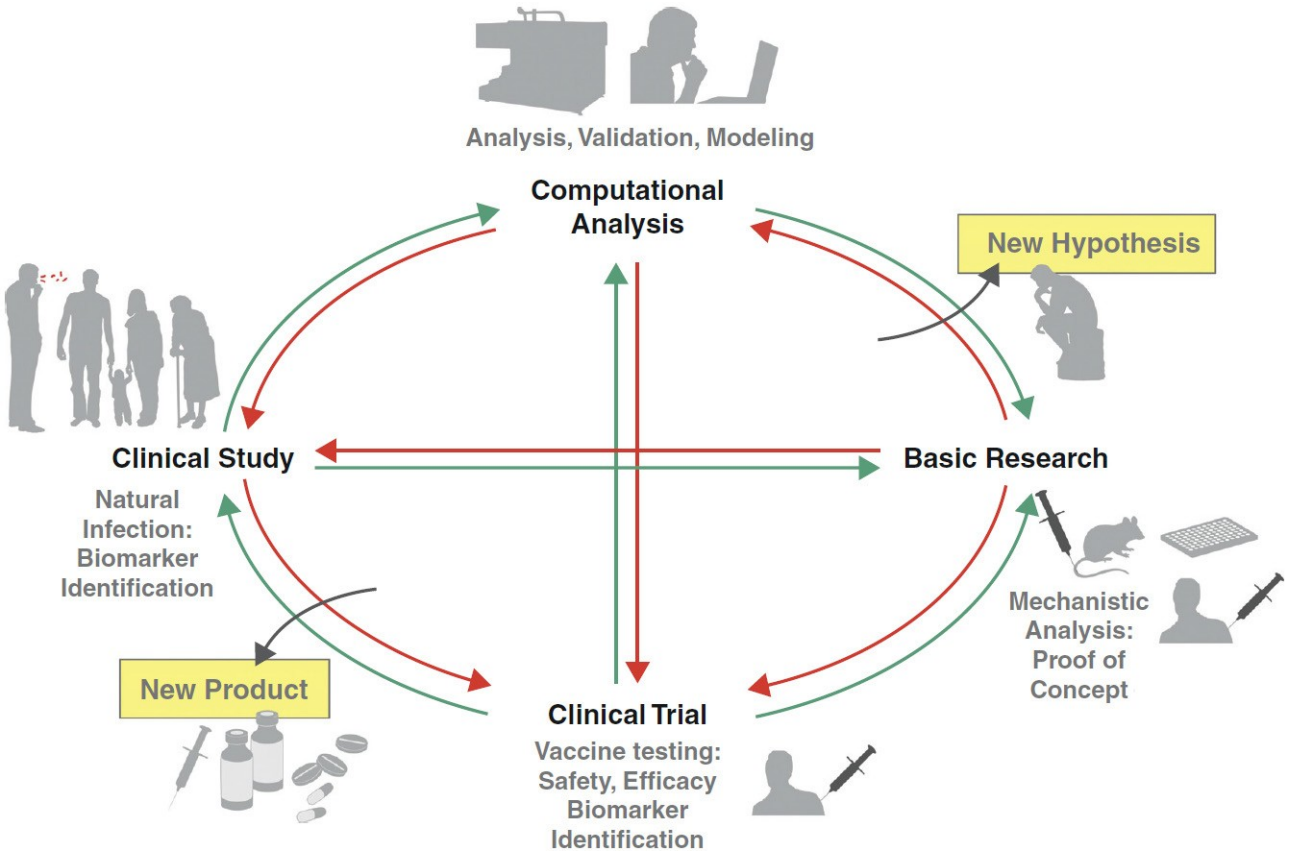

Figure 2- Research Strategy (adapted from Kaufmann et al, Curr Opin Immunol, 2014: Fig. 1, p 19).

At the cellular level, we focus on the crosstalk between Mtb and mononuclear phagocytes (MPs), which serve as both effector cells and as habitat for Mtb. At the tissue level, our focus lies on granulomas, which as solid granulomas contain Mtb, and as necrotic and caseous granulomas cause tissue damage and promote growth and dissemination of Mtb [4]. Granuloma formation and sustenance crucially depend on migration of and coordinated interactions among different leukocyte populations through cytokines, chemokines and surface receptors [5]. T lymphocytes are central regulators of protection and pathology. They depend on antigen-presenting cells, notably dendritic cells (DCs) and MPs, for appropriate activation. In addition, B cells and neutrophils are found in granulomas. The role of B cells remains elusive although recent evidence suggests that they perform regulatory functions [6;7]. The role of antibodies produced by B cell-derived plasma cells also remains incompletely understood. Recent studies into the role of neutrophils in TB point to a primarily harmful role for this cell type [8].

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Mtb influences the course of infection and disease by means of numerous factors which manipulate the host response, as well as by its ability to alternate between dormancy and metabolic and replicative activity. We therefore remain interested in TB as a highly attractive target for better understanding basic mechanisms of protection and pathology, as well as for developing novel intervention measures. We pursue these aims not through independent avenues but through a highly intertwined and reciprocal strategy that includes translation of basic research into a medical product, as well as reverse translation of findings obtained in clinical studies back to basic research questions (Figure 2).

References

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