

New vaccines for tuberculosis

with

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Any new concepts for treatment of tuberculosis?

The past decade has seen a resurgence in TB vaccine development, and there are now at least three new vaccines in the early stages of clinical trials (4). In parallel, new drugs are appearing,

such as moxifloxacin, PA-824, and R207910. How effective these treatments will be in the long term is unknown as yet, but there is clearly room for optimism.

The impact of tuberculosis?

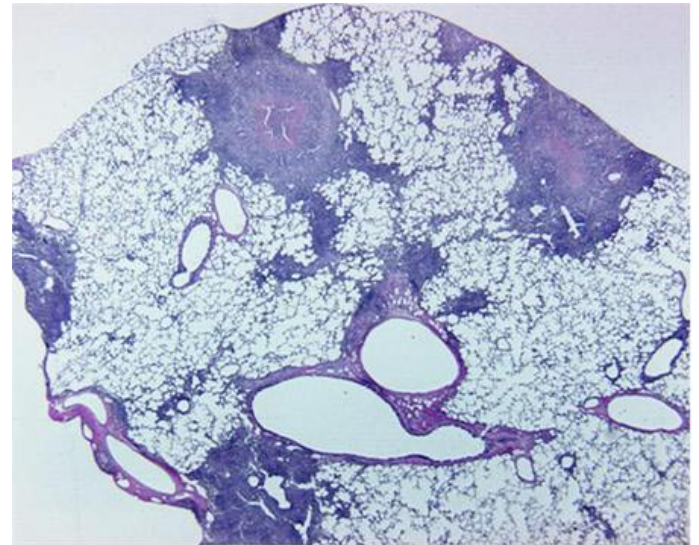
Tuberculosis continues as one of the three most serious global diseases, along with HIV and Malaria. Currently, there are about eight million new cases each year and close to 3 million deaths. In addition, many people get exposed to the bacillus but

do not show signs of disease. Many of these people, representing as many as a third of the global population, harbor a latent form of tuberculosis that has the potential to reactivate at a later date, or after another infection such as HIV (1).

Are animals useful for testing of new vaccines?

Yes, all long as one realizes they are not the “real thing”, they are models. Each has its own benefits and limitations. Mice are a good model of the human T cell response, but not the pathology. In contrast, there are considerable similarities between the pathology of the disease in guinea pigs and

that occurring in people (2). Moreover, screening and verification of a new vaccine candidate in animal models is inevitable in order to obtain FDA approval to go to clinical trials. In addition to protective effects of the vaccines, animal models are important to verify safety (Koch reactions, etc) and for toxicity testing.



Typical appearance of granulomas in guinea pigs infected with tuberculosis by low dose aerosol. Lesions are mixtures of lymphocytes and macrophages, with a caseous center. In the lesion on the top left this has significantly mineralized.

What is the role of T cells?

The T cell response is crucial to the expression of protective immunity to tuberculosis. Specifically, immunity is mediated by CD4 T cells of the so-called “TH1-type” which secrete the key cytokine gamma interferon (3). What is less clear is how this T cell subset changes over the course of the infection, or in response to effective vaccination. During the acute phase of the disease these cells are highly activated, and this continues well into the chronic phase. T cells with the capacity

to become memory T cells seem to undergo differentiation from activated effector to effector memory to central memory cells accumulating in lymphoid tissues and the bone marrow, but whether this happens in tuberculosis is much less clear. Our recent data suggests they may remain as activated effector cells and gradually disappear; this may explain why vaccination in children against tuberculosis wanes 10-15 years later in susceptible populations in developing countries.

REFERENCES

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