Vaccine Watch

PROGRAMMING INSTANT IMMUNITY

In this study, Popkov *et al.* combine elements of active and passive immunization through 'reactive immunization' and show that this approach can be used to generate instant immunity against tumours. Reactive immunization involves the generation of a reservoir of polyclonal antibodies that can assemble with chemical adaptors through a covalent bond. The adaptors are designed to direct the binding of the adaptor–antibody complex to a chosen target.

Here, the authors used two chemical adaptors to direct the binding of antibodies to $\alpha v\beta 3$ integrin and $\alpha v\beta 5$ integrin in three strains of mice with melanoma or colon tumours, which express these integrins. Treatment with either of the chemical adaptors resulted in instant antibody binding to the target and subsequent reduction in tumour size in all mouse strains. The antitumour mechanisms mediated by these chemically programmed antibodies involved antibody-dependent and complement-directed cytotoxicity.

So, this study describes the therapeutic potential of chemically programmable antibodies with implications for the treatment of diseases for which effective vaccines have not been developed using conventional approaches.

ORIGINAL RESEARCH PAPER Popkov, M., Gonzalez, B., Sinha, S. C. & Barbas III, C. F. Instant immunity through chemically programmable vaccination and covalent self-assembly. *Proc. Natl Acad. Sci. USA* 2 Mar 2009 (doi:10.1073/pnas.0900147106)

AUTOPHAGY ENHANCES VACCINE EFFICACY

Mycobacterium bovis bacillus Calmette–Guérin (BCG) has variable efficacy as a vaccine against tuberculosis. Now, Eissa and colleagues show that the induction of autophagy (which targets cytoplasmic components for lysosomal degradation) enhances antigen presentation of the immunodominant mycobacterial antigen Ag85B and thus increases vaccine efficacy.

M. tuberculosis is known to downregulate antigen presentation by infected macrophages and dendritic cells (DCs) by blocking fusion of infected phagosomes with lysosomes, but because *M. tuberculosis* and BCG secrete high levels of antigens, including Ag85B, it might be possible for these antigens to be delivered to lysosomes for antigen presentation through autophagy.

Pre-treatment of macrophages or DCs with rapamycin to induce autophagy followed by infection with *M. tuberculosis* or BCG resulted in increased mycobacterial killing and enhanced presentation of Ag85B. Furthermore, rapamycin treatment enhanced the ability of transferred DCs infected with BCG to protect against subsequent challenge with *M. tuberculosis in vivo*.

Infection of DCs with BCG that was engineered to overexpress Ag85B (BCG–OEAg85B) resulted in antigen accumulation in the cells, enhanced autophagy and increased antigen presentation. Importantly, immunization with BCG–OEAg85B protected mice against tuberculosis for a longer time than the conventional BCG vaccine.

ORIGINAL RESEARCH PAPER Jagannath, C. *et al.* Autophagy enhances the efficacy of BCG vaccine by increasing peptide presentation in mouse dendritic cells. *Nature Med.* **15**, 267–276 (2009)