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Improved vaccine approaches against pandemic influenza: Impact of novel adjuvants and prime-boost protocols on virus neutralization titers, epitope repertoires, antibody affinity maturation and cross reactivity

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Infection of humans with avian influenza (AIV) resulting in high morbidity and mortality rates were reported for H5N1, H7N7 and H7N9 AIV. Concerted efforts are under way to produce vaccines against avian influenza strains with pandemic potential. Most of the vaccines were based on vaccines formats that have been licensed for seasonal influenza, namely, split or subunit inactivated influenza vaccine (IIV) or live attenuated influenza vaccine (LAIV). However, both vaccine types gave very poor immune responses in humans. Combining AIV vaccines with novel adjuvants or prime-boost protocols were found to elicit significant hemagglutination inhibition (HI) against AIV strains. We analyzed the antibody responses elicited by the successful vaccination approaches to provide insights into the improved immune responses including complete antibody repertoires using whole genome phage display libraries (GFPDL) and antibody affinity measurements using SPR technologies. Several adjuvants (oil-in-water and saponin-containing particles) shifted the antibody focus from non-protective to protective targets in the globular head of the hemagglutinins of H5N1 and H7N9 AIV. SPR real time kinetics measurements demonstrated significant increase in total binding and increased affinity against functional HA1 proteins. LAIV prime with IIV boost resulted in similar changes in antibody quantity and quality similar to adjuvanted vaccines. In ferrets, increase in antibody affinity against the HA1 correlated with protection against lethal challenge with H7N7 and H5N1 HP avian influenza and reduced viral loads. Cross-protection against heterologous strains was also demonstrated. Therefore, new vaccine approaches along with novel analytical tools can improve the design of vaccine against pandemic influenza.

Biography

Hana Golding is the Chief of the Laboratory of Retroviruses at the Division of Viral Products, Center for Biologics Evaluation and Research (CBER), United States Food and Drug Administration (FDA), USA. She has received her PhD degree from Oregon Health Sciences University followed by Postdoctoral training at the Experimental Immunology Branch, NCI, NIH. She also is a Co-Manager of the Influenza Research Program in the Division of Viral Products, CBER, FDA. She has authored more than 150 research papers and book chapters on immunology, virology and infectious diseases. Her research areas include HIV, influenza, RSV, smallpox and novel adjuvants (safety and mode of action).

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