

## A rationally designed form of the TLR5 agonist, flagellin, supports superior immunogenicity of influenza B globular head vaccines

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**P**reviously, we demonstrated that for H1N1 and H5N influenza strains, the globular head of the hemagglutinin (HA) antigen fused to flagellin of *Salmonella typhimurium fljB* (STF2) is highly immunogenic in preclinical models and man. Further we showed that the vaccine format, or point of attachment of the vaccine antigen to flagellin, can dramatically affect the immunogenicity and safety profile of the vaccine. However, Influenza B vaccines based on these formats are poor triggers of TLR5 and consequently are poorly immunogenic. Through rational design, here we show that we have identified a fusion position within domain 3 of flagellin that improves TLR5 signaling and consequently, immunogenicity of multiple influenza B vaccines. Our results demonstrate that, similar to influenza A strains, the protective subunit of the influenza B HA can be fused to flagellin and produced in a standard prokaryotic expression system thereby allowing for cost and time efficient production of multivalent seasonal influenza vaccines.

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