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### Early NK cell activation as a result of MPL and QS-21 combination controls the adjuvant effect induced by the human Adjuvant System AS01

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ABSTRACTS

**Oral Abstracts**

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## Can Immunological Advances Enhance Vaccine Design?

contains both monophosphoryl-lipid A (MPL) and the saponin QS-21 and is used in the RTS,S malaria candidate vaccine. AS01 induces a transient activation of innate immunity, leading to increased number of activated antigen-presenting dendritic cells, but the impact of combining MPL and QS-21 on innate immune activation has not been investigated. We combined immunological and data analysis tools to identify the mechanism by which AS01 activates innate immunity, leading to improved adjuvant capability. Using a novel statistical framework for mRNA expression analysis, we unravelled the combinatorial effect of AS01 components and identified an emergent early IFN $\gamma$  signature elicited by AS01. The IFN $\gamma$  response was mediated by innate cells, including NK cells that secreted IFN $\gamma$  in the draining lymph nodes (dLN) as early as 2 h after injection of mice with AS01. Depletion strategies showed that NK cells were essential for the development of T cell immunity. Interestingly, a similar activation was observed in the dLN of AS01-injected macaques as well as in the blood of individuals receiving AS01-adjuvanted vaccine.

Our multidisciplinary, cross-species analysis of AS01 mode of action shows that combination of immunostimulants resulted in the induction of novel pathways associated with improved vaccine response. It also highlights a key role for early NK cell activation in AS01 adjuvant effect, providing novel hypotheses on the contribution of this adjuvant in the protection conferred by the AS01-adjuvanted vaccine in humans.

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### Early NK cell activation as a result of MPL and QS-21 combination controls the adjuvant effect induced by the human Adjuvant System AS01

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Combining immunostimulants in adjuvants can improve the quality of the immune response to vaccines. The Adjuvant System AS01