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Development of QS-21−inspired minimal synthetic saponins as novel vaccine adjuvants: Improving on nature

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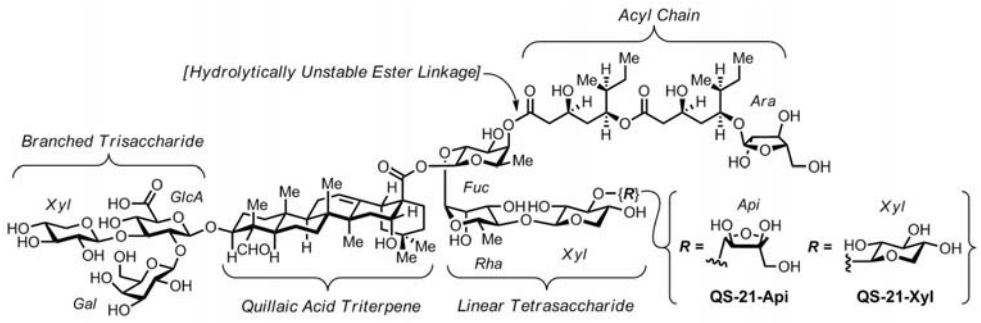
The immune response to vaccines is often enhanced by the presence of adjuvants – compounds that are themselves not necessarily immunogenic but augment significantly the immunogenicity of a coadministered antigen. Few adjuvants have both sufficient potency and acceptable toxicity for clinical use. QS-21, a saponin natural product, has shown promise in numerous vaccine clinical trials; however, its utility remains constrained by several factors, including scarcity, dose-limiting toxicity and chemical instability.[1] Further, its molecular mechanism of action is still largely unknown.

To address these challenges, we have rationally designed and synthesized novel simplified saponin variants with improved stability and high adjuvant potency.[2] Extensive structure-function exploration of the QS-21 molecule has provided important new insights into the key structural features that are critical for activity. This has led to the development of potent minimal saponin adjuvants that are synthetically accessible, non-toxic, and successfully decouple adjuvant activity from toxicity.[3] These efforts have enabled the development of QS-21−derived molecular probes with more favorable therapeutic profiles as a powerful platform for mechanistic studies of these saponins.



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