mRNA vaccine for *Staphylococcus aureus*

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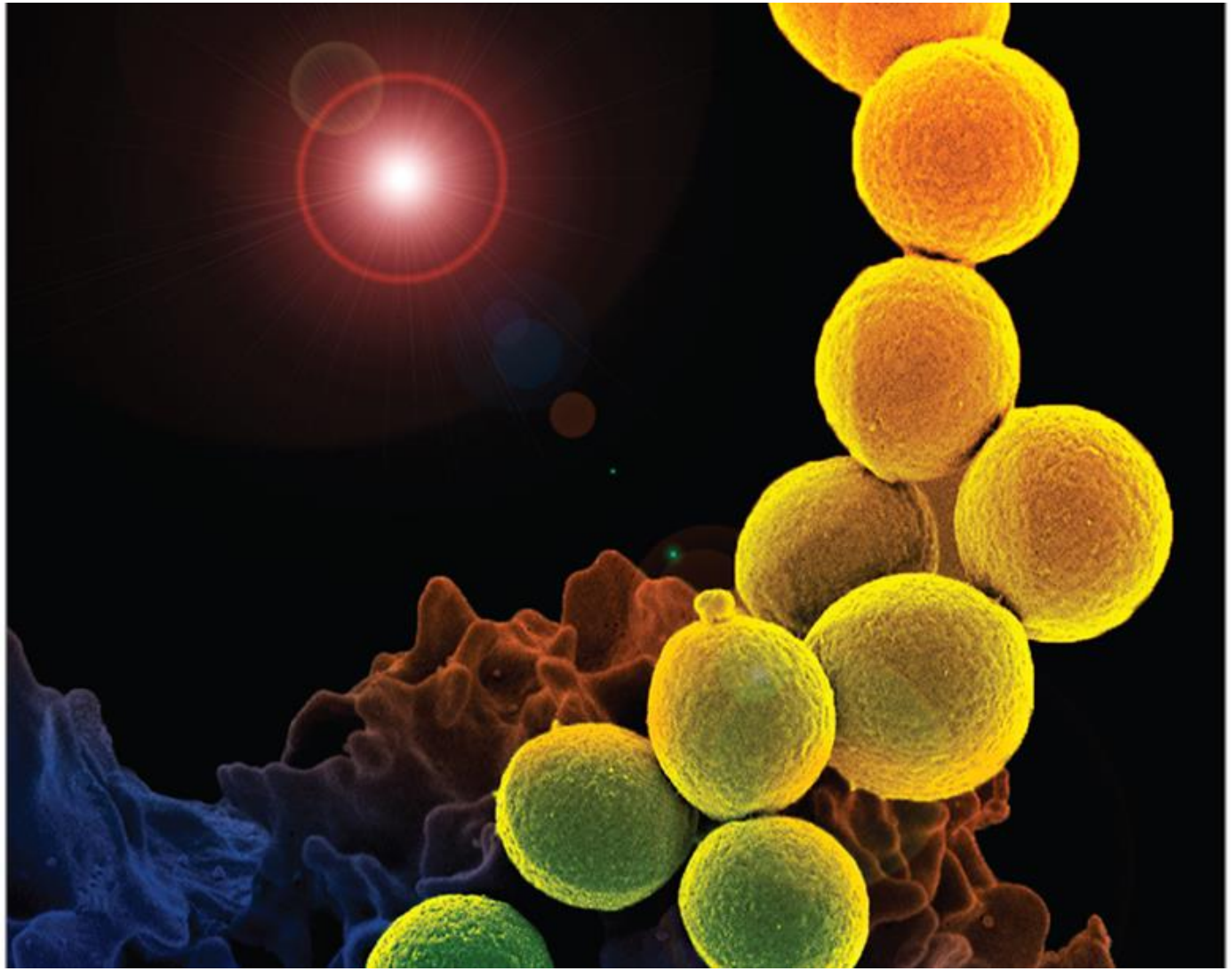
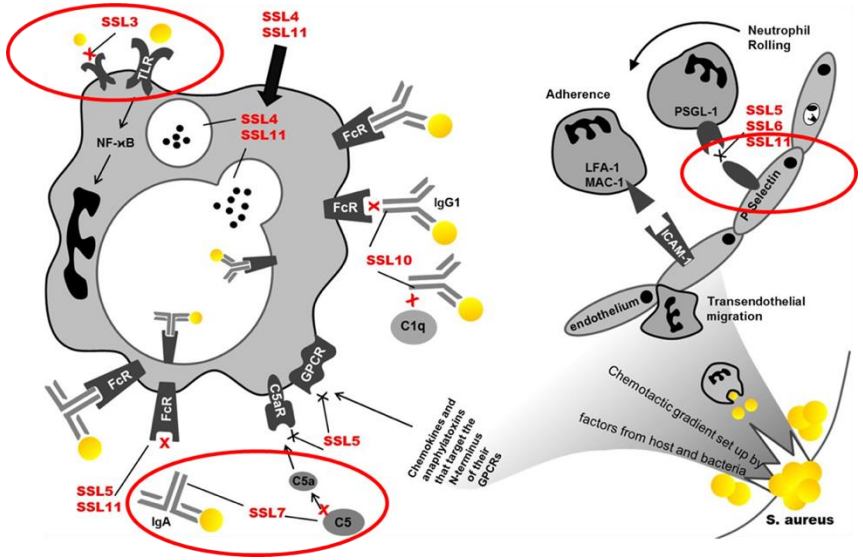


S. aureus vaccine targeting three virulence factors: Staphylococcal Superantigen-like (SSL) proteins

UBIQUITOUS SECRETED IMMUNE EVASION FACTORS

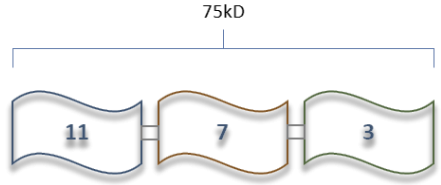
- Well characterised
- Inactivated by targeted mutation

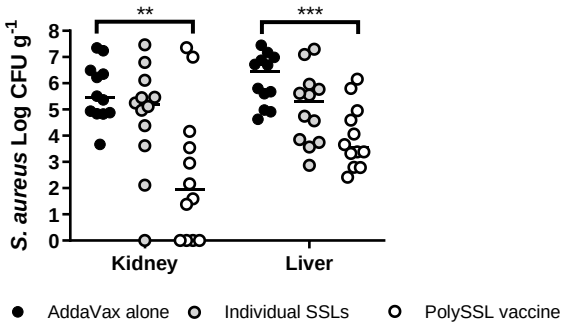


Langley, R.J., *et al.*, (2013), *Bact Toxins: Genet Cell Biol Practi Appl*. p. 129 -156.

RNA VACCINE BUILDS ON EXTENSTIVE PRECLINICAL INSIGHT FROM PROTEIN VACCINE

- Requires a fusion/poly protein (PolySSL)
- Adjuvant choice important
- Allelic variation covered with six PolySSL proteins
- Effective in mouse model of peritoneal infection





Chan JYH *et al.*, (2024) ICB, 102: 365.

Value Proposition: unique PolySSL vaccine targeting secreted toxins common to all strains

NZ has one of the highest rates of both invasive and non-invasive *S. aureus* in the developed world. $$$ in costs to our medical system and productivity.

S. aureus is a WHO priority pathogen due to antimicrobial resistance. A 2019 Global Burden of Disease Study identified *S. aureus* as the leading bacterial causes of death in 135 countries.

- IP held by UoA
- No similar drugs in the market
- Competitive advantage = reducing dependence on antibiotics
- Prophylactic treatment of at risk patients, e.g. prior to surgery or in aged-care facilities
- Scope for further Ag identification, transcript, & formulation design
- Pandemic preparedness: manufacture of mRNA through the platform (Malaghan & SPS)

Market: *S. aureus* is a leading cause of post-surgical infections [20-50 cases/100,000 of SAB in USA, unadjusted mortality of 10-30%]

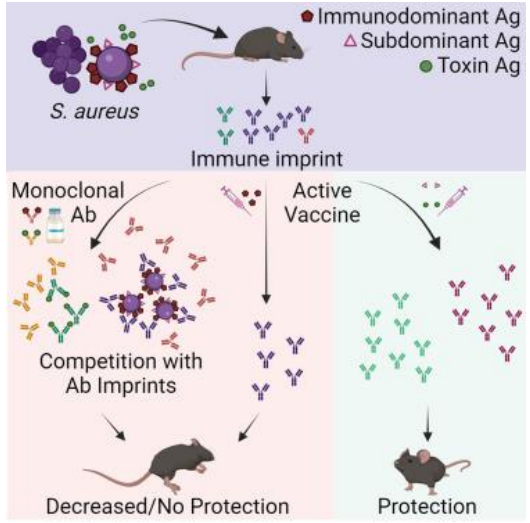
No approved vaccines
Several in early phase clinical testing

~14 failures, BUT substantial revenue anticipated if successful

Intercell and Merck's V710 staphylococcal vaccine (recently terminated), **forecast ~1.4bn in sales**

Pfizer's SA4Ag staphylococcal vaccine (also terminated), **~1.8bn in sales**

- Recent shift to secreted virulence factors, rather than dominant cell associated antigens, e.g. current Phase I trial for LBT-SA7 multivalent toxoid vaccine, designed to prevent skin and soft-tissue infections (SSTIs)
- Also recent expansion of focus to potential of childhood vaccination, before immune imprinting to *S. aureus* is established (JAMA, August 2024)



https://doi.org/10.1016/j.xcrm.2023.101360

SSL vaccine effective in *S. aureus*- immune imprinted mice

Capability

- Well characterized, immunogenic vaccine
- Models and *in vitro* assays to measure functional activities in place
- Expression of multiple antigens is a key requirement (payload design) and already demonstrated for this vaccine
- Areas of RNA product refinement identified

- Key strengths:
  - knowledge of *S. aureus* pathogenesis and capabilities around *in vitro* and *in vivo* testing of novel approaches
  - mRNA transcript design
- All major Pharma are interested in Staph vaccines and could be suitable partners

INTERNATIONALLY EXPERIENCED TEAM in RNA

INTERNATIONAL NETWORKS, EXPERTISE IN TRANSCRIPT DESIGN & TESTING

Duccio Medini

RiboPro

Sander van Asbeck

Design

- Transcript design from protein and production
- Codon-optimisation

University of Kent

Tobias von der Haar

King's College London

François Hallac
Harris Makatsoris

Packaging / Delivery

- RNA production/packaging
- Packaging

ACUITAS THERAPEUTICS

Penn Arts & Sciences University of Pennsylvania

- mRNA delivery/Novel dendrimers

Virgil Percec

Genome Institute of Singapore A*STAR GIS

Yue Wan

Refinement

- Circular RNA

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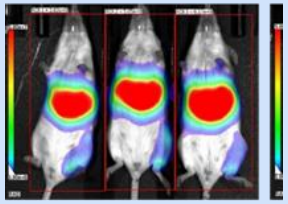
Vaccine candidate
Pathogen expertise
Translation from in vitro to in vivo

Mouse models
Reporter assays



Delivery and Refinement

- mRNA production

Victoria University of Wellington Te Herenga Waka

Rebecca McKenzie

- LNP formulations

Malaghan Institute of Medical Research

Gavin Painter
Sarah Draper

Development Potential: leverages strong product, platform strengths, and existing networks

- Further development requires support from all pillars of the RNA Platform
- Strong existing product with scope for design improvements
  - use of AI to rationally select additional antigens
  - refinement of transcript design – shift from secreted to transmembrane form
  - formulation development - capacity to tune LNPs
- Opportunity to engage with established network of infectious disease clinicians
- A phase I safety & efficacy trial might need around 20 participants. All could come from NZ. Maximum follow-up of 1 year.
- NZ and Aus are both suitable countries for a clinical trial

SNAP
Staphylococcus aureus
Network Adaptive Platform

Project Scope

Dimension	Description
People	Personnel with expertise in transcript design, relevant *in vitro* & *in vivo* assays, *S. aureus* models
Activities	1. Novel payload design, transcript re-design, production and testing of transcripts (year 1) 2. Animal model testing of new transcripts and/or formulations (year 1 through to year 2) 3. Serological testing of clinical samples for reactivity to relevant *S. aureus* antigens (years 1, 2)
Milestones	1. Identification & refinement of novel mRNA transcripts for a *S. aureus* vaccine 2. Identification of a formulation that stimulates >2 log reduction in *S. aureus* burden *in vivo* 3. Development of strong clinical linkages and relevant serological testing capabilities
Infrastructure	Key equipment & animal model in place for UoA project component, remaining infrastructure within the various pillars
IP	Novel vaccine antigens, development of new strategies for enhanced or altered transcript performance, identification of novel delivery approaches
Budget	$1.5 - 2 million over 2 years

Platform fit