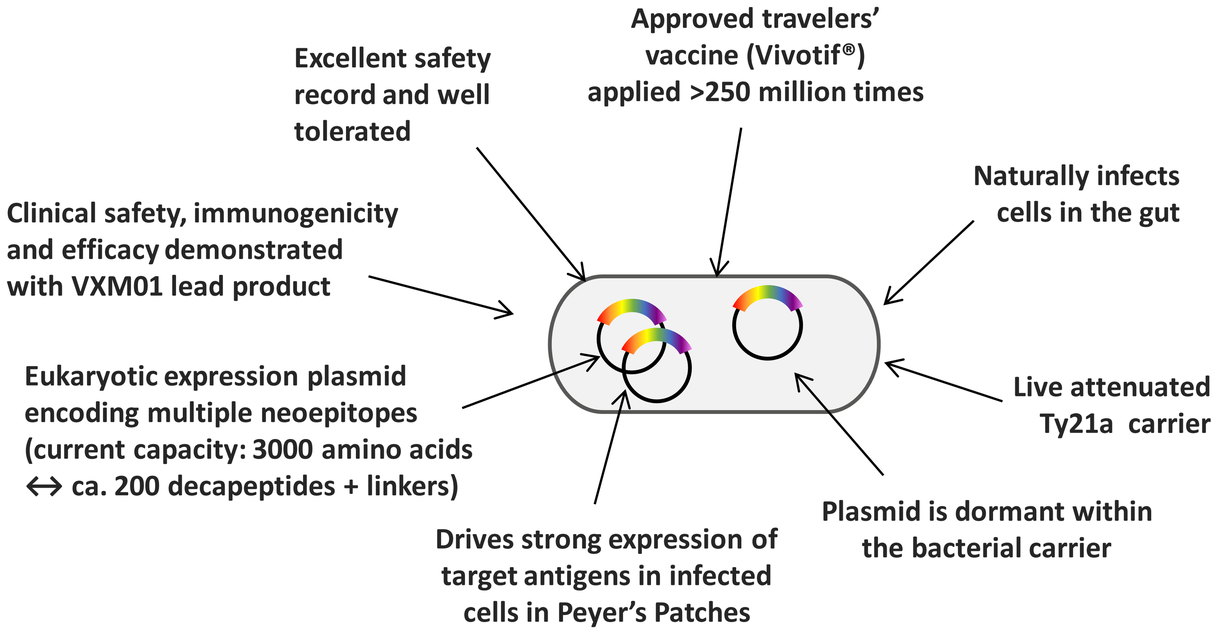
# A versatile live attenuated oral *Salmonella* DNA vaccination platform for modulating T cell immunity against tumor neoantigens

VAXIMM AG, Basel, Switzerland, and VAXIMM GmbH, Mannheim, Germany.

## High safety and good tolerability

### Readily combinable with other immune therapies

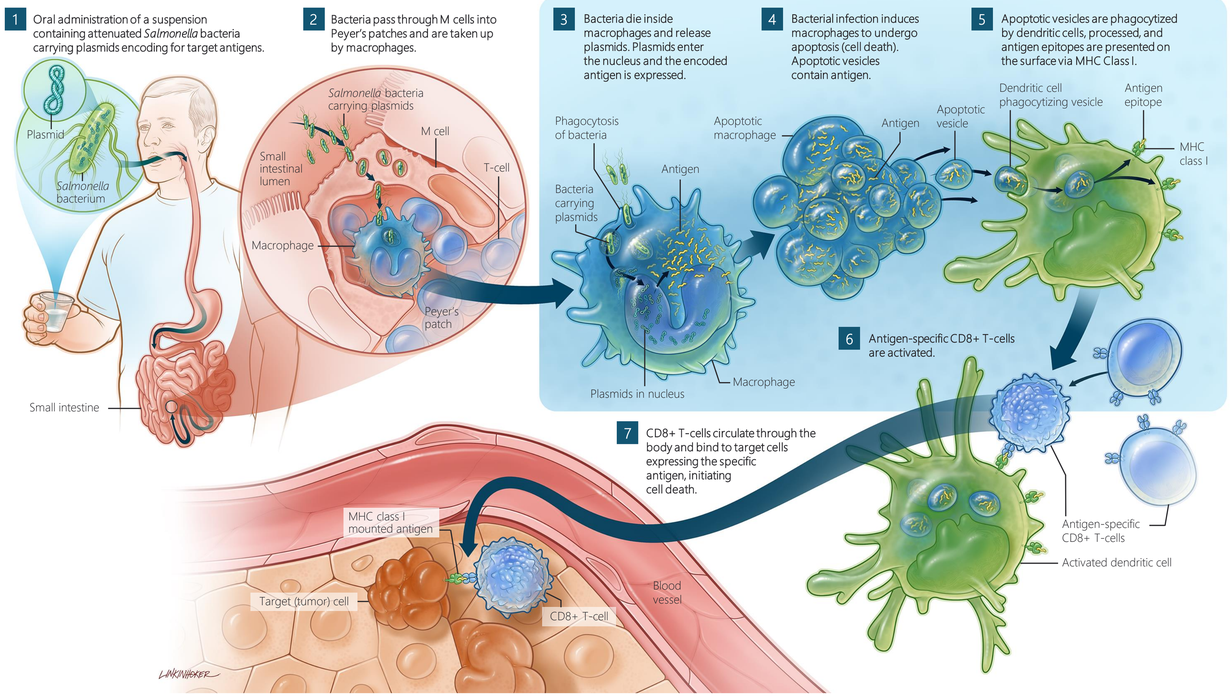
- Approved carrier bacterium, with excellent longstanding safety record
- Low therapeutic doses much below Vivotif® (typically $10^6$ – $10^7$ CFU)
- No anti-vector immunity and little to no vector-related side effects
- Suitable for multi target and neoantigen approaches




## Natural, efficient and easy way to activate T-cells

### Strong antigen expression allowing specific T-cells to target the tumor

- Oral delivery targeting the lymphatic tissue of the gut
- Boosting possible without anti-carrier immunity
- Self-adjuvanted through concomitant bacterial Ty21a infection
- Very low amount of genetic material administered corresponding to 1 ng of DNA in $10^7$ CFU, far below 500-1000 µg of RNA used in recent studies




## Best-in-class technology for neoantigen vaccination

### Novel approach for targeting neoepitopes

- Short time to oral administration
- Objective: neoantigen identification + 15 days
- Accelerated path to phase 1 POC data
- Unique administration mode
- Strong rationale to combine with checkpoint inhibitors

| Delivery Technology | N2N time |
|---|---|
| **VAXIMM** | Neoantigen discovery **+ 15 days** |
| Company A* | 115 days |
| Company B* | 90 days |
| Company C* | 75 days |

**according to published data*

| Delivery Technology | Ease of mfg. | Route of Administration |
|---|---|---|
| **VAXIMM** Ty21a based DNA vaccines | +++ | Oral |
| Listeria based vaccines | +++ | Intravenous |
| mRNA | + | Intravenous Intranodal Intradermal |
| Viral Vectors | + | Intradermal |
| Peptides | + | Intradermal |
| Dendritic Cells | + | Intravenous |
| DNA | +++ | Intramuscular |

## Fast, robust and flexible manufacturing

### Attractive cost of goods

- Plug and play system
- Established methods (GMP manufacturing, QA/QC, etc.)
- Stable formulation for 3 years independently of the insert
- No galenic formulation incompatibilities
- Neoantigen/ personalized vaccine approaches: 15-day turnaround time
- Large number of epitopes possible

**Plasmid**
- DNA synthesis and cloning
- Plasmid isolation
- Plasmid sequencing

**Bacteria**
- Master cell bank Ty21a
- Transformation of bacteria

**Drug substance**
- Preculture and QC
- Plasmid sequencing
- 1 L fermentation

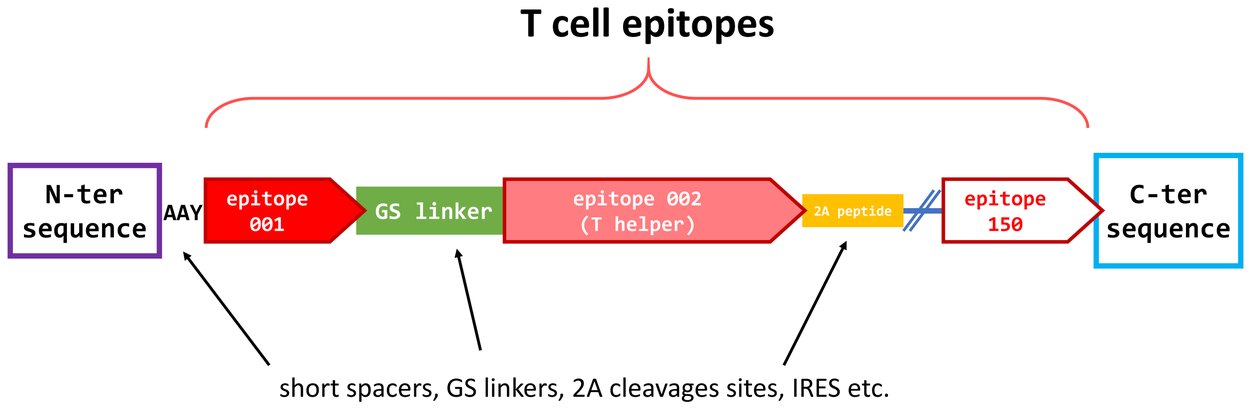
**Drug product**
- Dilution + Filling
- QC
- QP release

## Immunogenicity of different polyepitope constructs

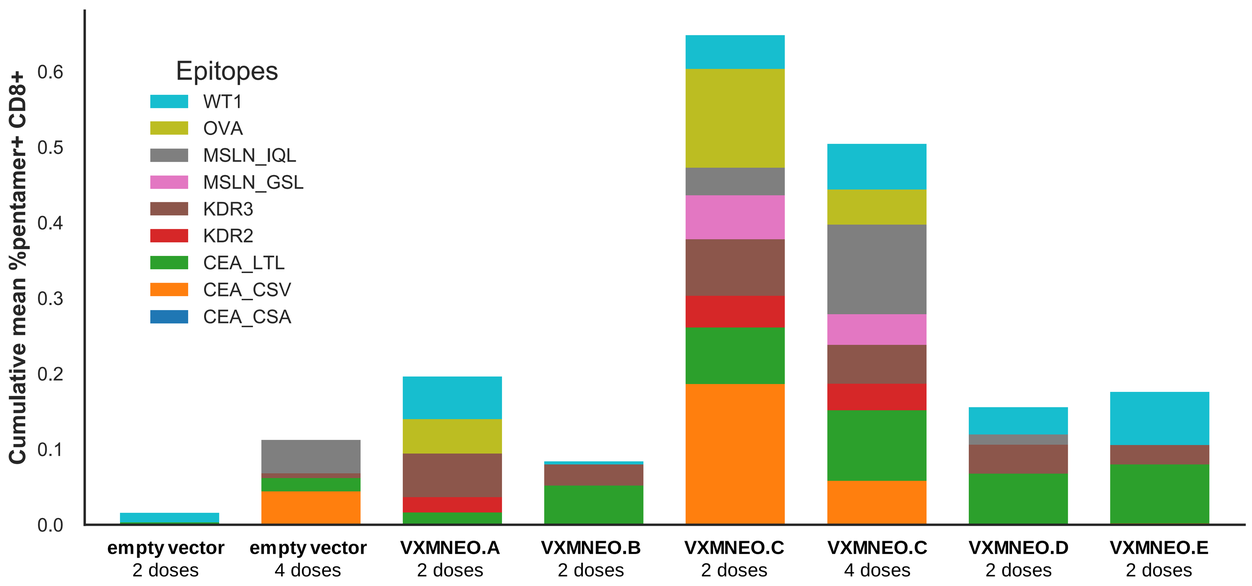
### Substantial systemic T-cell response detected

- Different constructs encoding multiple CD8 and CD4 T cell epitopes in a "string-of-beads"
- Dose, treatment schedule, ordering and linkage strategy greatly influences the immunogenicity

**100 – 300**
**T cell epitopes**




short spacers, GS linkers, 2A cleavages sites, IRES etc.




*Cumulative mean frequency of the indicated epitope-specific CD8+ T cell population in the splenocytes of C57BL/6 mice immunized via the oral route with different constructs encoding 9 CD8 epitopes and 1 helper epitope and doses up to $10^{10}$ CFU.*

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