

Immunobricks

A designer vaccine against Helicobacter pylori à la Synthetic biology

Kočar, Katja Kolar, Ana Lasič. Jan Lonzarić. Jerneja Mori, Anže Smole: Mentors: Moica Benčina. Monika Ciglič, Simon Horvat Karolina Ivičak. Roman Jerala, Nina Pirhe



Helicobacter pylori

20-90% population infected. Causes ulcers, cancer, gastric adenocarcinoma. 8th leading cause of death by 2010. Main virulence factors: flagellin, urease. Its flagellin avoids immune recognition (TLR5). No effective vaccine available.

Vaccine required

Effective vaccine must activate: Adaptive immunity (antibodies, T-cells) Innate immunity - adjutants, bacterial, and viral components - "immunologists' dirty little secret"



Synthetic subunit vaccines are safer than attenuated microbes.

Registered "Immuno"Biobricks

Reengineer TLR

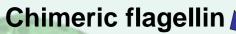
signaling network

Couple TLR activation to antigen processing

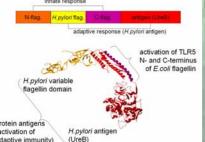
We have contributed 132 new constructs to the registry, which represents an "initial library" for the design of synthetic vaccines and engineering of TLR signaling.

Eradicate Helicobacter pylori!

Immunobricks for synthetic vaccines

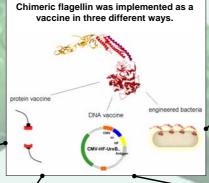


Make flagellin of H. pylori visible to the immune system

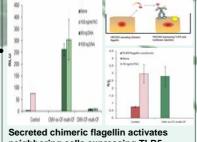


Designed synthetic multiepitope

Implementation



Chimeric flagellin with synthetic antigen is presented at the surface of E. coli strain with flagellin deletion.



neighboring cells expressing TLR5.

Chimeric flagellins were prepared, expressed in bacteria and purified. Protein is internalized by cells expressing TLR5 and in contrast to the original H. pylori FlaA activates TLR5 signaling.



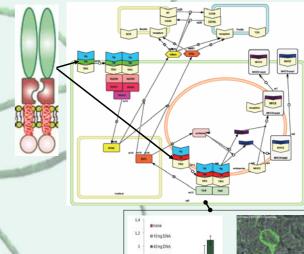
Fluorescent multi-TMTIR4 GFP is expressed in electroporated murine leg.

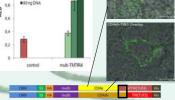


Serum of mice immunized with CFmulti (after only 3 weeks!) reacts with antigen and also with live H. pylori.

Beyond iGEM

- vaccine against bacteria that have TLR5 unresponsive flagellin (Bartonella, Campylobacter, Brucella...)
- potentially universally applicable principle to synergistically activate several signaling networks, also for tumor vaccines





Antigen-TLR fusions activate signaling and their localization can be selected by the type of TM segment.