

ORAL PRESENTATIONS

APPLICATION OF FUNCTIONALIZED SYNTHETIC LIPIDS IN BIOLOGY AND MEDICINE

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Membrane surfaces, which are common to all biological entities - including eukaryotic cells, prokaryotic cells, and virions - comprise a diverse array of biological molecules (proteins, glycans, and lipids) that mediate environmental interactions. The ability to precisely manipulate membrane composition holds immense potential for studying cellular interactions and for developing novel diagnostic and therapeutic strategies. Functionalized Lipid Constructs (FSL) technology offers a robust tool for the controlled modification of cellular and viral lipid membranes. The principle relies on the spontaneous insertion of amphiphilic molecules carrying well-defined epitopes into the lipid bilayer from a solution, without compromising cell viability, thereby enabling the programmable engineering of membrane surface properties.

Based on FSL constructs bearing peptide epitopes, highly sensitive diagnostic systems - termed "kodecytes" (modified erythrocytes) - have been developed for antibody detection in syphilis (sensitivity 98.6%, specificity 98.8%, outperforming the standard RPR test), leptospirosis, COVID-19, et. al. Molecular dynamics simulations, using a SARS-CoV-2 S-protein peptide as a model, confirmed that inserted peptides retain their native conformation and remain accessible to antibodies. Similarly, glycan-based FSL constructs enable the generation of erythrocytes displaying defined blood group antigens (ABO, Lewis, P, FORS), useful, e.g., for quality control or modeling of transfusion reactions in immunohaematology. FSL constructs bearing the xenogeneic Galili antigen (AGI-134), when injected into a solid tumor, label cancer cells with the non-human α -Gal antigen, prompting the naturally occurring anti- α -Gal antibodies to attack them. This triggers tumor cell death and converts the tumor into an autologous vaccine. In mouse experiments, the AGI-134 induced tumor regression and protected against metastases.

Beyond medical applications, FSL technology addresses fundamental biological questions, particularly in studying and modeling complement activation - a key mechanism of innate immunity. Using kodecytes modified with FSL constructs bearing specific glycans, it was confirmed that certain anti-glycan antibodies lack complement-activating capacity. Moreover, the hemolytic activity of complement in human serum was found to be twice as stable as previously assumed: 60% of activity was retained after one week at room temperature and two months at 4°C. Additionally, cholesterol-based lipid constructs enable targeted incorporation into lipid rafts - membrane microdomains central to cell signaling - opening perspectives for antigen-independent modulation of immune responses. Furthermore, fluorescent and biotinylated FSL constructs allow for the modification of enveloped viruses (e.g., influenza) for bioimaging of virions both *in vitro* and *in vivo*.

A key advantage of FSL technology is its ability to modify virtually any surface, including non-biological ones, without prior chemical activation. Applications include rapid biotinylation of magnetic microspheres for cell and protein immobilization, and glycosylation of implants to enhance biocompatibility.

In summary, FSL constructs represent a versatile platform for surface property modeling, combining ease of use with broad functionality. They demonstrate significant potential for translating fundamental chemical and biological research into clinically relevant applications.

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