Lithium niobate nanoparticles functionalization with proteins for cancer active targeting

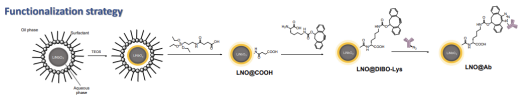
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Nowadays, cancer is a major health burden and has become the second leading cause of death in industrialized countries. Cancer mortality can be reduced through early stage detection and appropriate selective treatment. Conventional imaging techniques and cancer treatments lack sensitivity for early detection and show poor specificity, causing adverse side effects. Nanomedicine has emerged as an appealing tool to support early diagnosis and targeted tumor therapy[1],[2].

Harmonic nanoparticles (HNPs) are known for their efficient non-linear optical response by generation of second and third harmonic signals under ultrafast laser irradiation, which makes them appealing probes for bioimaging applications[3]. The HNPs can be functionalized with i) imaging probes for multimodal imaging; ii) photocaged cargos for controlled drug delivery; and iii) targeting ligands for active targeting of cancer cells. We herein present a functionalization strategy based on the silanization of $LiNbO_3$ (LNO) HNPs through water-in-oil microemulsion[4] to introduce surface reactive moieties followed by post-conjugation to targeting ligands, such as anti-EGFR antibodies. In order to enhance covalent immobilization over unspecific protein adsorption, surface covering with peptide mimics was investigated and showed promising anti-fouling properties. A small library of peptides was designed through solid phase peptide synthesis (SPPS) for further conjugation to antibodies using click reactions.

The long-term perspective of the project is to use protein-coated nanoparticles as theranostic nanoplatforms, focusing on the active targeting feature, through the use of monoclonal antibodies, or smaller engineered protein fragments, such as affibodies. Several grafting strategies will be investigated in the future. Potentially, these nanocarriers, simultaneously decorated with targeting ligands, anti-cancer drugs and imaging probes, could combine early detection and *in vivo* cancer treatment.



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[2] Stephanie D Steichen, Mary Caldorera-Moore, Nicholas A Peppas, *Eur J Pharm Sci,* **2013,** 48(3): 416-427.
[3] Andrii Rogov, Marie Irondelle, Fernanda Ramos Gomes, Julia Bode, Davide Staedler, Solène Passemard, Sébastien Courvoisier, Yasuaki Yamamoto, François Waharte, Daniel Ciepielewski, Philippe Rideau, Sandrine Gerber-Lemaire, Frauke Alves, Jean Salamero, Luigi Bonacina, Jean-Pierre Wolf, *ACS Photonics,* **2015,** 1416-1422.
[4] Adrian Gheata, Alessandra Spada, Manon Wittwer, Ameni Dhouib, Emilie Molina, Yannick Mugnier, Sandrine Gerber-Lemaire, *Nanomaterials,* **2023,** 13(3): 522.