Goldnanoparticle assemblies for SERS based detection of EGFR family expressing ovarian cancer cells in tumor xenografts

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For most tumors surgical dissection is still the most applied and effective treatment; however, it remains a challenge to secure the complete removal of the tumor. Explicitly the dissection of tumors with tendency to infiltrate the surrounding tissue within the peritoneal cavity. Intraoperative visualization of tumors can support the surgeon to see the edge of the tumor[1]. Hence tumor cells are targeted with biocompatible gold nanoparticles functionalized with antibody binding members of the EGFR family (anti-EGFR GNPs), on their overexpressed epidermal growth factor-receptors (EGFR) and confirmed with surface enhanced Raman spectroscopy (SERS)[2]. Thereby nanoparticle distribution, SERS signal strength and target selectivity is crucial and depends either on surface chemistry but also on GNP size and shape.

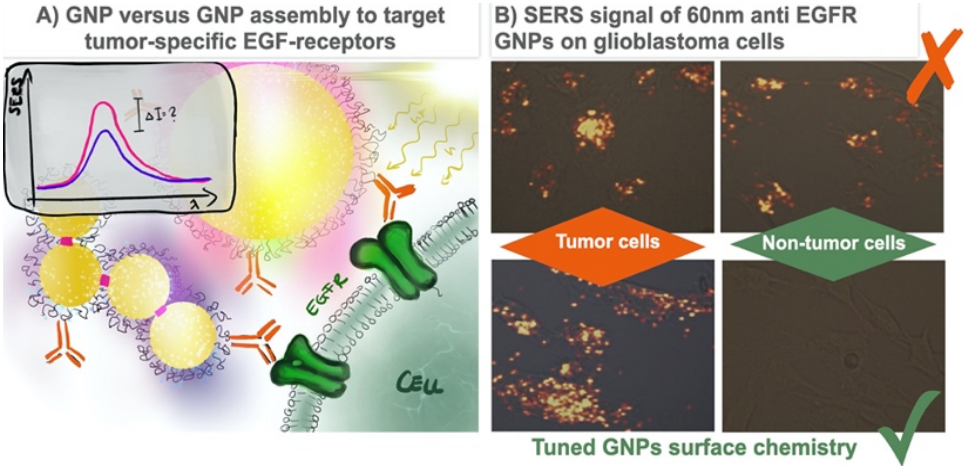

Figure 1 A) Sketch of the Goldnanoparticle assemblies versus single GNP targeting the EGFR receptor of the cell. **B)** SERS images of tumor (BS153) and non-tumor (IMA2.1) cells treated with anti EGFR gold nano particles (60 nm). Measured by F. Burgio *et al*. with confocal Raman microscope (WITec GmbH) at FHNW[2].

Within the proposed PhD project, we aim to determine the effect of GNP sizes (60-5nm) and shapes (e.g. spheres, rods, triangles) to optimize target selectivity and distribution. Moreover we will address the SERS intensity limit caused by GNP-diameter, by using assemblies of small GNPs (<20nm) connected with different types, lengths and concentration of linker molecules. Surface chemistry is characterized with inductively coupled plasma mass spectrometry, SERS, Quartz crystal microbalance and more. Assemblies are optimized based on SERS signal and fully characterized with scanning and transmission electron microscopy and atomic force microscopy. In order to measure the effect of the conjugates, we would like to test not only genetically manipulated ovarian cancer cells but also push this promising experimental setup further towards translational and interdisciplinary cancer research. CRISPR-Cas9-engineered ovarian cancer cells will be applied to a *in vivo* zebrafish embryo tumor xenograft model following on studying target specificity, distribution, SERS signal intensity and stability of large, single anti-EGFR GNPs to small, multi anti EGFR GNPs assemblies in a more complex but still well-known environment[3]. Importantly, the use of zebrafish tumor xenografts and PDX models allow visualization of single cells and can also be measured with SERS. To achieve this ambitious goal, this study takes advantage of established expertise and experimental capabilities in both collaborating labs.

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[3] a) F. Jacob et al. Cancer Res, 2018, 1, 78 (11), 2952 b) Huang et al. eLife, 2020 submitted

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