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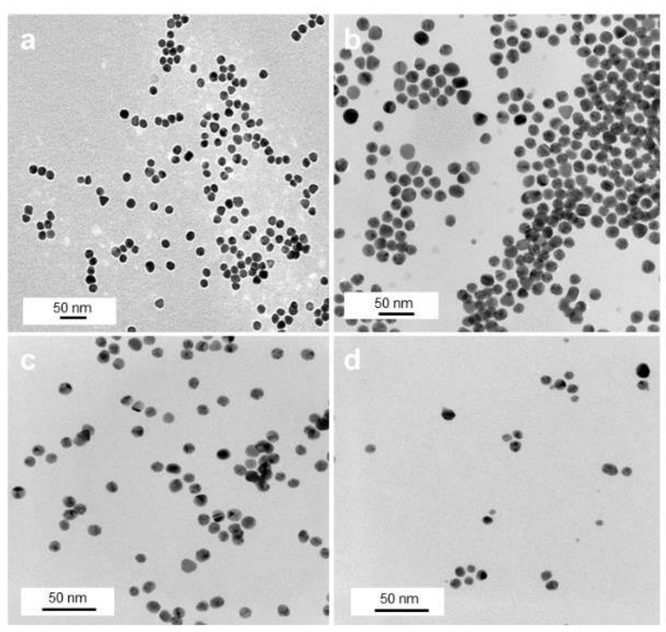
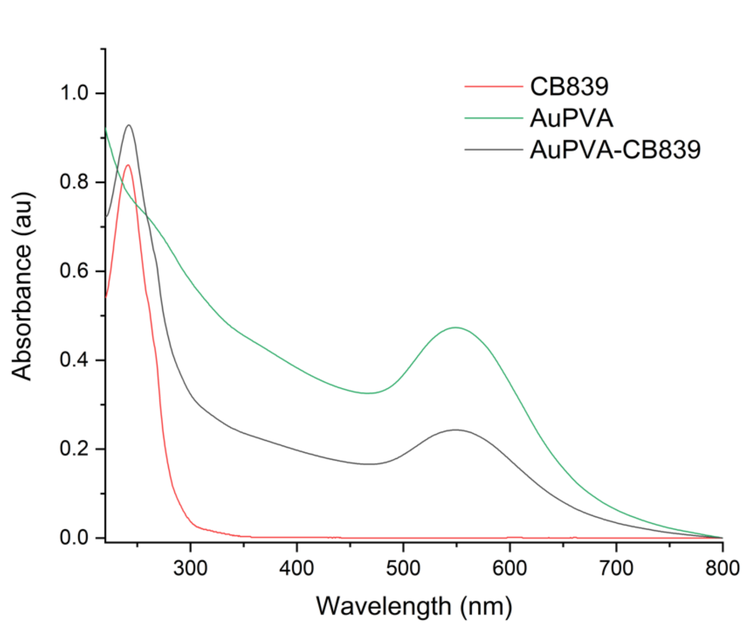
Augmentation of anti-cancer stem cell potential through nano-functionalization of Telaglenastat (CB-839)

Background:

- Nanomedicine is the medical application of nanotechnology which is estimated to cover a significant amount of your future economy
- Here we present results of transdisciplinary projects to develop nanodrugs to eradicate cancer stem cells.
- Glutaminase 1 (GLS1) is an metabolic enzyme that has been proposes to cover central roles in the maintenance of cancer stem cells in various tissues.
- Telaglenastat (CB-839) is a highly specific, pharmacological GLS1 inhibitor currently in is clinical stage testing for the treatment of different solid cancers

Results:





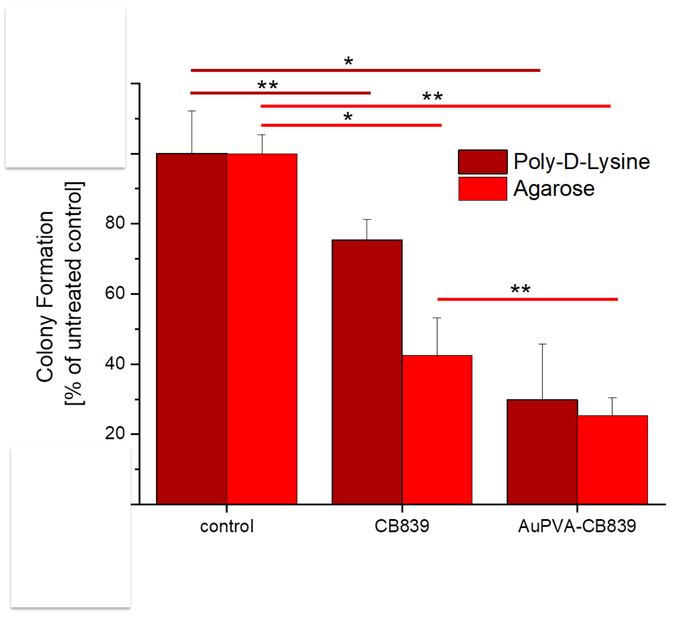
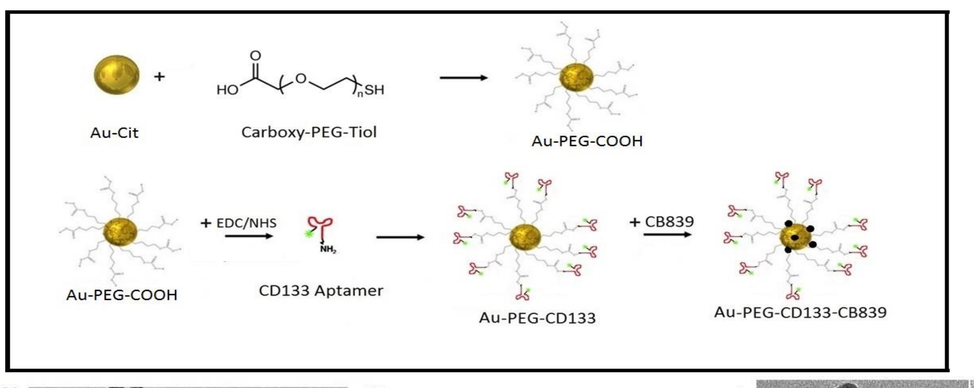
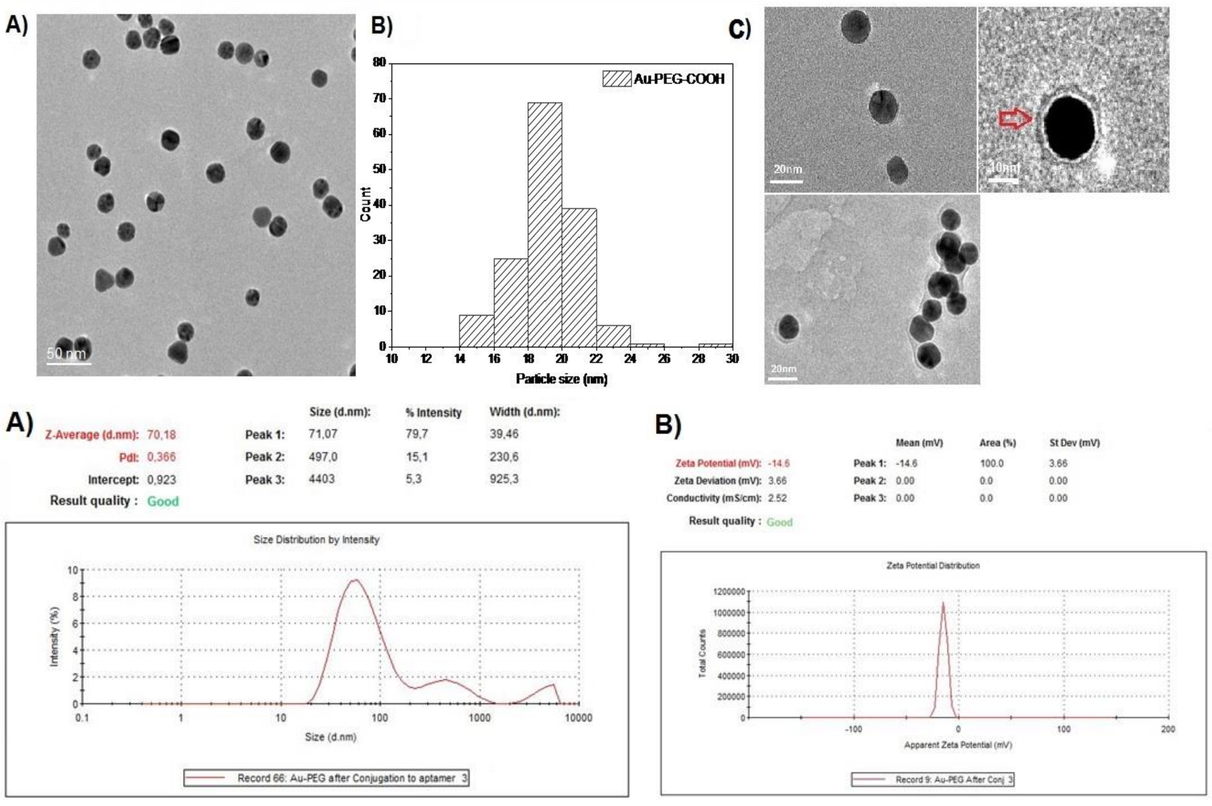


Fig1: Generation of gold nanoparticles (Au) based on the *in house* developed one-pot synthesis method (Giessen et al., 2020) equipped with CB-839 using polymer-assisted drug conjugation (our drug loading efficacy was highest when using polyvinyl alcohol /PVA as polymer). Pictures shows two assays applied for chemical characterization of the particles using transmission electron microscopy (TEM) or ultra violet imaging spectroscopy- quantified absorption. The third picture shows the example of functional assessment of the nanomedicine in one cancer stem cell line *in vitro*, revealing augmented anti-cancer potential as compared to the effects achieved when treating the cells with naïve drugs.





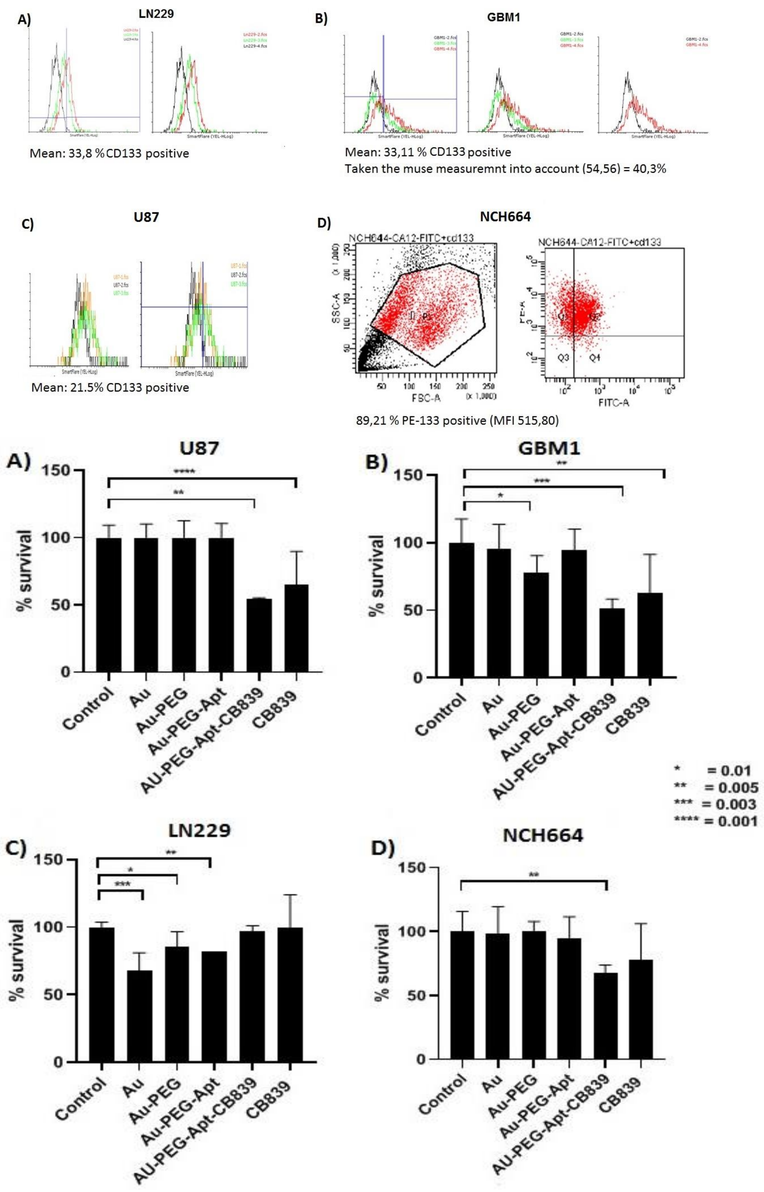


Fig2: Further development of our nanocarrier platform by functionalization of 15mer aptamers (5′-NH2-CCCUCCUACAUAGGG-3′, Eurofins, Germany) known to target anti (cancer) stem cell epitope CD133. In this synthesis design, the conjugation was ideally facilitated by polyethylenglycol (PEG) instead of PVA. The left panel of figures shows example of chemical characterization of aptamer-functionalized Au nanoparticles featuring size, form and zeta potential, whereas the right panel reveals results of the functional studies with CB-839 loaded onto anti-CD133 targeting nanomedicine.

References:

[1] Giessen et al., 2021; [2] Poonaki et al., 2022

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