Bioorthogonal click chemistry meets nanotechnology: covalent immobilization of magnetic nanoparticles on cell membranes

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Herein we describe the use of bioorthogonal click chemistry to immobilize magnetic nanoparticles (MNPs) on the membranes of living cells. We hypothesize that these MNPs could behave as membrane-localized nanoheaters and produce "hotspots" under magnetic hyperthermia (MH) triggers. The incorporation of azide reporters on cell membranes based on metabolic glycoengineering allows the "click" attachment of cyclooctyne-functionalized MNPs on cell membranes through strain-promoted [3+2] azide-alkyne cycloaddition (SPAAC) reaction.[1,2] Preliminary results concerning click immobilization of MNPs on living cell membranes are reported. The expression of azide groups on cell membrane was optimized on MCF-7 (breast cancer) cells and evaluated by SPAAC with a strained alkyne containing a red fluorescent probe, using confocal microscopy. A dose-dependent expression of azide groups on the cell membrane (Figure 1) and a half-life time of azides on membranes of around 8 h were observed. Hydrophobic 12 nm iron oxide MNPs were synthesized following a seed-mediated thermal decomposition methodology and transferred to water by coating with an amphiphilic polymer – poly (maleic anhydride-alt-1-octadecene), PMAO.[3] The MNPs were further functionalized step-wise with polyethyleneglycol (PEG) to increase colloidal stability and with a strained alkyne at different percentages of the total reactive groups on the MNPs.[4] Confocal microscopy results revealed an effective covalent immobilization of MNPs on cell membranes at a 50% strained alkyne-functionalization. We are currently investigating the MH behaviour of the immobilized MNPs.

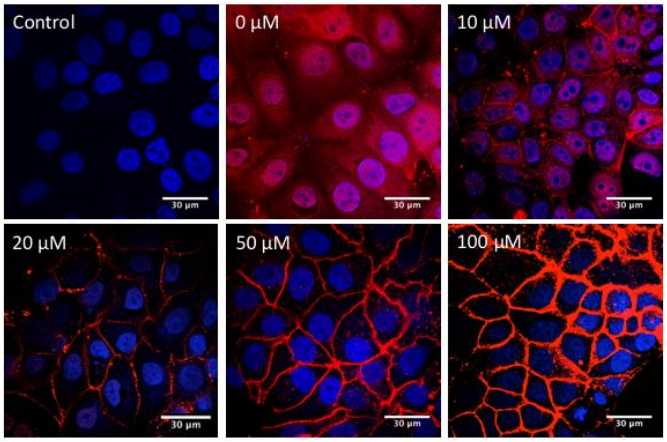

Figure 1. Dose-dependent expression of azide groups on MCF-7 cells. Scale bar: 30 µm.

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