ROS-generating Gold Nanorods as Sonosensitising Agents for Sonodynamic Therapy of Breast Cancer

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The application of sonodynamic therapy (SDT) as a non-invasive treatment for cancers is promising due to the non-radiative nature of ultrasound waves, which enables deep tumour tissue penetration.[1] To maximise the therapeutic efficacy of SDT, sonosensitisers with high potency and safety profiles are highly sought after. Gold nanorods (AuNRs) have been one of the most widely applied metal nanoparticles for photodynamic or photothermal cancer therapy due to their tunable optical properties and flexible surface functionalisation, but their suitability as sonosensitisers is yet to be investigated.[2] Herein, for the first time, we reported the potential of alginate-coated AuNRs ($AuNRs^{ALG}$) as sonosensitising agents. $AuNRs^{ALG}$ showed good heamocompatibility and cytocompatibility at concentrations up to 300 µg/ml. Under activation by ultrasound (1 MHz, 1 W/cm^2, 5 min), $AuNRs^{ALG}$ significantly enhanced cavitation bubble formation and increased temperature in the medium, suggesting their role as a source of bubble nucleation. The combined treatment of $AuNRs^{ALG}$ and ultrasound resulted in up to 8-fold higher production of reactive oxygen species (ROS) than other common metal sonosensitisers such as titanium dioxide.[3-4] $AuNRs^{ALG}$ exerted sonotoxicity on MDA-MB-231 breast cancer cells in a dose-dependent manner, achieving a maximum cell death of ~81% at 300 µg/ml (~1.5 nM of nanoparticles equivalent), showing the sub-nanomolar therapeutic potency of $AuNRs^{ALG}$ under the effect of ultrasound. Flow cytometry analysis revealed that $AuNRs^{ALG}$-mediated SDT induced cancer cell death mainly *via* apoptosis (~83% at 6 h post-treatment). These results unfold a new function of AuNRs as sonosensitising agents for breast cancer treatment.

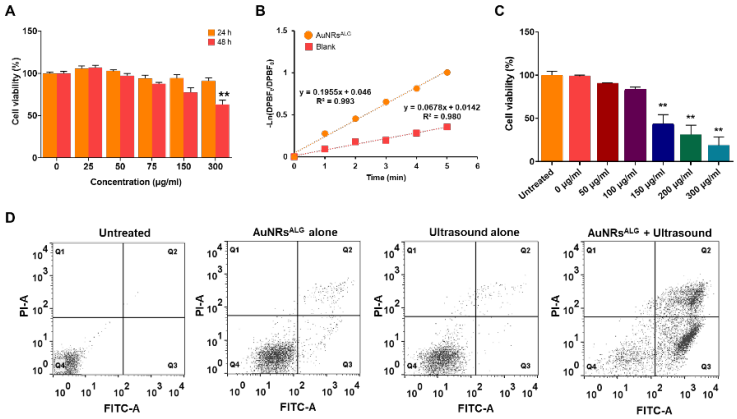

Figure 1: (A) Biocompatibility of $AuNRs^{ALG}$ in MDA-MB-231 at 24 h and 48 h. **(B)** First-order rate constant for ROS generation by $AuNRs^{ALG}$ under ultrasound. **(C)** Sonotoxicity of $AuNRs^{ALG}$ in MDA-MB-231 at 24 h. **(D)** Flow cytometry assay of MDA-MB-231 at 6 h following different treatment conditions. Data presented as mean ± SD (n=3). **p<0.001 obtained by one-way ANOVA.

References:

[1] Ma, A.; et al. *Small* **2019**, *15*, 1804028.
[2] Huang, S. H.; et al. *Colloids and Surfaces B: Biointerfaces* **2021**, *207*, 112014.
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[4] Cao, Y.; et al. *Chemistry of Materials* **2019**, *31*, 9105-9114.