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A Magnetically Triggered Gene Expression System Mediated by Heating of Nanoparticles

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Gene therapy promises a wide range of applications in medicine, including cancer treatment. Similar to chemotherapy, the therapeutic efficacy depends on the dosage (gene expression level) and timing. Thus, controlled gene expression is essential for gene therapy. Synthetic biology focuses on designing artificial gene expression systems. Numerous gene circuits have been developed to control gene expression. Among them, the tetracycline (Tet)-inducible system [1] and heat shock protein promoter system [2] have been used as effective inducible gene expression systems. Using a synthetic biological approach, we have previously constructed a heat-inducible transgene expression system incorporating a transcriptional positive feedback loop mediated by Tet-inducible system that enhances heat-induced gene expression [3].

Remote activation of target cells to trigger specific gene expression *in vivo* can provide a useful research tool and potential means to control gene expression in clinical settings [4]. For this purpose, nanotechnology is becoming increasingly important in medicine. Magnetite nanoparticles have been used for drug delivery systems and cancer diagnosis as contrast-enhancement agents in magnetic resonance imaging. Furthermore, magnetite (Fe_3O_4) particles absorb energy and generate heat in response to an alternating magnetic field (AMF) [5]. Thus, heat generation by AMF exposure can be a potent tool as a switch to induce target gene expression. Here, we combined synthetic biology with nanotechnology to convert a local heating signal using magnetite nanoparticles and AMF exposure into high-level gene expression at a specific site. We investigated the *in vivo* feasibility of this approach for cancer gene therapy using a tumor xenograft model.

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