Engineered Recombinant EGFP-Azurin Theranostic Nano-System for Targeted Therapy of Prostate Cancer

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The largest subfamily of receptor tyrosine kinases (RTKs), erythropoietin-producing hepatocellular (Eph) receptors and their ligands have emerged to be a novel class of cancer biomarkers due to their aberrant expression in many cancers[1]. The overexpression of EphA6 receptors has been corelated with increased metastatic potential in prostate cancer[2]. Azurin, a small redox protein is known to prevent tumour progression by binding to cell surface Eph receptors and thereby disrupting the Eph-ephrin signalling which results in the initiation of metastasis while stimulating adhesion, migration, invasion, and angiogenesis[3]. Hence, a self-assembled, theranostic nano-system of recombinant fusion protein his_6EGFP-azu (80-128) was designed by conjugating enhanced green fluorescent protein (EGFP) with the C- terminal region of azurin (80-128), specific for Eph receptor binding. This design was inspired by the *in silico* binding study where the analogue his_6EGFP-azu (80-128) showed higher binding affinity for EphA6 receptor than the ephrin A ligands. The his_6EGFP-azu (80-128) nano-system which existed as spherical nanoparticles was tested for the simultaneous detection and killing of prostate cancer cells, LNCaP overexpressing EphA6 receptors. Interestingly, while these his_6EGFP-azu (80-128) nanoparticles showed selective binding for EphA6 positive LNCaP cells, they lacked binding to EphA6 negative human normal lung cells, WI-38. Herein, we reveal anti-proliferative, apoptotic, antimigratory and anti-invasive behaviour of this nano system on LNCaP cells, while having no similar effects on normal cells. In summary, this study presents development of an alternative robust protein-based theranostic tool for prostate cancer.

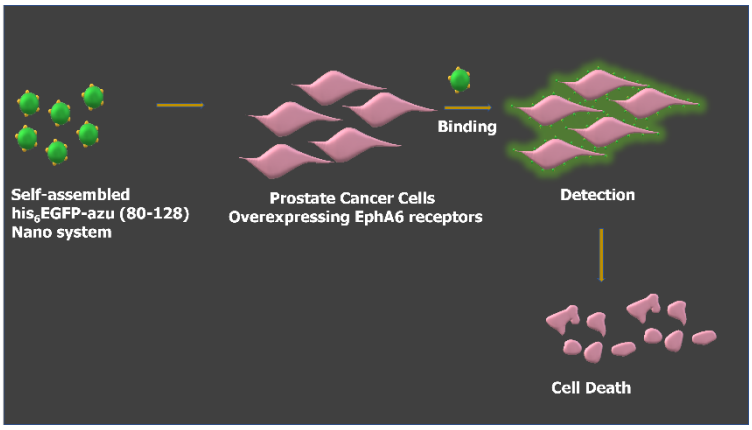

Figure 1. Graphical abstract

References:

[1] Lodola, A. et al. *Eur Jl of Med Chem* **2017,** 147, 152-162.
[2] Li, S.; et al. *Oncotarget* **2015,** 6, 22587-22597.
[3] Chaudhari, A.; et al. *Biochemistry* **2007**; *46:* 1799-1810.