SYNTHETIC CELLS SYNTHESIZE THERAPEUTIC PROTEINS INSIDE TUMORS

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The existing dogma is that protein medicines need to be produced in large factories, and then injected to the patient. We propose that miniature artificial inert factories can be injected to the patient, to produce a protein of interest directly in the diseased tissue. We engineered artificial cell-like particles with an autonomous capacity to synthesize protein drugs after receiving an external signal. The protein is tuned to the patient's needs based on a predetermined DNA code we incorporate inside the particles. This approach increases treatment efficiency and reduces adverse effects to healthy tissues.
We developed a new T7-S30 based cell-free protein synthesis system, which contains all the transcription and translation machines and molecules required for protein production (Krinsky *et al*., *PloS one* 2016). This system was used to prepare liposomes that act as artificial cells, capable of producing proteins autonomously in response to a physical trigger. Functional enzymes (luciferase and tyrosinase) and fluorescent proteins (GFP) were successfully produced using the new cell-free protein synthesis system and inside the particles both *in vitro* and *in vivo*. In addition, we demonstrated the therapeutic capabilities of the protein producing particles by producing *Pseudomonas* exotoxin A, an extremely potent protein, for treating cancer. Applying the particles on 4T1 cells (a triple-negative breast cancer cell-line) *in vitro* or injecting them into a 4T1-induced tumor *in vivo*, resulted in high cytotoxicity due to the effective production of the therapeutic protein inside the vesicles (Krinsky *et al*. *Advanced Healthcare Materials,* 2017).
Synthetic cells serve as autonomous, trigger-able, artificial particles that produces a variety of proteins. This platform has promise to address a wide range of fundamental questions associated with protein synthesis in nature, as well as applicative protein delivery needs.

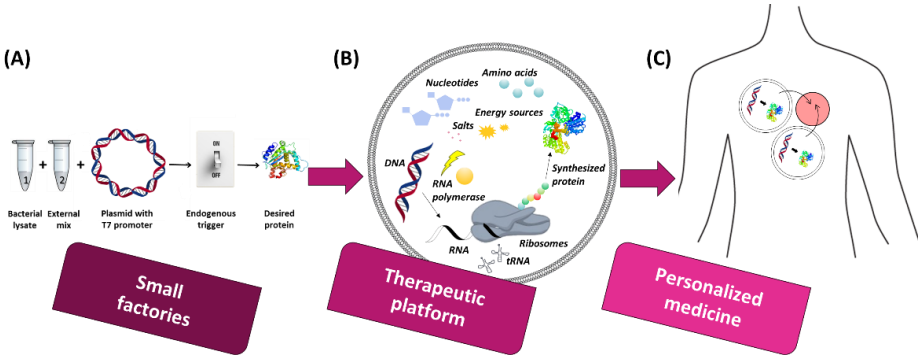

Figure 1 - the therapeutic platform. Onsite synthesis of protein medicines inside the body is achieved by encapsulation of all the transcription and translation factors required for protein production inside a liposome. (A) Cell-free protein synthesis (CFPS) work flow. (B) Protein producing particle. (C) Personalized medicine; triggered protein production inside the patient's body at the diseased tissue.