Barcoded Nanoparticles for Personalized Cancer Medicine

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Laboratory for Targeted Drug Delivery and Personalized Medicine Technologies

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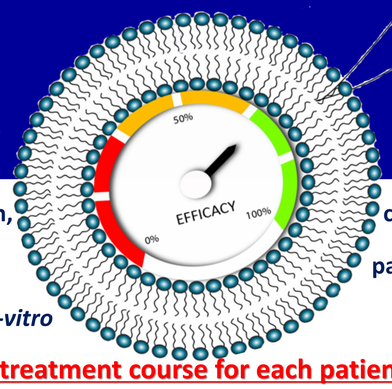
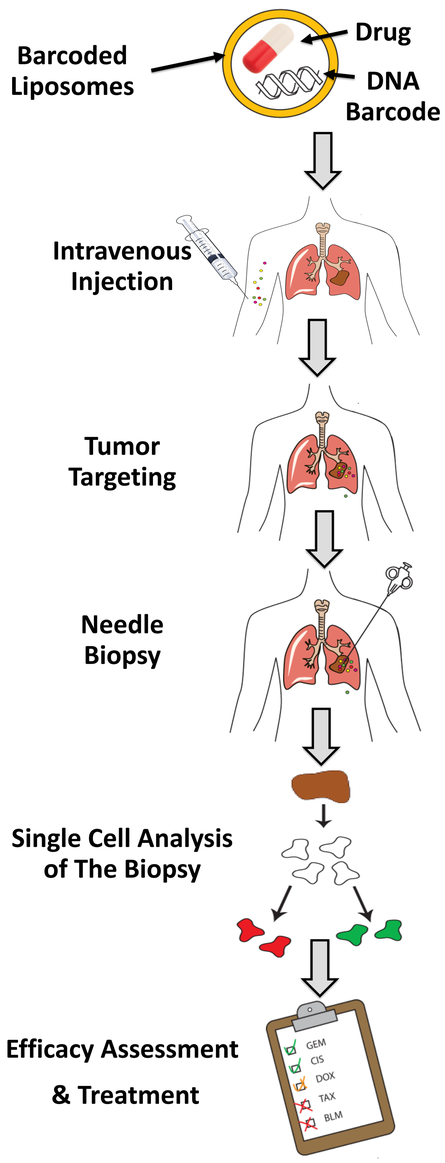


Selecting proper therapeutic that will address each patient's **unique** disease presentation, can significantly improve the treatment outcome. Patient-specific biomarkers have helped to advance personalized medicine, however, much remains unknown when predicting whether a certain patient will or will not respond to therapy. **Prescreening for drug activity inside the patient's tumor and metastasis** will generate an improved treatment predictor in comparison to *in-vitro* or *ex-vivo* assays. In this study, a nanoparticle-based technology for **predicting the therapeutic potency of drugs** was developed. This technology will improve care by **personalizing the treatment course for each patient** and provide **better tools for strategizing cancer care**.

Research objective

Predict the patient specific potency of anticancer drugs by simultaneous screening of low doses of multiple drugs inside the patient's tumor microenvironment.

In-Patient Diagnostics



Designing the Barcode

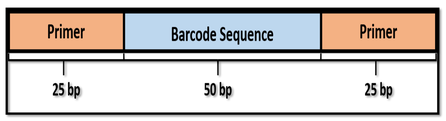


Figure 1. **Barcode structure.**

Strands are long enough to be sequenced and short enough to be encapsulated easily in the liposomes.

Results

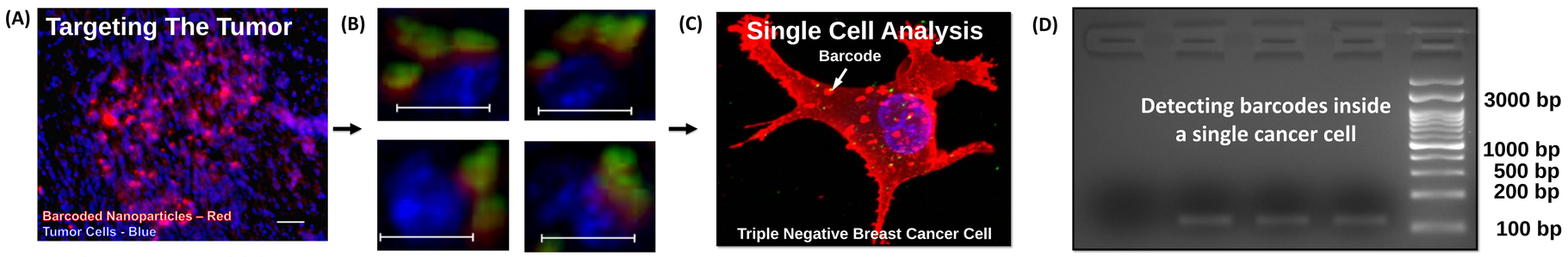


Figure 2. **Single cell sensitivity.** **(A) Barcoded Nanoparticle uptake by triple negative breast cancer cells.** Barcoded Nanoparticles were detected inside murine 4T1 triple negative breast cancer tumor tissue. **(B)** Co-localization of the barcodes and the particles inside single cells that compose the tumor tissue. **(C)** Confocal image of barcoded nanoparticles inside 4T1 breast cancer cell. Barcodes were stained with Fluorescein (green) , nanoparticles were stained with Rhodamine, plasma membrane was stained with DID (red) and the nuclei was stained with Hoechst (Blue). Scale-bar represents 50µm in **(A)**, and 10µm in **(B)**. **(D)** The barcodes were extracted from single cells using Fluorescence Activated Cell Sorting. After amplification by Poly Chain Reaction (PCR), the barcodes were detected using gel electrophoresis

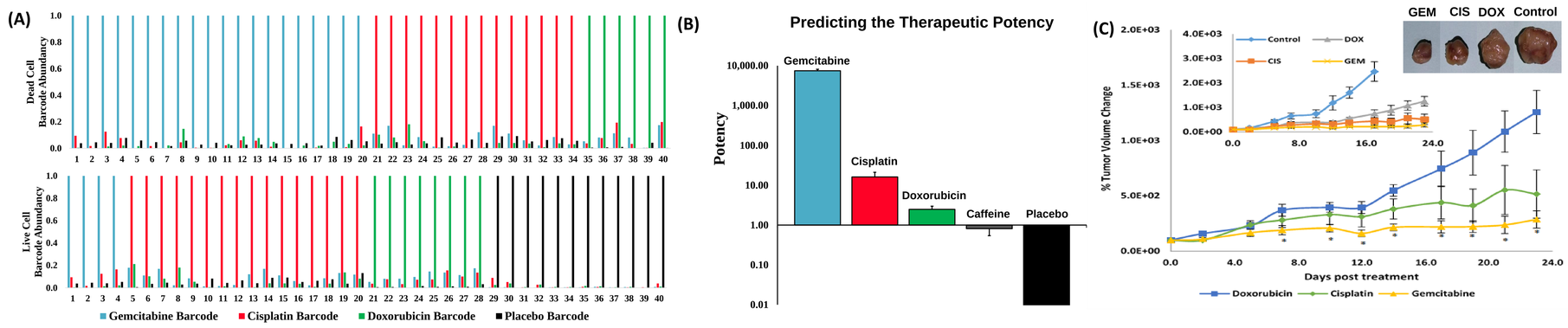


Figure 3. **Therapeutic Efficacy.** The barcodes were extracted from single live and dead cells using Fluorescence Activated Cell Sorting (FACS), and detected by amplification using Poly Chain Reaction (PCR). **(A)** Comparison between drugs barcodes levels in single live and dead cells. The placebo liposome contained barcode only . Y axis represents the ratio of the most abundant barcode relatively to the other barcodes per cell. **(B)** The potency of the drugs was calculated by dividing the barcodes extracted from dead cells by those that extracted from the living cells. The values are presented in logarithmic scale. **Therapeutic Treatment based on Barcoding Analysis**. **(C)** Comparing tumor volume change between different therapeutic groups. Each group got a weekly dose of chemo drug Doxorubicin, Cisplatin, or Gemcitabine. Representative tumor dimensions of each group.

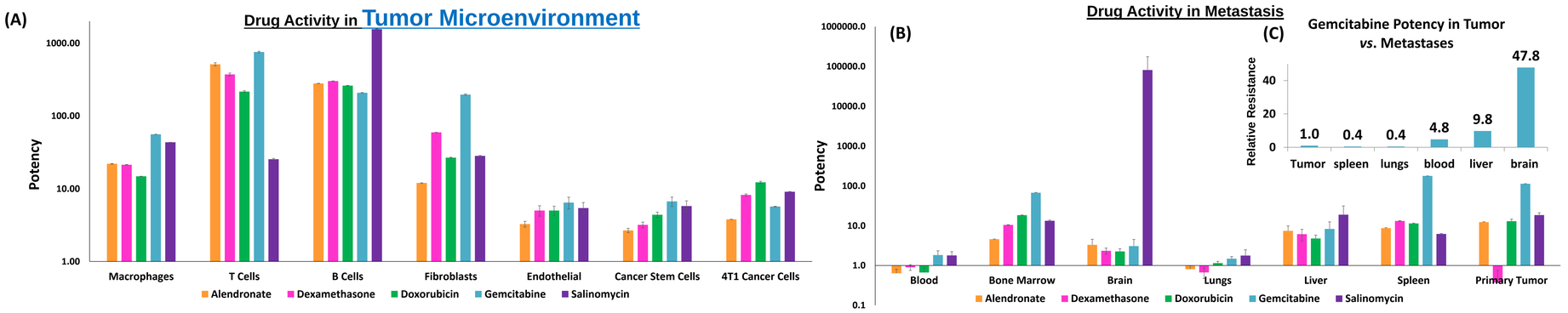


Figure 4. **Treating Tumor Microenvironment and Metastasis.** **Screening five medications in (A) several cell types which compose the tumor microenvironment and (B) several metastasis.** The panel includes placebo particle in addition**.** Following tumor dissociation into single cell suspension, the cells were labeled using fluoresce abs and sorted using FACS into dead/live populations. Potency of the drugs was calculated as mentioned above. The bars are normalized to the placebo barcode. **(B)** The metastasis cells were isolated from the organ using FACS based on the mCherry signal the cancer cells produced. The bars are normalized to the placebo barcode. **(C)** Representative resistance panel for Gemcitabine. Relative resistance was defined as the ratio between barcode/cell in metastasis and the primary tumor. The bars are normalized to the primary tumor values.

Take Home Message

- **Nanotechnology that allows detecting and tracking drug activity *in vivo*.**
- **The system grants single-cell sensitivity of drug activity inside the patient's tumor.**
- **Sub-Sets of cells in the tumor microenvironment respond differently to medications.**
- **Metastasis ≠ Primary Tumor cells regarding drug sensitivity.**

References

- **Theranostic Barcoded Nanoparticles for Personalized Cancer Medicine, *Nature Communications,* 2016.**
- **Collagenase nanoparticles enhance the penetration of drugs into pancreatic tumors, ACS Nano 2019, 13 (10), 11008-11021**

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