Nanorobots as sensors for cancer microenvironment

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Key ideas:

- Nanorobots can be driven in 3D tissue co-culture consisting of both cancerous and non-cancerous cells, a system which approximates an in-vivo malignant breast tumor.
- Nanorobots can sense physico-chemical changes in cancer-sculpted extracellular matrix (ECM).

Experimental Setup

- Nanorobots move due to rotating magnetic field generated by triaxial Helmholtz coil.
- Nanorobots are injected into tumor-like environment and moved for 30 minutes along a random direction.

α 2,3-linked sialic acid may be the primary cause of adhesion

- Adhered nanorobots are spatially co-located with sialylated cancer ECM.
- The extent of sialic acid spread was measured to be $\sim 40 \mu$ m

Nanorobots adhere to the cancer ECM but not near non-cancerous ECM

Trajectory of nanorobot near a cancer cell:
Nanorobot gets adhered to the ECM in the vicinity of cancer cell

Trajectory of nanorobot near a normal cell:
Nanorobot can be maneuvered near a normal cell

- A total of 376 cells were sampled, of which 203 cells were cancer cells and 173 were normal cells.
- Total 71 cells were found to have adhered nanorobots in their vicinity, of which 58 were cancer cells and 13 were normal cells.

Negatively charged PFO coated nanorobots do not get adhered

Anisotropy of nanorobot adhesion is correlated to ECM sialylation

Cell Type: MCF7

Anisotropic adhesion of nanorobots

Anisotropic distribution of Sialic acid

Cell Type: MDA-MB-231

Isotropic adhesion of nanorobots

Isotropic distribution of Sialic acid

Adhesion force is correlated to metastatic potential

- Plot of average force (F) vs adhesion distance (x) for four breast cancer cells is shown. Within each graph, open circles correspond to a single nanorobot, highlighting a self-referenced method of measurements.

- The fitting formula $F = F_0 \exp(-\frac{x}{l_p})$ provides characteristics force (F_0)

- Physical effects of invading cancer cells are manifest up to a length of $\sim 40 \mu$ m from the cell surface within the ECM surrounding them.

- Estimated F_0 for various cell lines.
- F_0 increases for cells with higher metastatic potential.

Summary

- Dynamics of nanorobot $\rightarrow$ spatially differentiate cancerous and non-cancerous cell microenvironment.
- Nanorobot adhesion near cancer cells $\rightarrow$ different charge conditions of the cancer sculpted ECM.
- Physical effects of invading cancer cell $\rightarrow \sim 40 \mu$ m from the cell surface.
- Specific sialic acid linkages within the ECM secreted by the cells.
- Implications for future in-vivo cancer targeting.

Patent: Charge-based methods for studying a biochemical micro-environment, Debayan Dasgupta, Dharma Tejaswar Reddy Pally, Deepak Saini, Ramray Bhat, Ambarish Ghosh, Indian patent (provisional) application, 2019

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