Targeting Tumors Using Invasive Assays Through Magnetospirillum Magneticum

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Magnetospirillum magneticum AMB-1 are a species of magnetotactic bacteria that are capable of orienting along the earth’s magnetic field lines through their organelles called magnetosomes. Many studies have shown that certain engineered-bacteria can infect the tumor cells resulting in a controlled death of a tumor. This work deals with a technique utilizing AMB-1 along a predefined path through magnetotaxis, which can pave a way for selective doping as well as isolation of the tumor cells from a group of healthy cells through a magnetic invasive assay (MIA). For such a control, tiny mesh of vertical electrical coils each having a diameter of ~ 5 mm is fabricated, which establishes the path for the bacteria to move along the magnetic field lines. The molecular dynamics simulations at the interface of the bacterial cell surface proteins (MSP-1 & flagellin) and Chinese Hamster Ovary (CHO) cell surface containing cytoplasmic and extracellular proteins (BSG, B2M, SDC1, AIMP1, and FOS) will establish an association between the invading AMB-1 and the host CHO cells. The experimental demonstration involves the CHO invasion by the AMB-1 and isolation of selected CHO cells. Statistical analysis along with the relevant electron and force microscopy data will confirm the number of AMB-1 and CHO cells involved before and after invasion and the role of directional control.

Materials and Methods

- Experimental:
  - 32 AWG magnetic wire, cavity slide [20 (dia.) x 30 mm (deep)], current source and gaussmeter for the experimental setup.
  - Light Microscopy: To check the morphology of AMB-1 and magnetotaxis verification.
  - Scanning Transmission Electron and Atomic Force Microscopy: To be done to confirm the CHO cells invasion by AMB-1 through a typical invasive assay protocol.
  - Inverted Microscope:
    i. Isolation of the invaded CHO cells from the non-invaded cells using vertical coil based arrangement through magnetotaxis.
    ii. Real time invasion of the CHO cells using the magnetically guided and directionally controlled AMB-1 cells - magnetic invasive assay (MIA).

- MD Simulations:
  - Interactive protein system modeling using VMD and simulations using NAMD.
  - All simulations will be carried out for a time period of 100ns.
  - CHARMM force field and TIP3 water model with ions including Na, Cl, Mg and K according to the experimental procedure.
  - Periodic boundary conditions based on a constant temperature of 300K (MIA) and 310K (incubation) at a constant pressure of 1 Atm.
  - Data analysis for the interactions taking place between the AMB-1 cell surface proteins and CHO proteins in the extracellular, plasma membrane and cytosol region.

Conclusions

- The AMB-1 was found to be sensitive to the magnetic field after four days of the sub-culture until seven days whereas the CHO cells are found to be more confluent by the 4th day of culture.
- The movement of the AMB-1 cells is found to be towards the coil carrying current and random otherwise.
- A controlled switching of the current through the multiple coils provides a guided path for the AMB-1 and invaded CHO cells.
- Molecular dynamics simulations quantify the interactive energies between the AMB-1 cell surface proteins and the CHO proteins.
- Interaction of the extracellular CHO proteins (SDC-1 & B2M) and AMB-1 protein (Flagellin) further confirm the hypothesis concerning the role of AMB-1 surface proteins in invasive assays further supporting the experimental results.
- The NAMD simulations and VMD data analysis would justify the interactions of the surface proteins giving more credibility to our aim.

Future Work

The quantitative analysis of the AMB-1 and CHO cells, pre and post analysis would determine the number of AMB-1 per CHO cell statistically.

References


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