Abstract

Lung cancer is the leading cause of death from cancer worldwide, with a dismal 16% average 5-year survival rate. It is known that this is largely due to the fact that the majority of lung cancer therapies fail in the metastatic setting; metastasis accounts for over 90% of deaths in cancer patients. Cytokines are implicated in metastasis in various cancers such as breast and melanoma. The role of the SDF-1/CXCR4 axis in tumor metastasis is the most well defined, however, we hypothesize that other cytokine receptors are also involved in the migration and metastasis of lung cancer cells. The role of cytokine receptors that stimulate the migration of human lung cancer cells will be identified in a cell culture screen and analyzed for a functional role in lung cancer. The migration capacity of A549 cells, a human lung adenocarcinoma cell line, in response to 200 human cytokines arrayed in a library will be tested with Corning 96-transwell permeable membrane Migration assays. The receptors of the “hit” molecules, that stimulate migration, will be neutralized with antibodies to demonstrate specificity in these assays. This work will identify which cytokine receptors may be crucial for human lung adenocarcinoma metastasis; and broadly, these studies will determine if and how stem cell biology approaches can be applied to understanding lung cancer biology.

Metastasis

When cancer cells migrate from their primary site to other parts of the body, the trafficking of stem cells and metastatic cancer cells may be similar.

Cytokines

Cytokines are small proteins released by cells that have a specific effect on:
- Interactions between cells
- Communication between cells
- Behavior of cells

Figure 1

Figure 2

Figure 3

Migration Assay Scheme

Figure 4

The Cytokine Screen Process

Figure 5

Optimization of 96-Well Migration Assay Protocol

Figure 6

Migration Assay Test Screen with 96-Well Plates and the help of the ES Cell Core to Verify Controls

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