The myosin II inhibitor, blebbistatin, more potently inhibits 3D cell invasion than 2D cell migration in a human metastatic tumor cell

Thomas Nelson, Meagan Roddy, Daniel M. Appledorn, Vince Groppi
Essen BioScience, Ann Arbor, MI

Abstract

The IncuCyte FLR Direct

Our metastasis Kinetic RWD (%)

Cell Invasion Methodology

Results

Blebbistatin more potently affects cell invasion than cell migration

The 96-Well WoundMask

Figure 3: We used GM6001 to investigate the effect of MMP inhibition on cell invasion and migration. GM6001 downregulated both migration and invasion of the highly invasive MDA-MB-231 cell line but not the not invasive MCF-7 cell line. Unlike GM6001, blebbistatin had only a marginal effect on cell migration and invasion of MCF-7 cells. Box plots show data are representative of three biological replicates.

Figure 4: The 96-well WoundMask was used to examine the phase of cell migration and invasion using the MDA-MB-231 cell line and compared to MCF-7 cells. Unlike MDA-MB-231 cells, MCF-7 cells were not able to form a wound at the center of the plate.

Introduction

Metastasis is a multidisciplinary process driven by growth and migration of local, sentinel, and systemic microenvironments that contribute to the phenotypic character of tumor cells.

The basement membrane is a thin, continuous sheet of interstitial matrix that surrounds organ and represents a barrier that tumor cells must invade and transverse to establish metastatic colonies.

This study demonstrates a novel, automated, label-free, 96-well strategy to measure both cell migration and cell invasion in the IncuCyte FLR using the IncuCyte FLR-Cell imaging system.

This automated, flexible, kinetic, label-free, quantitative strategy was then used to examine the pharmacology of the inhibitors blebbistatin, bisantrene, GM6001, and the MMP inhibitor, GM6001.

Our results indicate that all compounds were more potent inhibitors of cell invasion than cell migration.

Automated Image Analysis

Invasion vs. Migration in 2D Gel

Invasion vs. Migration in 3D Matrix

Invasion vs. Migration in 3D Matrix

Figure 5: B (Left): Invasion vs. Migration in 2D Gel

Conclusions

Direct comparison of cell invasion and migration assays on the same plate, at the same time, provides the best opportunity for determination of the potency of drugs and the utility of potential drug targets.

Simultaneous evaluation of the effects of blebbistatin, GM6001, and U0126 on cell invasion and migration.

Automated data acquisition: After the experiment is initiated, the data is collected automatically.

Label-free: The IncuCyte HD optics and software package obviates the need to label the cells.

Integrated RWD metric: Results are quantitative and reproducible.

Morphological data: HD images are acquired at every time point and can be assembled into time-lapse movies for convenient viewing.