Melanoma Cell Malignancy Does Not Correlate with Migratory Rates in Three Different Highly Metastatic Cell Lines

Amos, Tyler (School: Chantilly High School)

Malignant melanoma is characterized by its ability to metastasize, and is responsible for 90% of skin cancer mortality. Metastasis requires cell migration from a primary tumor to blood and lymph vessels, where the cells then proliferate in distant organs. Cell migration requires remodeling of the cytoskeleton and integrin-based focal adhesions (FAs). It's unclear whether metastatic potential correlates directly with cell migration behavior. We examined cell migration and the cytoskeleton in 3 human melanoma cell lines with differing metastatic potential: Lu1205 (highest), A375m (intermediate), and SKMEL28 (least). Cell motility was measured in wound healing assays, and velocities were measured using kymograph analysis. SKMEL28 migrated 2x faster than Lu1205 and A375m. To evaluate a correlation between FA organization and migration, we performed immunofluorescence analysis using antibodies to myosin-IIA and paxillin, and stained the actin filaments with Alexa-565-phalloidin. SKMEL28 cells presented small FAs and dense myosin-IIA ribbons, while A375m and Lu1205 cells had larger FAs and peripheral arcs of myosin-IIA filaments. We then used gel-electrophoresis and western-blot to analyze FAK signaling. This showed that Lu1205 presented the most phosphorylation of FAK (p-FAK), while SKMEL28 had the least p-FAK. Higher p-FAK correlates with strong integrin-ECM binding, which could correlate with slower FA turnover and slower migration. In SKMEL28 cells, lower p-FAK, small focal adhesions and well organized myosin likely results in faster migration. The slow-migrating Lu 1205 cell line has a higher metastatic potential than the fast-migrating SKMEL28, therefore our results suggest that there is no correlation between metastatic potential and in vitro motility.

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