

# Heterogeneity of Cancer Cell Motility

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**H**ETEROGENEITY of cell phenotypic core traits within homogenous cell populations (e.g., cell lines) is increasingly addressed with quantitative methods. Regardless of its source (genetics, epigenetics, signaling noise), this heterogeneity has implications for normal and pathologic tissue organization. Quantifying cell trait heterogeneity opens avenues to address its long suspected role in cancer, especially in clonal selection and adaptation during cancer progression. We are quantifying cell-to-cell variability of motility within cancer cell lines by large-scale single-cell tracking (approximately 500 cells/cell line) and high content automated microscopy. Cell-to-cell variability of spontaneous, non-directed motility in non-cancer (MCF10A) and cancer (AT1 and CA1d) breast epithelial cell lines was evaluated with respect to speed, step-length, motile cell fraction and a novel metric, Instantaneous Motion Fraction, under two culture conditions, full or serum/EGF-depleted media. Intrinsic speed fluctuation was greater in cancer cells, and increased in depleted media. The range of cell-to-cell speed variability was also greater in cancer cell lines, and likewise expanded in depleted media. Regardless of conditions, only a minority of cells was highly motile in any cell line. The motile cell fraction was highly variable across experiments in cancer cells. Changes in persistence time did not differ among cell lines, but a novel metric, Instantaneous Motion Fraction increased significantly in cancer cells in depleted media. In spite of this widespread variation, cell step-lengths appeared to be organized around a power-law distribution, suggesting stabilizing mechanisms (perhaps both intrinsic and extrinsic to cells) that dampen variation and may be deregulated in cancer cells.