Collective Migration Models in 2D and 3D: Dynamic Modeling of Single Cells

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Abstract:

Collective cell migration, an essential physiological mechanism where cells move either in loosely or closely associated groups, plays important roles in key pathological or normal processes, such as tissue regeneration and cancer metastasis. However, current molecular biology techniques for studying collective cell migration, such as PCR or immunohistochemistry, do not allow for dynamic cell monitoring due to the need for either cell fixation or lysis. Additionally, both invasive cancer tumors and healing wounds are distinctly heterogeneous in nature, developing discrete subpopulations of cells at the migrating front, further complicating matters. To solve these problems we have developed a fluorescent oligonucleotide strand displacement probe (dsLNA) that hybridizes with the target mRNA or miRNA inside living cells, preserving spatiotemporal gene expression. The probe is not only stable inside cells for up to 72 hours post-transfection, but it can also monitor both increases and decreases in RNA expression from external biochemical or physical stimuli. In addition, the dsLNA probe is capable of quantifying the RNA concentration inside cells. By coupling the dsLNA probe to other advanced collective migration techniques such as multiphoton and live cell imaging we investigated fundamental biological processes in both 2D and 3D culture models, revealing key genes regulating cancer invasion and tissue regeneration as well as additionally providing potential therapeutic target genes for medical therapy and treatment.