Physical limits of cell migration

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Using a model for cancer cell migration through 3D collagen matrices as well as through polycarbonate filters of different porosity, we here show the physical limits of cell migration and identify the deformabillity of the nucleus as rate-limiting compartment. Decresing pore size of the migration substrate lead to complete migration arrest with a rate-limitng cut-off below 3 µm pore diameter for different cell types. Using RNA knockdown of nuclear lamins, nuclear deformability and, accordingly, migration rates were increased in matrices of small pores. Conversely, availability of pericellular proteolysis executed by MT1-MMP/MMP-14 resulted in the widening of matrix pores and reduction of nuclear deformation and, thus, enhanced migration rates. In conclusion, interstitial tissue transmgration is a process determined by the pore size present in the tissue, the proteolytic capability of the cell to widen preexisting pores, and the deformability of the nucleus.