Understanding the migration of cancer cells

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Activity of regulatory proteins for the growth of filopodia and lamelopodia clarified

Lamellipodia are veil-shaped protrusions of the plasma membrane, that can turn into upward-curled ruffles if they fail to adhere to the substrate. A dendritic meshwork of short and highly branched actin filaments might constitute their main structural component. The other type of protrusion, the filopodia, are finger-like and consist of parallel, long and unbranched actin filaments. Interestingly, fast-crawling cells mainly form lamellipodia/ruffles while poorly migrating or non-motile cells often show the coexistence of both lamellipodial and filopodial protrusions. These observations suggest that the lamellipodia-to-filopodia selection might regulate cell migration. Moreover, the pivotal contribution of lamellipodial and filopodial protrusions to important developmental and homeostatic processes certainly requires tight regulatory mechanisms.

Unfortunately, while the microscopic morphology, dynamic development and protein signature of both lamellipodia/ruffles and filopodia have been investigated, little is known about the mechanisms whereby cells co-ordinate these actin-based extensions. Therefore, we urgently need to better understand this basic process to ultimately increase our therapeutic intervention arsenal against the metastatic progression of cancers.

It is known that the activity of regulatory proteins for the growth of the actin cytoskeleton Arp2/3 complex along with WAVE and mDia2 produce a burst of actin polymerization required for the formation of

lamellipodia/ruffles and filopodia, respectively. In the forthcoming issue of *Nature Cell Biology* Metello Innocenti and coworkers report that, starting from the unexpected observation that mDia2, WAVE and Arp2/3 form a complex, they discovered how filopodia extensions are generated and integrated with lamellipodia/ruffles in human cancer cells. At the molecular level, WAVE and Arp2/3 jointly promote lamellipodia/ruffles outgrowth and cell migration and at the same time inhibit mDia2-dependent filopodia formation. Moreover, emission of filopodia occurs only after the disassembly of the mDia2-WAVE-Arp2/3 complex. Thus, it is likely that suppression of filopodia by the ruffling-making machinery is needed for cancer cells to move efficiently.

Their results pave the way to a cogent molecular analysis of the interplay between lamellipodia/ruffles and filopodia in regulating both the migratory and invasive abilities of cancer cells. The researchers anticipate that new and more specific therapies to counteract cancer will be developed exploiting these exciting findings.

Source: Goethe University Frankfurt