# Mechanical interplay between invadopodia and the nucleus in cancer cells

**Or-Yam Revach [1],Allon Weiner [2], Katya Rechav[3], Ilana Sabanay [1,3]Ariel Livne[1], and Benjamin Geiger [1*]**

[1] Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot 7610001, Israel

[2] Department of Materials and Interfaces, The Weizmann Institute of Science, Rehovot 76100, Israel

[3] Electron Microscopy Unit, Department of Chemical Research Support, Weizmann Institute of Science, Rehovot 76100 Israel

* Corresponding Author Benny.geiger@weizmann.ac.il

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Invadopodia are actin-rich protrusions of the plasma membrane that attach to the extracellular matrix and induce its degradation. They are commonly formed by cancer cells and believed to promote tumor invasion and metastasis. In this study, we explored the mechanics of invadopodia in cultured A375 melanoma cells, using a combination of multi-color-fluorescence microscopy, focused ion beam ablation, and scanning electron microscopy approaches. This study demonstrated that the core actin bundle of most invadopodia physically interacts, with distinct cellular structures; at its basal aspect, it transiently associates with integrin-mediated matrix adhesions; along its length, it is flanked by a dense web of microtubules, and at its apical aspect, it physically interacts with the nuclear envelope and indents it. Live cell imaging, using total internal reflection fluorescence microscopy demonstrated that abolishment of invadopodia by Src or microtubule inhibitors, leads to the disappearance of these nuclear indentations, suggesting that the actin bundle physically pushes against the nuclear envelope. Estimation of the forces applied to the nucleus by the invadopodia, based on the indentation profile and the viscoelastic properties of the nucleus, suggest that the force is in the nano Newton range. It is conceivable that such forces also reinforce the protrusive activity of the invadopodia. The existence of molecular cross-talk between the apical and basal aspects of invadopodia is further suggested by experiments showing that knockdown of LINC complex components nesprin 2 and SUN1, leads to substantial increase in the prominence of the adhesion domains in invadopodia. We discuss the mechanical interplay between the apical and basal domains of invadopodia, and their respective roles in the penetration of invadopodia into the underlying matrix.