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Deciphering the role of HGF in invadopodia formation and associated activity in breast cancer

The role of growth factors like EGF, HGF in triple-negative breast cancer (TNBC) invasion is well documented(1,2). Though HGF is shown to increase invasion in MDA-MB-231(2), the underlying molecular mechanism is yet to be elucidated.

Here, we investigated the effect of HGF on invadopodia formation and associated activity. HGF treatment led to a significant increase in the invadopodia number in MDA-MB-231 cells. It also altered the trafficking of MT1-MMP, a major invadopodia-associated membrane protease. Recent studies indicate that MT1-MMP contributes to invadopodia formation independent of its proteolytic activity(3). To validate the role of MT1-MMP in invadopodia biogenesis we generated several deletion and point mutants in the cytosolic tail as it serves as a platform for protein-protein interactions. We propose to exploit these mutants in rescuing invasive phenotype in MT1-MMP depleted MDA-MB 231 cells in the presence and absence of HGF stimulation. Differential proteomics of the MT1-MMP tail along with inhibitor-based studies will be carried out to decipher the mechanism of HGF stimulated invadopodia formation. Moreover, whether the two major invadopodial proteases, MT1-MMP and MT2-MMP, share any redundant role in invadopodia formation will be addressed.

1. Mader CC, Oser M, Magalhaes MAO, Bravo-Cordero JJ, Condeelis J, Koleske AJ, et al. Molecular and Cellular Pathobiology An EGFR-Src-Arg-Cortactin Pathway Mediates Functional Maturation of Invadopodia and Breast Cancer Cell Invasion. Available from: http://cancerres.aacrjournals.org/
2. Rajadurai C v., Havrylov S, Zaoui K, Vaillancourt R, Stuible M, Naujokas M, et al. Met receptor tyrosine kinase signals through a cortactin-Gab1 scaffold complex, to mediate invadopodia. Journal of Cell Science. 2012 Jun 15;125(12):2940–53.
3. Ferrari R, Martin lle, Tagit O, Guichard A, Cambi A, Vassilopoulos phane, et al. MT1-MMP directs force-producing proteolytic contacts that drive tumor cell invasion. Available from: https://doi.org/10.1038/s41467-019-12930-y