Review of: "Vimentin Regulates Collagen Remodeling Through Interaction with Myosin 10"

Óscar Javier Cordero[1]

1 Universidad de Santiago de Compostela

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Increased vimentin (Vim) expression and reduced cytokeratin and E-cadherin are hallmarks of epithelial-mesenchymal transition (EMT) progression. EMT is a biological phenomenon in which non-migratory epithelial cells acquire the migratory behavior of mesenchymal cells, this being one of the first steps of metastasis in many types of cancer. However, the role of this protein in EMT is not totally known.

In this manuscript, authors have found Vim filaments' interaction with, and regulation of, Myo10, a protein trafficking to the tips of the cell extensions. Many data suggests that Vim and Myo10 may move together during filopodial/invadopodia formation.

This mechanism enhances tractional remodeling of fibrillar collagen (Col), organized into complex and diverse hierarchical networks in the matrix of connective tissues. Cancer cells avidly contract and compact collagen, so they can escape from the primary tumor.

It is proposed that Myo10 control MT1-MMP secretion or translocation to membrane, this MMP one of the collagenases that can degrade ECM Col.

These data altogether suggest that suppression of the Vim-Myo10 interaction might affect the progression of colon cancer, and the development of experiments to prove it may facilitate the development of novel therapeutics for cancer or fibrosis.

The methods used in this manuscript are impressive and I only suggest that a further round of language edition will sharp some difficult-to-understand sentences.

A couple of suggestions for future research are:

1. As well as Vim has been found bound to membrane glycoprotein CD44 or NMIIA/B, and MMP1 and MMP2 catalytic activity is reduced when Myo10 is silenced in certain tumors, there are additional proteases that have been found involved in the collagenase activity at invadopodia of migratory cells, and therefore in desmoplasia, for example CD26/DPP4, or MMPs 7 and 9. The concomitant to Vim upregulation of other EMT markers such as N-cadherin, the E-cadherin repressor slug, as well as twist or fibronectin would also be incorporated to this model.
2. Most experts focus on cancer stem cells (CSCs) as the true originators of tumors and metastases. CSCs exist both in epithelial and mesenchymal states, but EMT favors migration of cancer cells while inhibiting cell proliferation. Thus, MetSCs should be found in the epithelial state in the primary tumor, in the mesenchymal state in the peripheral blood, and in the epithelial state in the host organ. Perhaps, the mechanism proposed in the manuscript, where fibroblasts or

tumor cells were used, was different in CSCs, or evolve according to their cell state.