Andrew Leask, J Clin Exp Dermatol Res 2016, 7:4(Suppl)
http://dx.doi.org/10.4172/2155-9554.C1.029



6th International Conference on
Clinical and Experimental Dermatology
May 04-06, 2016 Chicago, USA

# The role of the tumor microenvironment: The matricellular protein CCN2/CTGF is essential for melanoma metastasis

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Melanoma, the second most common invasive cancer in young adults, is highly metastatic: ~5% of patients diagnosed with metastatic melanoma survive for 5 years after diagnosis. 40-60% of all cutaneous melanoma patients possess mutations in BRAF; in these patients, tumors shrink in response to the *BRAF* inhibitors. However, patients develop resistance to these drugs, necessitating the development of alternative therapeutic targets. The matricellular protein connective tissue growth factor (CCN2) is overexpressed in melanoma; however, how CCN2 contributes to melanoma progression is unclear. Herein, we use melanoma cell lines and mice in which CCN2 is deleted in the tumor stroma to demonstrate that loss of CCN2 in the tumor microenvironment impedes melanoma invasion. Specifically, loss of CCN2 in melanoma cells diminished their ability to invade through collagen *in vitro* and loss of fibroblast derived CCN2 decreased metastases of melanoma cells from the skin to the lungs *in vivo*. CCN2 deficient B16(F10) cells showed reduced expression of periostin; addition of recombinant periostin rescued the *in vitro* invasion defect of these cells. Analysis of CCN2 deficient mice confirmed loss of periostin expression in the absence of CCN2. CCN2 and periostin mRNA levels are positively correlated with each other and with the stromal composition of human melanoma lesions but not *BRAF* mutations. These results are consistent with the idea that metastatic ability results from CCN2 mediated interactions between tumor cells and the stroma. CCN2 promotes invasion and metastasis via periostin and should be further evaluated as a possible therapeutic target for *BRAF* inhibitor-resistant melanoma.

## Biography

Andrew Leask has completed his BSc from the University of British Columbia and PhD from the University of Chicago and Postdoctoral studies from Stanford University School of Medicine. He was a Staff Scientist at FibroGen and University College London. He has published more than 130 peer reviewed journals, has an h factor of 47 and is Managing Editor of *Journal of Cell Communication and Signaling* and the Editorial Board Member of several other journals.

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