Cheng-Han Tsai, J Mol Genet Med 2015, 9:3
http://dx.doi.org/10.4172/1747-0862.C1.009

OMICS International
conferenceseries.com

3rd International Conference on
Genomics & Pharmacogenomics
September 21-23, 2015 San Antonio, USA

Over-expression of cofilin-1 suppressed growth and invasion of cancer cells is associated with up-regulation of let-7 microRNA

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Cofilin-1, a non-muscle isoform of actin regulatory protein that belongs to the actin-depolymerizing factor (ADF)/cofilin family is known to affect cancer development. Previously, we found that over-expression of cofilin-1 suppressed the growth and invasion of human Non-Small Cell Lung Cancer (NSCLC) cells in vitro. In this study, we further investigated whether over-expression of cofilin-1 can suppress tumor growth in vivo, and performed a microRNA array analysis to better understand whether specific microRNA would be involved in this event. The results showed that over-expression of cofilin-1 suppressed NSCLC tumor growth using the xenograft tumor model with the non-invasive reporter gene imaging modalities. Additionally, cell motility and invasion were significantly suppressed by over-expressed cofilin-1, and down-regulation of Matrix Metalloproteinase (MMPs) 1 and 3 was concomitantly detected. According to the microRNA array analysis, the let-7 family, particularly let-7b and let-7e, were apparently up-regulated among 248 microRNAs that were affected after over-expression of cofilin-1 up to 7 days. Knock-down of let-7b or let-7e using chemical Locked Nucleic Acid (LNA) could recover the growth rate and the invasion of cofilin-1 over-expressing cells. Next, the expression of c-myc, LIN28 and Twist-1 proteins known to regulate let-7 were analyzed in cofilin-1 over-expressing cells, and Twist-1 was significantly suppressed under this condition. Up-regulation of let-7 microRNA by overexpressed cofilin-1 could be eliminated by co-transfected Twist-1 cDNA. Taken together, current data suggest that let-7 microRNA would be involved in over-expression of cofilin-1 mediated tumor suppression in vitro and in vivo.

Biography

Cheng-Han Tsai has completed his PhD from National Yang-Ming University and now is the first year Post-doctoral studies from the same institute. His studies focuses on changes of physiological characteristics as well as related genes profile including miRNA of lung cancer cell in vitro and in vivo while the actin associated protein, ADF/cofilin is manipulated. Some of studies have been published on reputed journals and other manuscripts are under prepared for further submissions.

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