J Clin Toxicol 2015 2015, 5:3
http://dx.doi.org/10.4172/2161-0495.S1.016

OMICS International
conferenceseries.com
4th Global Summit on
Toxicology
August 24-26, 2015 Philadelphia, USA

Genetic dissection of signaling network during mammalian secondary palate development and cleft palate

Jixiang Ding
University of Louisville Birth Defects Center, USA

Cleft palate is a common birth defect that affects approximately 1:700 births. Palate formation during embryonic development is a complex process involving a series of steps such as vertical growth of palate shelf, palate re-orientation or elevation to horizontal level and horizontal growth until meet and fusion along the facial midline. Each step is under strict regulation to avoid possible developmental disruption and cleft palate. In this study, we used genetic approaches to investigate the functions and interactions of major signaling pathways during mouse secondary palate development and cleft palate. *Zeb1* encodes a transcription modulator that regulates the activities of SHH and TGF-βsignaling pathways. Genetic inactivation of the *Zeb1* gene causes cleft palate due to delayed palate re-orientation/elevation. By examining the re-orientation process in *Zeb1* mutant line, we found that palate re-orientation is initiated by cell migration and outgrowth from the side of vertical palate shelf. Considering the critical role of FGFs in controlling embryonic cell migration and movement, we investigated the function of FGF8 in palate re-orientation by tissue specific deletion of Fgf8 gene in palate mesenchymal cells and disclosed varied cleft palate phenotype associated with defects in palate re-orientation including vertical palate and shortened horizontal palate. In addition, we found that FGF8 carries out its role in palate development by interacting with WNT, another important signaling pathway. Since *ZEB1* is a TGF-β modulator, we re-visited the issue of TGF-β1, 2 in palate and found that Tgf-β1 and Tgf-β2 double mutants display cleft palates in strain dependent manner.

j0ding03@louisville.edu

Anticancer effects of Hinokitiol: The pivotal role on inhibiting MMPs 2 and 9 and modulating antioxidant enzymes in mouse melanoma cells

Thanasekaran Jayakumar, Chien-Hsun Huang and **Joen-Rong Sheu**
Taipei Medical University, Taiwan

Numerous reports have been shown that inhibition of matrix metalloproteinases (MMP) expression and/or inhibition of their enzyme activities can be used as early targets for preventing cancer metastasis. MMP-2 (72-kDa gelatinase A) and MMP-9 (92-kDa gelatinase B) are involved in the invasive metastatic potential of tumor cells. Number of recent evidence has revealed that natural dietary antioxidants are capable of inhibiting cancer cell growth. Moreover, these natural antioxidants are reported to have the ability to enhance the activities of detoxification enzymes. Decrease in the activities of the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT) noted in tumor group is regarded as markers of malignant transformation. Therefore the significant elevation of SOD and CAT may be the potential targets for anticancer therapy. Thus, great attention is focused on developing agents or drugs that can inhibit metastasis via inhibiting MMPs and modulating antioxidant defense. Hinokitiol, a natural bioactive compound found in *Chamacyparis taiwanensis*, has long been used in hair tonics, cosmetics, and food as an antimicrobial agent. In this study, it appeared to achieve hinokitiol reduces the expression of MMP-2 and 9 by suppressing the phosphorylation of mitogen- activated protein kinase (MAPK) signaling molecules followed by inhibiting the phosphorylation of p65 nuclear factor kappa B (NFκ-B) in melanoma (B16-F10) cells. In addition, hinokitiol increased the activities of CAT and SOD detected by native polyacrylamide gel electrophoresis in this cell. Moreover, electron spins resonance (ESR) study shown that hinokitiol suppressed hydroxyl radical (OH°) formation in a concentration dependent manner. These findings suggest that hinokitiol holds a potent anticancer effect via inhibiting MMPs 2 and 9, modulating antioxidant defense and suppressing OH° formation in B16-F10 melanoma cells. These results may accelerate the development of novel therapeutic agents for the treatment of malignant cancers.

tjaya_2002@yahoo.co.in