褪黑激素可望成為對抗肺癌之新契機！

Clinical science (London, England : 1979)

Vol.133/ issue 5/page 709-722

2019/05/15

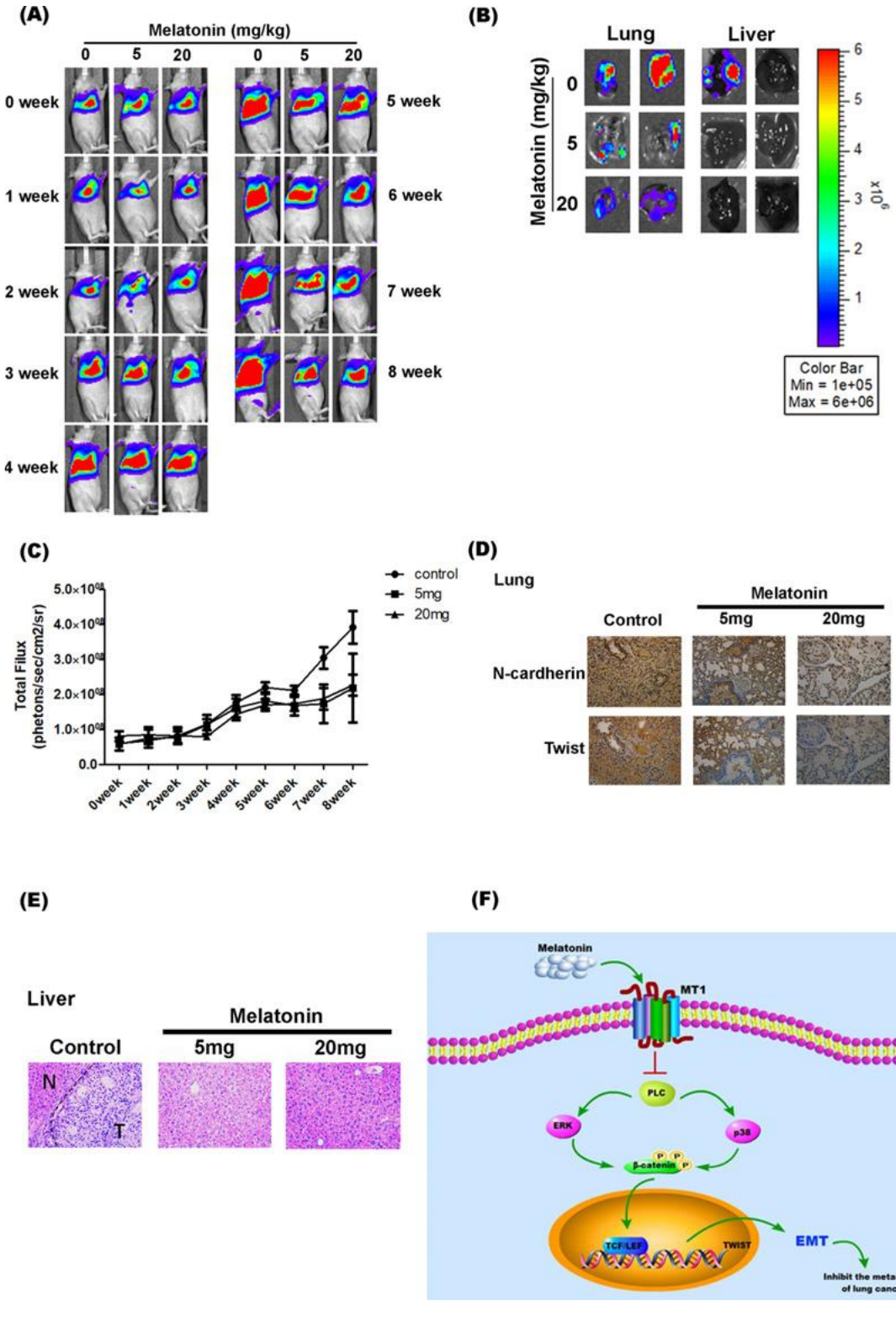
趙家佳副教授/醫學院呼吸治療學系

褪黑素通過標靶 Twist 基因抑制上皮-間質轉化並抑制肺癌轉移

褪黑激素(melatonin)為松果體生成之荷爾蒙，主要功能為調節生理時鐘。然而在近年的研究中也被指出具有抗癌、抗氧化及抗發炎的功能。由醫學院呼吸治療學系趙家佳副教授團隊所進行的抗肺癌研究有成，發現褪黑激素在細胞實驗及臨床前小鼠動物實驗中，都能有效抑制肺癌生長及轉移。她的團隊在深入探討後發現褪黑激素是藉由抑制上皮－間質轉化(Epithelial-mesenchymal transition; EMT)過程，進而達到抗腫瘤轉移效果。本研究成果期望未來能將褪黑激素應用在臨床肺癌治療中。

肺癌長期位居十大癌症死亡率之首，儼然已成為公認之國病。肺癌之治療雖已有多種方式，然而其五年存活率仍具有相當大的改善空間。因此在基礎及臨床研究上紛紛投入許多資源研發新穎之抗肺癌藥物。上皮－間質轉化(Epithelial-mesenchymal transition; EMT)的本為胚胎發育之重要過程，然而許多證據指出腫瘤轉移時上皮細胞將進行 EMT 之轉化，並且因此轉變成較具運動性及侵襲性之癌細胞。先前已有許多研究證據指出，褪黑激素具有抗氧化的作用和保護細胞抵抗致癌物質的影響，進而避免腫瘤的進展。然而，在針對 EMT 以及肺癌轉移中，褪黑激素的效果目前並未瞭解。

趙家佳老師研究團隊發現褪黑激素會透過抑制 Twist/Twist1(twist 家族 bHLH 轉錄因子 1)表現來抑制 EMT。也進一步釐清此作用是由 MT1 receptor, PLC, p38/ERK and β-catenin 訊息傳遞所調控的。同時也發現在肺癌組織當中，Twist 表現與腫瘤分期呈正相關，與 MT1 表現呈負相關。此外，在活體小鼠實驗中也證實了褪黑激素能抑制 EMT 分子標記的表現和肺癌的轉移肝臟現象。最後，褪黑激素在肺癌轉移的治療中顯示了潛力，而此值得進一步研究。



相關連結 https://doi.org/10.1042/CS20180945

Melatonin could be serve as an anti-tumor agent in lung cancer therapy

Clinical science (London, England : 1979)

Vol.133/ issue 5/page 709-722

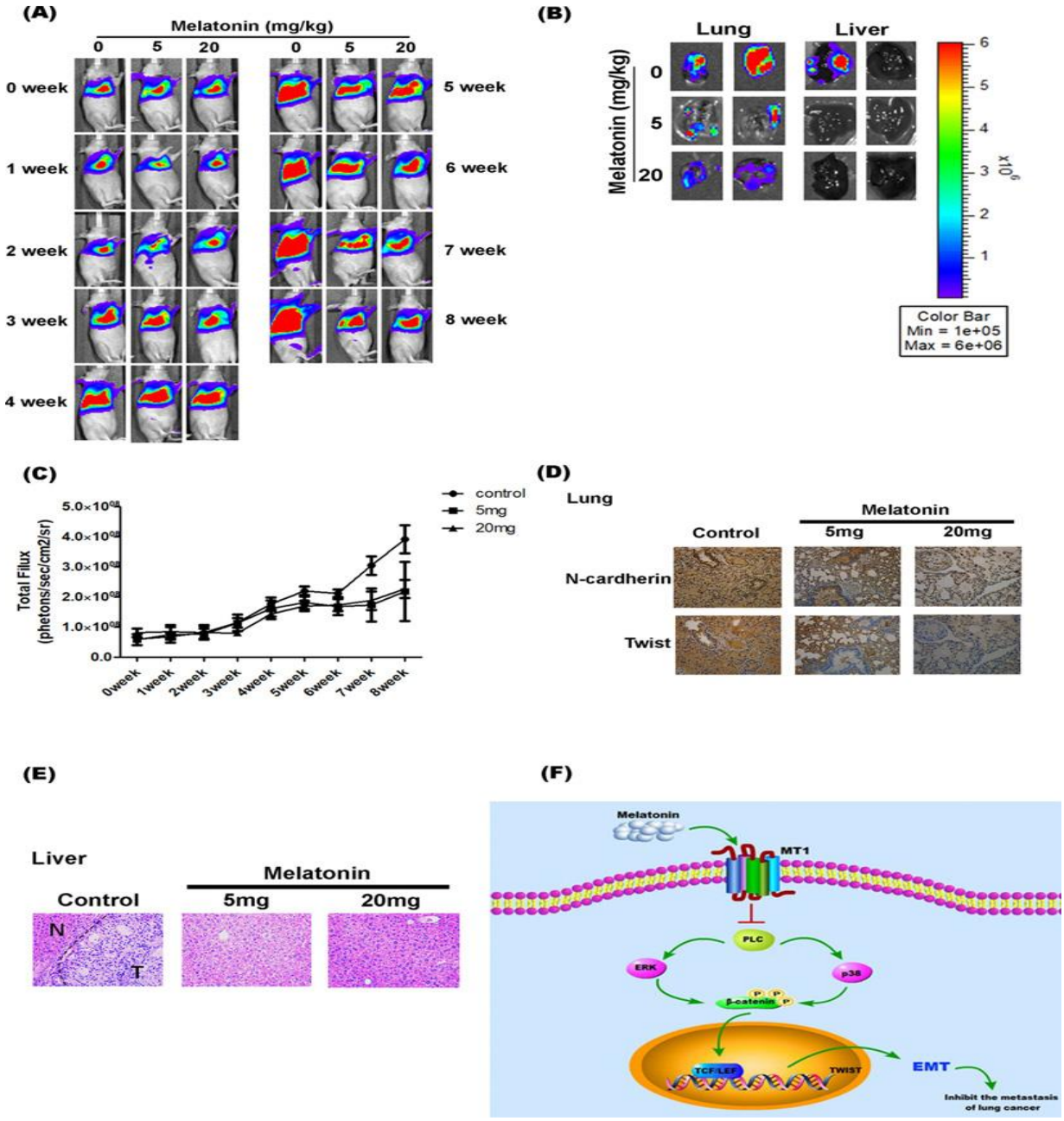
2019/05/15

Chao chia chia Ph.D., Associate Professor
Department of Respiratory
College of Medicine

Melatonin suppresses lung cancer metastasis by inhibition of epithelial mesenchymal transition through targeting to Twist

Melatonin is a hormone secreted by pineal gland which has various capacities. For example: anti-tumor, anti-aging, anti-inflammatory, and antioxidant effects. A research team lead by Dr. Chia-Chia Chao at Department of Respiratory Therapy, has found melatonin can prevent lung cancer growth and metastasis in in vitro and in vivo studies. Dr. Chao's team also found that the anti-metastatic effects of melatonin was mediated by targeting epithelial-mesenchymal transition (EMT). The current finding could develop melatonin as therapeutic strategy against lung cancer in the future.

The epithelial-mesenchymal transition (EMT) phenotype, whereby mature epithelial cells undergo phenotype transition and differentiate into motile, invasive cells, has been indicated in tumor metastasis. The melatonin hormone secreted by the pineal gland has an antioxidant effect and protects cells against carcinogenic substances that reduce tumor progression. However, the effects of melatonin in EMT and lung cancer metastasis are largely unknown. We found that melatonin downregulated EMT by inhibiting Twist/Twist1 (twist family bHLH transcription factor 1) expression. This effect was mediated by MT1 receptor, PLC, p38/ERK and β-catenin signaling cascades. Twist expression was positively correlated with tumor stage and negatively correlated with MT1 expression in lung cancer specimens. Furthermore, melatonin inhibited EMT marker expression and lung cancer metastasis to liver in vivo. Finally, melatonin shows promise in the treatment of lung cancer metastasis and deserves further study



Link to the article : https://doi.org/10.1042/CS20180945