

RESEARCH ARTICLE

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p300 promotes proliferation, migration, and invasion via inducing epithelial-mesenchymal transition in non-small cell lung cancer cells

Xue Hou^{1,2,3*}, Run Gong^{4*}, Jianhua Zhan^{2,3*}, Ting Zhou^{1,2,3}, Yuxiang Ma^{2,3,5}, Yuanyuan Zhao^{1,2,3}, Yaxiong Zhang^{1,2,3}, Gang Chen^{1,2,3}, Zhonghan Zhang^{1,2,3}, Shuxiang Ma^{1,2,3}, Xi Chen^{1,2,3}, Fangfang Gao^{1,2,3}, Shaodong Hong^{1,2,3}, Fan Luo^{1,2,3}, Wenfeng Fang^{1,2,3}, Yunpeng Yang^{1,2,3}, Yan Huang^{1,2,3}, Likun Chen^{1,2,3}, Haolian Yang^{2,3,6,†} and Li Zhang^{1,2,3,†}

Abstract

Background: Histone acetyltransferase p300 is a crucial transcriptional coactivator and has been implicated as a poor prognostic factor in human cancers. However, little is known about the substantial functions and mechanisms of p300 in NSCLC proliferation and distant metastasis.

Methods: We constructed p300 down-regulated and up-regulated cell lines through RNAi and recombinant plasmid transfection. Cell Counting Kit-8 assays were used to test the cell proliferation and confirmed by colony formation assays. Wound healing assays and transwell chamber assays were used to test the migration and invasion ability. Based upon these results, we measured the epithelial markers and mesenchymal markers after regulating p300 expression to explore epithelial-mesenchymal transition as a potential mechanism of p300 promoting NSCLC metastasis.

Results: In NSCLC cells NCI-H1975 and NCI-H1993, down-regulation of p300 leads to inhibition of cell proliferation and colony formation. Cells with reduced p300 expression also demonstrate inhibited migration and invasion ability. Contrarily, up-regulation of p300 significantly enhanced the proliferation, colony formation, migration and invasion ability of NCI-H460. Importantly, further investigation shows that decreased p300 expression is associated with reduced expression of mesenchymal markers and increased expression of epithelial markers, while up-regulated p300 expression correlated with decreased expression of epithelial markers and increased expression of mesenchymal markers.

Conclusions: As a crucial tumor promoter, p300 promotes cell proliferation, migration, and invasion in NSCLC cells. Epithelial-mesenchymal transition is a potential mechanism of p300 promoting NSCLC metastasis.

Keywords: Epithelial-mesenchymal transition, Invasion, Non-small cell lung cancer, p300, Prognosis

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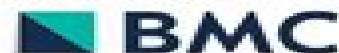
[†]Xue Hou, Run Gong, Jianhua Zhan, Haolian Yang and Li Zhang contributed equally to this work.

Xue Hou, Run Gong and Jianhua Zhan share the first authorship.

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Epithelial Mesenchymal Transition Promotes Proliferation Non Small

**Xiaohua Yan, Peter Ten Dijke, Long
Zhang, Keiji Miyazawa**



Epithelial Mesenchymal Transition Promotes Proliferation Non Small:

The Epithelial-to-Mesenchymal Transition (EMT) in Cancer Joëlle Roche, 2018-04-09 This book is a printed edition of the Special Issue The Epithelial to Mesenchymal Transition EMT in Cancer that was published in Cancers

Epithelial-Mesenchymal Transition (EMT) as a Therapeutic Target in Cancer Tao Sun, Guojun Sheng, Weilong Zhong, Dingzhi Huang, 2023-03-03

Links between Fibrogenesis and Cancer Esteban C. Gabazza, 2019-11-18 Tissue fibrosis may occur for unknown causes or be the consequence of many pathological conditions including chronic inflammatory or infectious diseases autoimmune disorders graft rejection or malignancy On the other hand malignant tumors have been identified in fibrotic tissues decades ago and now accumulating evidence suggests that fibrotic lesions enhance the risk of cancer in several organs such as liver lungs and breast Disruption of an organ parenchymal cells and of its normal structural scaffold during tissue fibrogenesis appears to induce loss of cell polarity promoting uncontrolled cell proliferation that may eventually lead to cancer development Many cellular and molecular abnormalities including aberrant expression of microRNAs genetic and epigenetic alterations evasion or delayed apoptosis unregulated intracellular signal pathways and dysregulation or defective intercellular communications have been proposed to explain this link between fibrogenesis and carcinogenesis However the precise mechanisms of this fibrosis to cancer transition remain unclear This book presents a collection of reviews and original articles summarizing recent advances in understanding the molecular mechanisms of cancer development in fibrotic organs

Epigenetics in Precision Medicine Jose Luis Garcia-Gimenez, 2021-11-12 In recent years knowledge of epigenetic mechanisms underlying disease onset and progression has proven crucial for the development of novel early diagnosis and prognosis biomarkers for patient stratification and precision medicine Epigenetics in Precision Medicine a new volume in the Translational Epigenetics series provides a thorough discussion and overview of current developments in clinical epigenetics with special emphasis on epigenetic biomarkers that can be used for clinical diagnosis prognosis patient stratification and treatment monitoring Disease types discussed include cancer metabolic disorders neurodegenerative diseases bone disease and immune related disorders The book examines the challenges of advancing epigenetics research and translating findings to the clinic and drug discovery in each of these areas as well as current solutions chapter authors discuss how to leverage epigenomic technologies applications and tools such as next generation sequencing to discover new epigenetic biomarkers in disease and drug studies Epigenetics in Precision Medicine focuses on complex epigenetic mechanisms in several pathologies and explores how epigenetics can power the advance of precision medicine not only by improving in vitro diagnostic and prognostic tools but by providing new therapeutic approaches to treat human disease Provides a thorough grounding in epigenetics driven precision medicine with emphasis on developing and implementing early diagnosis and prognosis biomarkers and supporting patient stratification Empowers researchers and clinicians to incorporate epigenetics in new disease research drug discovery and clinical practice Features

chapter contributions from international leaders in the field lncRNAs in Cancer Metastasis and Therapy Resistance Aamir Ahmad, Palmiro Poltronieri, Shahab Uddin, 2023-10-30 lncRNAs long non coding RNAs are the relatively longer more than 200 nucleotides long subtypes of ncRNAs non coding RNAs i e the RNAs that do not code for any proteins However even without themselves being translated lncRNAs impact the cellular gene expressions and functions in ways that are just beginning to be explored The metastasis of human cancers as well as acquired resistance against the administered therapeutics are two major factors responsible for the cancer associated mortality **The Role of ncRNAs (non-coding RNAs) in Regulating**

Tumor Immune Microenvironment Yanyan Tang, Shiv K. Gupta, Zong Sheng Guo, 2022-09-14 **Non-coding RNA as Prognostic and Diagnostic Biomarkers in Thoracic Oncology** Desi Shang, Wei Jiang, Yan Gu, Huihui Fan, 2022-03-09

Genetic and proteomic biomarkers in solid tumor detection and treatment Jitian Li, Apeng Chen, Ruowen Zhang, Changwei Li, Jian-Guo Zhou, 2023-06-07 *Altered Expression of Proteins in Cancer: Function and Potential*

Therapeutic Targets Varda Shoshan-Barmatz, Carlos Pérez-Plasencia, Sandra Casimiro, Marta Martins, João Pessoa, 2022-08-03

TGF- β and BMP Signaling in Cancer Xiaohua Yan, Peter Ten Dijke, Long Zhang, Keiji Miyazawa, 2022-10-12 Targeting the Wnt/ β -catenin Signaling Pathway in Cancer Simone Patergnani, Donald Buchsbaum, Gary Piazza, 2022-11-01

Epigenetic Regulation and Tumor Immunotherapy Mingzhu Yin, Qin Yan, Jian Cao, Bihui Huang, 2022-05-27 Epigenetic Cancer Therapy Steven Gray, 2023-05-03 Epigenetic Cancer Therapy Second Edition provides a comprehensive discussion of healthy and aberrant epigenetic biology along with new discoveries to improve our understanding of cancer epigenetics and therapeutics The book encompasses large scale intergovernmental initiatives as well as recent findings across cancer stem cells rational drug design clinical trials and chemopreventative strategies As a whole the work articulates and raises the profile of epigenetics as a therapeutic option in the future management of cancer Since the publication of the first edition of this book the field of epigenetics has undergone significant change New epigenetic therapies have been designed and approved for clinical use Our knowledge of the plasticity of the epigenome in cancer and disease has expanded dramatically with increasing evidence linking pollution to epigenetic changes in cancer development This second edition has been fully updated to address these changes along with promising therapeutic programs such as CRISPR Cas9 mediated approaches CAR T based therapies epigenetic priming histone modifications and similar transformative advances across synthetic biology and cellular engineering Concisely summarizes the therapeutic implications of recent large scale epigenome studies Covers new findings in the interplay between cancer stem cells CSCs and drug resistance thus demonstrating that epigenetic machinery is a candidate target for the eradication of these CSCs Provides a fully updated resource on new topics including the epitranscriptome oncohistones single cell analysis epigenetic priming CRISPR therapy CAR T therapy and epigenetics and pollution Features chapter contributions from leading experts in the field Chemical and Molecular Approach to Tumor Metastases Gianni Sava, Alberta Bergamo, 2018-07-05 This book is a printed edition of the Special Issue Chemical and

Molecular Approach to Tumor Metastases that was published in IJMS **Genetics and Epigenetics of RNA Methylation System in Human Cancers** Shicheng Guo,Shenying Fang,Dingyuan Luo,Xiang Shu,Zhifu Sun,Xiangqian Zheng,2022-02-17

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Handbook of Animal Models and its Uses in Cancer Research Surajit Pathak,Antara Banerjee,Atil Bisgin,2023-01-31 This reference book compiles together different animal models in cancer research It provides knowledge and a better understanding of the advancement of the molecular and cellular mechanisms associated with the progression formation and clinical results of various types of cancer from the evidence collected from animal models utilized for cancer research It discusses animal models for screening anti cancer drugs and exploration of gene therapy It presents different methods used to construct cancer animal models and the progress of each animal model in tumor research The book also highlights the applications of genetic engineering including CRISP Cas9 in designing and developing animal models for cancer research Further it discusses strategies for modeling animals for investigating growth metastasis tumor associated inflammation and microenvironment cancer stem cells tumor heterogeneity and therapeutic resistance This book is s a valuable resource for basic and translational cancer researchers clinicians and health care **Mechanisms of Melanoma Tumor Progression** Vladimir Spiegelman,Vijayasaradhi Setaluri,2022-02-21 *Methods and Applications: Computational Genomics* Guanglin Li,Tao Huang,Lei Wang,Yang Gao,2022-07-28

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