

# The ability of long non-coding RNA IGFBP4-1 to modulate Cellular Metabolism is a potential breakthrough in Lung Cancer Therapy

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## Article Info

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## ABSTRACT

Lung cancer being one of the leading causes of cancer-related deaths around the world has significantly added to the global burden of disease. Late diagnosis, unavailability of definitive treatment and an unclear pathophysiological mechanism behind the role of various genes expressed in lung cancer make it a challenge that needs new techniques and better understanding of the underlying pathology and role of genetics. Long non-coding RNAs, once considered insignificant, are now being elucidated to have major roles to play in the regulation and development of carcinogenesis. In this review, the ability of a lncRNA, lncRNA IGFBP4-1 to modulate cellular metabolic processes, eventually affecting lung cancer progression and consequently being a potential biomarker for lung cancer diagnosis has been discussed.

## Introduction

In recent studies, it has been shown that long non-coding RNAs (lncRNA) can regulate and develop cancer progression by facilitating cell growth and proliferation. In our recent study, "Overexpression of lncRNA IGFBP4-1 reprograms energy metabolism to promote lung cancer progression"<sup>1</sup>, an attempt has been made to elucidate the connection between lncRNA and cell metabolism in tumour cells which could be a new thinking not only in exploring a valuable biomarker in early diagnosis but also in being a potential path in lung cancer therapy.

## Global Burden of Lung Cancer

Cancer has been shown to be one of the leading causes of mortality and morbidity around the world. There have been around 14 million new cases reported in the year 2012 and lung cancer deaths have amounted to 19 percent of all mortalities caused by any cancer<sup>2</sup>. As per the World Cancer Report published in 2017, lung cancer is one of the leading causes of mortality around the world and has caused 1.69 million deaths in 2015<sup>3</sup>. The clinical treatment of lung cancer has developed in leaps and bounds especially with the advent of precision medicine, but the overall survival rate has still not improved significantly due to the paucity of cancer biomarkers in early diagnosis and as a result leading to a late diagnosis of the disease often involved with lymph nodes involvement and metastasis into other organs.

## Role of lncRNAs

The role of lncRNA and its mutation and aberrant expression causing physiological changes such as cell growth and apoptosis, and pathological changes such as metastasis and invasion, consequently contributing to development and promotion of tumour cells in carcinogenesis has been illustrated in recent studies<sup>4-6</sup>. The communication between proteins associated with various lncRNAs had distinct molecular processes and the lncRNAs were found to have functional interrelation with the sense genes<sup>7</sup>. There was significant difference in the lncRNA expression in normal tissues and in non-small lung cancer tissues illustrating the possible role of specific lncRNA screening tests<sup>8</sup>. These lncRNAs have been shown to regulate metabolism and metastasis in tumour cells thus providing evidence that they are potential biomarkers. Similarly, lncRNA insulin-like growth factor receptor binding protein (IGFBP4-1) has been shown to influence cell metabolism and proliferate lung cancer.

## Role of lncRNA-IGFBP4-1

lnc-IGFBP4-1 is located in the upstream section of IGFBP4 gene and these proteins are known to be regulation factors involved in the metabolism of cancer cells by competing with insulin-like growth factor receptor (IGFR), combining with insulin-like growth factor (IGF) and as a result, modulating the physiological functions of the IGF<sup>9</sup>. There is evidence that lnc-IGFBP4-1 has been significantly overexpressed in lung cancer tissues in respect to adjacent normal histological tissues and the high localization of lnc-IGFBP4-1 in the nucleus of cancer cells hints at its transcriptional regulation ability. The upregulation of lnc-IGFBP4-1 increased the cell proliferation ability significantly in lung cancer cell lines, and there is proof of increased migration and invasion of cancer cells with an overexpression of lnc-IGFBP4-1. Similarly, downregulation of lnc-IGFBP4-1 decreased cell migration and invasion and increased apoptosis of lung cancer cells pointing to the influence of this lncRNA in lung cancer cell growth and proliferation *in vitro* and *in vivo*<sup>10-11</sup>. The energy (ATP) levels were significantly elevated in cancer cells that had an overexpression of lnc-IGFBP4-1, the increase in metabolic enzymes in upregulated lnc-IGFBP4-1 tumour cells and *vice versa*, thus indicating the role lnc-IGFBP4-1 plays at a transcriptional level in modulating lung cancer cell metabolism<sup>1</sup> which is a hallmark of cancer.

## Potential of lnc-IGFBP4-1 in Lung Cancer therapy

Long noncoding RNA lnc-IGFBP4-1 seems certain to be a major regulator in the development, progression and spread of lung cancer by promoting cell growth and inhibiting apoptosis, however, there are a few limitations. Unfortunately, there is still no comprehensive understanding

of the mechanisms behind how lnc-IGFBP4-1 modulates the lung tumour cells at a transcriptional level to change their pathophysiological properties to the extent that it affects their metabolism and growth. There is further room for research and investigation on lncRNAs like lnc-IGFBP4-1 and their associated oncogenes which have connections with tumour promoting activities. Once these molecular mechanisms are thoroughly understood, and there is prognostic review knowledge of lnc-IGFBP4-1, there is clear indication that this lncRNA will not only be an essential biomarker in early lung cancer diagnosis but also an encouraging nouveau point of target for lung cancer therapeutics.

## Conflict of interest

The authors have declared no conflicts of interest.

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