INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: **An Investigation of the Role of Lipocalin Receptor in the Development of Lung Cancer**

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SHORT ABSTRACT

Lung cancer is the most prevalent malignancy globally. Tobacco smoking in all forms is the predominant risk factor for lung carcinogenesis. This aggressive disease has a very low overall 5-year survival rate with approximately 15% in developed countries and 5% in developing countries which can be attributed to its late-stage diagnosis due to lack of suitable biomarkers and efficacious therapeutic strategies. Increasing lines of evidence suggested that neutrophil gelatinase-associated lipocalin receptor (NGALR) is strongly implicated in the development and progression of various human malignancies including glioma, colon, oesophagus, endometrial, liver cancer, etc. However, the expression and role of NGALR in the pathogenesis of lung cancer have not been elucidated thus far. Interestingly, our study showed for the first time that NGALR is significantly upregulated in lung cancer tissues compared to the normal adjacent tissues. It was also found to be upregulated in different stages and grades of lung cancer tissues, thus indicating its involvement in the positive regulation of lung carcinogenesis. In addition, this is the first report to show that knockout of NGALR decreased the proliferation, survival, and migration of lung cancer cells via downregulation of a wide range of intracellular signals including Akt/mTOR, NF-κB, JAK/STAT-3 and EGFR/MAPK signaling pathways. Furthermore, this lipocalin receptor was also found to be involved in the positive regulation of NNK (nicotine-derived nitrosamine ketone), tumor necrosis factor (TNF)-α and TNF-β induced proliferation, survival and migration of lung cancer cells through modulation of proteins involved in different cellular processes. This is the first study that shows the invaluable role of NGALR in the pathogenesis of lung cancer along with its involvement in tobacco as well as TNF-mediated lung carcinogenesis. Our findings not only increase the understanding of this important lipocalin receptor but also provide a potential therapeutic target for developing novel and efficacious therapeutic interventions for lung cancer patients.