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Hypothesis

Linking common non-coding RNAs of human lung cancer and *M. tuberculosis*

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Abstract:
Lung cancer and pulmonary tuberculosis caused by *Mycobacterium* are two major causes of deaths worldwide. Tuberculosis linked lung cancer is known. However, the precise molecular mechanism of *Mycobacterium* associated increased risk of lung cancer is not understood. We report 45 common human miRNAs deregulated in both pulmonary tuberculosis and lung cancer. We show that sRNA_1096 and sRNA_1414 from *M. tuberculosis* have sequence homology with human mir-21. Hence, the potential role of these three small non-coding RNAs in rifampicin resistance in pulmonary tuberculosis is implied. Further, the linking of sRNA_1096 and sRNA_1414 from *M. tuberculosis* with the host lung tumorigenesis is inferred. Nonetheless, further analysis and validation is required to associate these three non-coding RNAs with *Mycobacterium* associated increased risk of lung cancer.

Keywords: Genetic predisposition; lung cancer risk; microRNA; *Mycobacterium tuberculosis*, sRNA

Background:
Viral involvements and their causal roles in oncology are well accepted for various cancers including ovarian neoplasms **[1]** hepatocellular carcinoma **[2]** and lung cancer **[3]** among others. Although, bacterial infections are not considered as major threats to cancer, yet a number of bacterial pathogens are reported to be associated with several cancers. Some examples include: *Mycoplasma* in prostate malignancy **[4],** *Robinsoniella* in pancreatic cancer **[5],** *S. typhi, H. bilis, H. hepaticus*, and *E. coli* in carcinoma of the gallbladder **[6],** *Chlamydia* in cervical cancer **[7]** and *Mycobacterium* in lung cancer **[8-14].**

Lung cancer is the leading cause of all cancer related deaths with a recently estimated 1.6 million deaths worldwide **[15].** Similar to lung cancer, pulmonary tuberculosis caused by *M. tuberculosis* is a global health problem. It is one of the major causes of death amongst infectious diseases and according to WHO 2013 report, it is estimated that 9 million people are infected and 1.5 million died from tuberculosis in 2012 **[16].** Several reports have documented the co-existence of tuberculosis and lung cancer **[14, 17-20],** and pulmonary tuberculosis is a risk factor for developing lung cancer **[17-20].** However, it is not yet fully established at the molecular level, how the *Mycobacterium* increases susceptibility to lung cancer. Some reports say that *M. tuberculosis* induces ROS mediated DNA damage pathway and produces epiregulin growth factor to induce cell proliferation **[21];** while an other study indicates mechanisms along with COX-2 mediated activation of inflammatory pathway in *M. tuberculosis* associated carcinogenesis **[22] .**

Bacterial small regulatory RNAs (sRNAs) are a class of small non-coding RNAs of 40-500 nt in length that regulate various essential patho-physiologies in bacteria such as outer membrane protein biogenesis, virulence, quorum sensing etc. sRNA functions through complementary base-pairing with 3′- or 5′-UTRs of target mRNAs to inhibit translation, alters activity of a