non-malignant cells. Analysis of PCNA structure revealed that the L126-Y133 region forms part of a pocket suitable for binding by a small molecule. We designed and tested a series of small molecules that target this binding pocket and identified AOH1160, a potent PCNA inhibitor, which kills small cell lung cancer (SCLC) cells at high nanomolar concentrations, but causes no significant toxicity to a broad range of non-malignant cells up to a concentration of 10 μM. AOH1160 is orally available to animals and inhibits tumor growth without causing any observable side-effects, including weight loss, in mice. These studies demonstrated the feasibility of inhibiting the growth of SCLC cells by targeting a specific region of PCNA without causing unacceptable toxicity to normal tissues. Further development of AOH1160 may lead to a novel anti-cancer therapy.

Translational application of microRNA profiling for early detection of lung cancer: A comparison of sputum and blood

Jennifer E. Gyoba, Rene Razzak,
Sunita Ghosh, Linghong Guo, Wilson Roa,
Eric L.R. Bedard University of Alberta, Edmonton, AB, Canada

Background: Lung cancer has the highest mortality rates of all the cancers in Canada with a 5 year survival rate of less than 15%. Asymptomatic in its early stages, methods to screen high risk individuals are in dire need to allow earlier diagnosis and curative intent treatment. MicroRNAs (miRNAs) are small, non-coding strands of RNA that are shown to lead to carcinogenesis when dysregulated. They are promising candidates for biomarkers as they are stable, detectable in small quantities and are expressed in a tissue specific manner. Through the use of a miRNA panel developed by our group that demonstrated good sensitivity and specificity using sputum as a medium to measure miRNA, we aimed to compare the efficacy of measuring miRNA in sputum and blood to develop a miRNA profile for non-small cell lung cancer (NSCLC).

Objective: To examine miRNA profiles of NSCLC cases versus healthy controls to compare the efficacy of sputum and blood for potential screening purposes using microarray analysis.

Methods: A case control study of stage I/II cancers, matched with controls having similar smoking history, age, and gender, was performed. Participants were recruited at the Royal Alexandra Hospital in Edmonton, Alberta, Canada. Both sputum and blood are collected and analyzed via Qiagen miRNA kits. 10 cases and 10 controls miRNA samples were submitted for microarray analysis. miRNAs were labelled, hybridized, and quantified using single-color experimental design. Specific miRNAs from past literature were then compared in cases and controls using Mann Whitney U test.

Results: Sputum does not have consistent levels of miRNA present when compared to blood, and principle component analysis (PCA) plots show more random patterns in sputum when compared to blood. By using heat maps and hierarchical clustering, no apparent clusters are seen when compared cases and controls in both sputum and blood. A type II error could be responsible for this finding due to the small sample size. In an independent analysis looking at specific miRNAs seen to be dysregulated in past literature, miR-147a is significantly different in sputum, and miR-126-5p is significantly different in blood.

Conclusions: Microarray analysis shows that sputum is less consistent when measuring miRNAs compared to blood overall. These findings have already been applied to the next phase of our research which will examine miRNA levels in high risk individuals as a means of establishing it as a robust screening test for lung cancer.

Targeting immunosuppressive mechanisms in KRAS mutant lung cancer

Lauren Smith Havel, Dingcheng Gao,
Jennifer S. Daniel, Nasser K. Altorki,
Vivek Mittal Neuberger Berman Foundation Lung Cancer Center, Weill Cornell Medical College, New York, NY

Clinical trials with single agent immune checkpoint inhibitors, mainly the anti-PD-1 antibody, have achieved noteworthy benefit with an objective response rate in 17% of non-small cell lung cancer (NSCLC) patients. However, minimal or no response in a large proportion of patients suggest that additional immune suppression pathways need to be identified in the tumor microenvironment to define combination immune therapies for future therapeutic intervention. We have focused our studies on the KRAS mutant subset, as it accounts for >30% of NSCLC patients with high mortality rates due to a conspicuous lack of effective FDA approved targeted therapies.

To enable selection of appropriate immunotherapies, we have performed comprehensive analysis of immune microenvironments in a mouse model of