correlation coefficient of 0.51 for the change between day 0 and day 7 (p=0.02) and of 0.59 for the change in the second week of RT (day 7 and 14, p=0.02). This correlation was not observed for other cytokines. Moreover, IL-6 levels were higher in patients showing no metabolic response compared to responders: day 0 resp. 18.9 ± 7.6 and 6.0 ± 0.9 (p=0.06), day 7 resp. 31.0 ± 13.0 and 9.5 ± 3.0 (p=0.03) and for day 14 resp. 25.3 ± 12.2 and 8.5 ± 1.9 (p=0.10). Seventy days after RT, levels of IL-1b (r=-0.55, p<0.04) as well as neopterin (r=0.58, p<0.04) were positively correlated with clinically symptomatic pneumonitis (>grade 1). Furthermore, the dyspnea score at this time point showed a graded correlation with plasma levels of neopterin (r=0.76, p<0.01) and the cough score with osteopontin levels (r=0.81, p<0.01), while these phenomena were not observed during RT.

Conclusions: Changes in SUVmax were positively correlated with changes in IL-6 levels during radiotherapy, suggesting that changes in FDG uptake might be partly explained by inflammation. Seventy days after radiotherapy, levels of neopterin were correlated with both symptomatic pneumonitis and dyspnea score, assuming cell-mediated immune activation in the development of pneumonitis. Furthermore, levels of osteopontin, a lungfibrosis related protein, were correlated with cough score after radiotherapy.

PD2-1-4 Cancer Genetics and Tumor Biology, Tue, 16:00 - 17:30

Genome features predict response to chemotherapy for non-small cell lung cancer

Buys, Timon P. 1 The Genome Canada Lung Pharmacogenomics Group. 2,3

1 BC Cancer Research Centre, Vancouver, BC, Canada 2 British Columbia Cancer Agency; Vancouver, BC 3 Ontario Cancer Institute/Princess Margaret Hospital, Toronto, ON, Canada

Background: While standard chemotherapy for non-small cell lung cancer (NSCLC) confers a survival benefit to patients and improves quality of life, a complete response to therapy is uncommon, especially for patients with advanced disease. Uncovering genomic signatures that predict drug response for specific tumors will allow for the rational selection of effective treatments for individual patients and lay the foundation for personalized treatment strategies.

Objective: To determine if genomic features present in pre-treatment tumor cells can predict response to chemotherapy and to identify novel genes associated with drug resistance.

Methods: A panel of archived pre-treatment lung tumor biopsies with recorded patient response to a standard doublet regime (cis-platinum/vinorelbine) were selected and subdivided into “responders” and “non-responders” based on clinical parameters. Following pathology review, tumor cells were isolated and DNA was extracted from formalin-fixed, paraffin-embedded tissue sections. Molecular profiling of tumors was undertaken by whole genome tiling-set array comparative genomic hybridization (aCGH). The SeeGH and SIGMA software programs were used for visual analysis of all aCGH profiles. A segmentation algorithm was applied to array data to identify DNA copy number alterations in each tumor. Statistical analysis of processed tumor genome data was used to define regions of significant difference between the “responder” and “non-responder” subgroups.

Results: Comparative analysis of high resolution genome profiles for “responder” and “non-responder” tumors revealed segmental genomic gains and losses specific to each group. Genes within these regions of alteration are known to play a role in cellular processes that affect response to chemotherapeutic agents, including DNA repair and apoptotic signalling. Functional experiments for candidate loci are ongoing.

Conclusions: High resolution analysis of pre-treatment tumor genomes reveals molecular signatures that can predict response to chemotherapy. Clinical application of such signatures will allow cancer treatments to be tailored to individual patients. In addition, candidate response genes within identified signatures may provide insight into drug resistance mechanisms and serve as novel therapeutic targets.

Funding for this work was provided by Genome Canada/Genome BC and Amgen, Inc.