A Translational Approach Towards More Cost-Effective Lung Cancer Treatments

Tuula Klaavuniemi
University of Eastern Finland, klaavuniemi@proton.me

Subhash C. Chauhan
The University of Texas Rio Grande Valley

Ville Paappanen
University of Eastern Finland

Artturi Mäkinen
Tampere University Hospital

Tuomas Rauramaa
Kuopio University Hospital

See next page for additional authors

Presenter Information (List ALL Authors)
Tuula Klaavuniemi, Subhash C. Chauhan, Ville Paappanen, Artturi Mäkinen, Tuomas Rauramaa, Juha Väyrynen, Arja Jukkola, Hanne Kuitunen, and Outi Kuittinen

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Tuula Klaavuniemi1 Subhash Chauhan2, Ville Paappanen1, Artturi Mäkinen3, Tuomas Rauramaa4, Juha Väyrynen5, Arja Jukkola6, Hanne Kuitunen7, Outi Kuittinen1

1 Institute of Clinical Medicine, University of Eastern Finland

2 South Texas Center of Excellence in Cancer Research, Department of Immunology and Microbiology, University of Texas Rio Grande Valley, US

3 Department of Pathology, Tampere University Hospital, Finland

4 Department of Pathology, Kuopio University Hospital, Finland

5 Department of Pathology, Oulu University Hospital, Finland

6 Faculty of Medicine and Health Center, Cancer Center, Tampere University, Finland

7 Cancer Center, Oulu University Hospital, Finland

Lung cancer, globally the second most common cancer, causes 1.8 million deaths annually with 2 million new cases. It's also one of Finland's deadliest cancers. Chemotherapeutic agents, targeted drugs and radiation therapy have been the mainstay in oncologic treatment for lung cancer patients for decades. Checkpoint inhibitors (e.g. nivolumab, pembrolizumab, atezolizumab) have changed the landscape also in lung cancer. These drugs awake patients own immune system to attack cancer cells. These drugs are widely used in different cancers and they have efficacy also in lung cancer, but only in a minority of patients. Checkpoint inhibitors also induce autoimmune side effects. Majority are mild, but often irreversible, such as hypothyroidism or diabetes. Life-threatening and fatal adverse events are rare, but they also occur. Neither treatment response nor adverse effects can be predicted individually. In Finland, these drugs cost app. 10 000€ per month per one patient increasing the economic burden to our society. Thus, we need better understanding of lung cancer biology to be able to offer individual therapies in patient-centered manner, but also within the limits of the carrying capacity of our society. In 10-15% of lung adenocarcinomas there is a
driver EGFR-mutation. Checkpoint inhibitor are ineffective in this type. However, EGFR pathway targeted agents, such as osimertinib, deliver often sustainable responses, but unfortunately resistance mechanism arise in this subtype as well. We need to better understand also the resistance mechanism in EGFR mutated subtypes to better tailor the best optimal treatment sequences to our patients. Translational research, that combines the basic science of lung cancer biology with patient characteristics and treatment outcomes, is a crucial tool in responding to these demands. Tumor microenvironment plays an important role in carcinogenesis, as well as in treatment response, especially acidic environment is immunosuppressive and promotes cancer cell survival. Mucins are a large family of transmembrane glycoproteins expressed on epithelial membranes, including airways. They form the protective immunogenic glycocalyx against microbes as well as pollutants, e.g., carcinogens in tobacco smoke. They are involved in lung cancer formation and in drug resistance forming an important compartment of the tumor microenvironment protecting cancer cells from immune system. Mucins function also as a signaling platform orchestrating cell proliferation, migration and metastasis. Our hypothesis is that dysfunctional regulation and expression of mucin 13, a member of mucin family, provides an immunosuppressive environment and associates with poor response to checkpoint inhibition and poor survival. Mucin 13 is also involved in EGFR signaling. Analyzing mucin 13 with advanced biomolecular techniques using tumor and serum samples of Finnish lung cancer patients

combined with clinical characteristics and treatment outcomes will elucidate the biological mechanisms and improve patient selection for optimal treatments.