Contribution ID: **4** Type: **Oral (8 min)**

Characterising pulmonary carcinoids through molecular analyses within the lungNENomics project

Thursday, 23 November 2023 09:10 (12 minutes)

Introduction

Pulmonary carcinoids are well differentiated low to intermediate grade lung neuroendocrine tumours (LNETs), that belong to the group of lung neuroendocrine neoplasms which also include highly aggressive lung neuroendocrine carcinomas (LNECs). Carcinoids are further divided into atypical and typical, based on mitotic count and presence of necrosis. Although pulmonary carcinoids show relatively good prognosis in comparison to carcinomas, metastatic disease and relapse do occur. In a previous study we introduced the concept of molecular groups of carcinoids: A1, A2, and B, which, importantly, contained a mixture of the two histological types. Additionally, we identified six tumours, termed supra-carcinoids, that displayed genuine carcinoid-like morphology, but had clinical and molecular characteristics of LNECs. The focus of our work is to better understand the biological and clinical characteristics of these molecular groups of carcinoids.

Methods

To address this aim we have designed the lungNENomics study, an international cohort of over 250 cases of pulmonary carcinoids, with clinical data and central pathology review, as well as whole-genome sequencing, RNA sequencing, DNA methylation array, and digital spatial profiling data. These data have been combined with previously published LNET data to perform integrative analysis using multi-omics factor analysis (MOFA), resulting in a molecular map of lung neuroendocrine neoplasms for exploration. To these data we applied the evolutionary theory of task specialisation (ParetoTI) to identify and characterise distinct archetypes, i.e. molecular subtypes, of LNETs.

Results

Multi-omics integration analysis of 319 carcinoids resulted in a molecular map forming a distinctive tetrahedron. ParetoTI theory identified four tumour archetypes within the tetrahedron, corresponding to the three previously reported molecular groups, and the fourth enriched for the aggressive supra-carcinoids. Each archetype was characterised by specific clinical, genomic, and microenvironmental features.

Conclusion

While progress has been made in recent years in the characterisation of pulmonary carcinoids, little is known about the underlying biology or developmental origins of these molecular groups, hampering efforts to identify predictive markers and suitable therapeutic options. The lungNENomics project aims to address these important questions, and will continue to improve the biological understanding of this exceedingly rare and understudied disease.

Primary authors: SEXTON OATES, Alexandra (IARC); FERNANDEZ CUESTA, Lynnette (IARC); FOLL, Matthieu (IARC); ALCALA, Nicolas (IARC / WHO)

Presenter: SEXTON OATES, Alexandra (IARC)

Session Classification: Oral Presentations