Iron dynamics and microbiome dysbiosis during tobacco-associated lung adenocarcinoma development
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Background
Our group has shown that loss of the airway lineage-specific G-protein-coupled receptor 5a (Gprc5a) leads to lung adenocarcinoma (LUAD) development particularly in animals exposed to the tobacco-specific carcinogen nicotine-derived nitrosamine ketone (NNK) (1). Lipocalin 2 (Lcn2), an immunomodulatory protein that we showed to exert protective roles against LUAD development (2), is involved in microbiome homeostasis and prevents non-commensal bacterial overgrowth that causes inflammation and potential carcinogenesis (3). Lcn2 was shown to bind to iron-laden siderophores proteins that are needed by non-commensal bacteria to thrive (4). However, interplay between Lcn2, iron dynamics, and lung microbiome changes in relation to LUAD development is yet to be determined. Towards this, we probed iron and microbial changes during LUAD oncogenesis.

Hypothesis
Microbial dysbiosis and changes in iron levels are associated LUAD development. These may be further exacerbated by loss of Lcn2.

Methods

Results

Gprc5a−/−

Gut

Lung

Figure 2. Changes in diversity of gut (left panels) and lung (right panels) microbiomes with time. *p<0.05.

Figure 3. Changes in iron levels in BALF from WT and Gprc5a−/− mice. *p<0.05, **p<0.01, ***p<0.001.

Discussion
- Iron levels increase in the lung late during oncogenesis.
- In Gprc5a−/− mice, free iron and ferritin circulating in the serum are less pronounced than iron levels onsite during lung oncogenesis.
- Loss of Lcn2 further attenuates microbial diversity and ferritin levels suggesting that this immunomodulator counteracts microbiome dysbiosis during LUAD development.

Future Directions
- Investigation of the interplay between iron levels and immune response during LUAD development.

References
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3. Mochsen AR, Lipocalin 2 Orshts from Inflammation and Tumorigenesis Associated with Gut Microbiota Alterations, Cell Host & Microbe, 2016

Acknowledgements: This presentation is supported by the National Cancer Institute grant R01CA248731 and through the US4 CA096297/CA096300; UPR/MDACC Partnership for Excellence in Cancer Research Training Program. For further information, please contact Rhiannon Morris at RMorris2@mdanderson.org.