Background and Objective:
MIBC is genetically and immunogenically heterogenous disease. Recent molecular classification of MIBC identifies six different molecular subtypes that differ in the immune features. Bladder cancer patients show a high variability in response to treatment, which includes the recently approved checkpoint inhibitors as well as chemotherapeutic interventions. To study the different molecular subtypes and their inter-play with the immune microenvironment that enables the tumors to escape immune surveillance, we have developed immune competent syngeneic BURP (BBN induced Urothelial carcinoma Roswell Park) model of bladder cancer.

Methods: BURP tumor lines were developed by serial sub-cutaneous passaging of BBN induced primary bladder tumors into sex-matched wild-type C57BL/6 mice. The tumor models were first classified by histological features following identification of molecular subtypes by applying the consensus molecular subtype classifiers to the bulk RNA-seq data of each tumor line. Immune cell composition of the BURP lines was determined by applying CIBERSORT deconvolution algorithm using the ImmuCC immune cell signatures. We treated two BURP lines of different molecular and immune subtype with cisplatin and compared the difference in tumor growth rates between them.

Results: We have established eight BURP tumor lines, that differ in their histological, molecular and immunological characteristics. Histologically, the tumor lines show squamous and sarcomatoid differentiation. Molecularly, the tumor lines are divided into basal/ squam, stroma-rich and neuroendocrine subtypes. All the tumor lines have a low estimated CD8+ T-cell fraction, but differ in their estimated fraction of macrophages and differentiated CD4+ T-cells. The BURP tumor line classified as stroma-rich subtype (BURP16) showed a strong response to cisplatin treatment but BURP24, classified as basal/ squam subtype, was resistant to cisplatin treatment.

Conclusion: The BURP tumor lines are suitable model systems to study the dynamics between molecular sub-types and the tumor immune microenvironment. The difference in response to cisplatin treatment between the BURP tumor lines, indicates that the BURP tumor lines can provide a deeper understanding of the interplay between the molecular drivers and immune cell players in inherent treatment response and resistance.