Urothelial carcinoma (UC) of the bladder is the 4th most commonly diagnosed cancer and the 8th most common cancer-related death in males in the United States as reported in 2016. High prevalence of UC occurred in Taiwan is also found. Gemcitabine/cisplatin (GC) regimen is commonly used for treatment with locally advanced and metastatic UC due to its low toxicities. However, drug-resistance and rapid relapse/recurrence are the major reasons for treatment failure. This reveals the needs for the understanding of GC-resistant mechanisms to develop a novel strategy for effective treatment.

Tumor microenvironment (TME) is a critical factor to affect chemoresistance, including cancer-associated endothelial cells, cancer-associated fibroblasts (CAFs), adipocytes, mesenchymal cells, mesenchymal stem cells, and tumor-associated macrophages (TAMs). Chemotherapy-resistant CSCs have also been proven in various solid tumors, including UC. The modes of action and interplay between stemness and TAMs activation at the TME of chemoresistant UC will be explored.