AUA
2020

Mitomycin C sensitive tumor cells generate an inflammatory secretome capable of inducing anti-tumor immune responses

Presenter: Bianca Oresta

Chiara Pozzi, Daniele Braga, Rodolfo Hurle, Massimo Lazzeri, Piergiuseppe Colombo, Giorgio Guazzoni, Maria Rescigno

Humanitas Clinical and Research Center, Rozzano (Milan) Italy

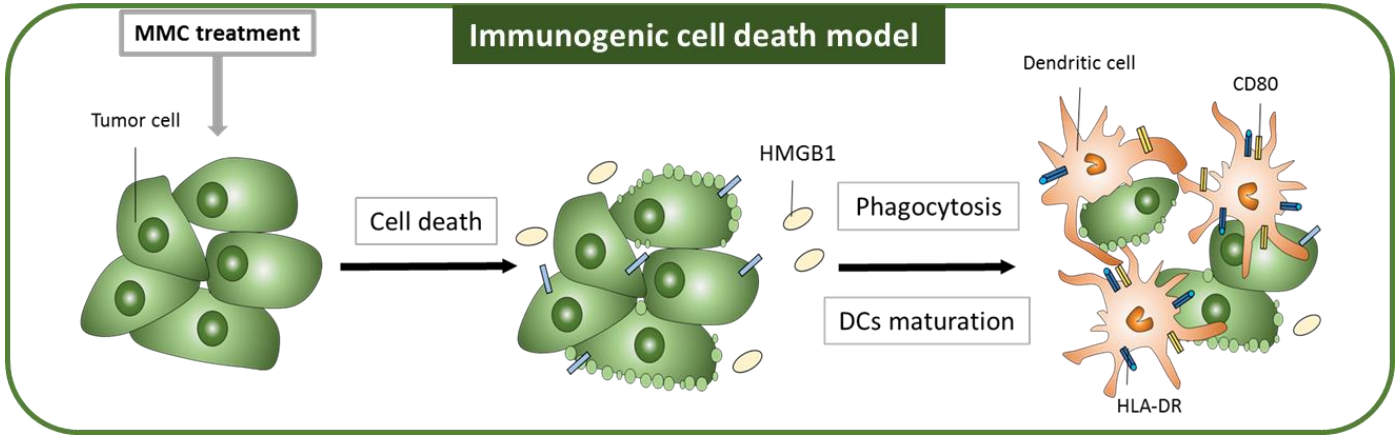
MP01-07

AUA
2020

I have no potential conflict of interest to report

Background & objective

Despite preventing recurrence of non-muscle invasive bladder cancer (BC), the chemotherapeutic drug Mitomycin C (MMC) is effective only in a proportion of patients. We speculated that treatment success might not only rely on MMC cytotoxic potential, but also on its ability to trigger immunogenic cell death (ICD). In this study, we assessed MMC-induced ICD in a panel of BC cell lines and we investigated the molecular differences between ICD-responsive and ICD-resistant resistant BC cells to identify potential underlying mechanisms of MMC efficacy.



Results

Treatment with MMC fostered ICD in some BC cells, but not all. RNA sequencing analysis of ICD-responsive and ICD-resistant tumor cells showed that responsive cells were characterized by the expression of a specific signature characterized by the upregulation of genes involved in immune functions. Moreover, we observed that pathways related to the regulation of cell cycle, spindle formation, sister chromatid segregation, and protein processing were specifically downregulated in ICD-responsive cells, indicating that MMC treatment in these cells induced an early block in the replication machinery, stopped in cell cycle progression, leading to cytotoxicity. On the contrary, ICD-resistant cells did not upregulate the expression of inflammatory mediators.

Conclusions

We showed a novel immune-related mechanism of action of MMC that may be exploited to optimize bladder cancer management and identify ICD-related biomarkers.