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Bladder Cancer: Basic Research I
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567: NEW IMMUNOTHERAPY FOR NON MUSCLE INVASIVE BLADDER CANCER (NMIBC): EFFECTS OF IMMUNOMODULATOR P-MAPA

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Introduction and Objectives

Immunotherapy represents one of the approaches for the treatment of cancer. Compounds which are able to act as toll-like receptors (TLRs) agonists may represent promising candidates to be developed as medicines against cancer. BCG is used as a therapeutic tool for some cancer types, including the urothelial cancer. P-MAPA is an acronym for Protein Aggregate Magnesium-Ammonium Phospholinoleate-Palmitoleate Anhydride having significant in vivo antitumor. Thus, the aims of the hereby study were to characterize effects of the P-MAPA on TLRs in vitro and in vivo, as well as to verify its potential as adjuvant therapy for NMIBC. For its purpose, the efficacy of P-MAPA was compared versus BCG in the NMIBC mouse model.

Methods

Thirty female Fisher 344, 7 week old, rats were anesthetized and received 1.5 mg/kg dose of n-methyl-n-nitrosourea (MNU), intravesically every other week for 7 weeks. After MNU treatment, the 30 rats were divided into 3 groups: The MNU group received 0.30 ml dose of 0.9% physiological saline for 8 weeks; The BCG group received 106 CFU dose of BCG for 8 weeks; The P-MAPA group received 5 mg/kg dose of P-MAPA for 8 weeks. After 15 weeks, all bladders were collected for immunological and Western Blotting analysis for TLR 2, TLR 4, p53, Ki-67 (cellular proliferation) and apoptosis detection. The activity of P-MAPA on TLRs was assayed in vitro through NF-κB activation in HEK293 cells.

Results

The P-MAPA samples exhibited significant stimulatory effect on human TLR2 and TLR4 at 50 µg/mL corresponding to about 88% and 32% of the control ligands respectively. The highest TLR4 and TLR2 protein levels were found in the P-MAPA groups when related to BCG and MNU groups. The p53 protein level was significantly higher in the P-MAPA groups than in the BCG and MNU groups. Furthermore, this level was significantly higher in the BCG group when compared to the MNU group. The apoptosis and cellular proliferation indexes were increased in all experimental groups. However, these processes were decreased in the BCG and P-MAPA groups in relation to the MNU group.

Conclusions

In conclusion, P-MAPA acted as TLR ligand in vitro and improved the immunological status in vivo, including TLR2 and TLR4 protein levels. P-MAPA immunotherapy was more effective in restoring p53 and TLRs reactivities and showed significant antitumor activity than other immunotherapies. The activation of TLRs and p53 may provide a hypothetical mechanism for the therapeutic effects found in NMIBC. Taking together, the data warrant the further assessment of P-MAPA as a potential candidate for treatment of NMIBC.