03. Vaccine therapy

P03.01 EFFICACY AND TOXICITY OF BCG THERAPY IN BLADDER CANCER

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Background Bacillus Calmette-Guérin (BCG) has been successfully used as immunotherapy to treat non-muscle invasive bladder cancer (NMIBC) for more than four decades. BCG is the only intravesical agent shown to reduce the risk of progression of NMIBC to muscle-invasive disease. Unfortunately, BCG therapy is not a universal panacea and it still fails in up to 40% of patients. Many of these patients, especially in the high-risk category (T1 high-grade disease, carcinoma in situ) will require aggressive therapy like cystectomy or in selected cases, bladder-sparing options like chemo-radiation. This prospective cohort study was designed to document efficacy and toxicity of half dose (40 mg) BCG.

Materials and Methods Eligibility criteria include intermediate and high-grade NMIBC and carcinoma in situ after 3 weeks of TURBT. Weekly BCG therapy (40 mg, half dose) was given for 6 weeks as induction and a weekly dose for 3 weeks at 3, 6, 9 and 12 months was given as maintenance therapy. The entire procedure was done as an outdoor procedure.

Results 18 patients were included in the study from 2018 to 2021. Cystitis is the most common symptom experienced by all patients to varied extent but fortunately all are self-limiting. 2 patients had fever which subsided with paracetamol. No serious adverse effect observed in any of the 18 patients, and all were discharged on the same day of admission. After 36 months of mean follow up period, 8 patients had recurrence, 1 patient died, and 1 patient had stuck foley catheter after BCG vaccine instillation which was managed conservatively.

Conclusions BCG therapy is an effective treatment in intermediate and high-grade NMIBC and carcinoma in situ after TURBT. With half dose of BCG toxicity is low and the cost of treatment is just over 20$ per dose.

S. Acharya: None.

P03.02 DEVELOPMENT OF AN ANTITUMOR VACCINE APPROACH BASED ON THE DELIVERY OF MESSENGER RNA USING A CELL PENETRATING PEPTIDE

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Background In the last decades, therapeutic cancer vaccines have proven to induce strong immune responses with little-to-no adverse effects. Capable of eliciting exceptionally strong immune responses, RNA has emerged as an attractive vaccine platform for cancer therapy. Current mRNA vaccines are based on cationic lipid formulations which were shown to potentially induce anti-formulation immunity, impairing the use of the same nanoparticles for future vaccines. Thus, developing suitable next-generation mRNA-based nanoparticles for vaccination is a major challenge. Recently, cell penetrating peptides (CPPs) received attention as a promising alternative mRNA carrier, especially for their biocompatibility and the inherent ability of some of them to target the immune compartment. Thus, we examined multiple new CCPs as carriers for mRNA based anti-tumour vaccines.

Materials and Methods We investigated the ability of new CPPs to efficiently transfect 5-methoxyuridine-modified (5MoU) mRNA into antigen presenting cells (APCs), using murine cell lines for macrophages (RAW264.7) and dendritic cells (DC2.4). We used mRNA coding for the reporter gene GFP, alongside multiple adjuvants to evaluate transfection efficiency, cytotoxicity and APC maturation. We then used an mRNA encoding for ovalbumin (OVA) to evaluate the ability of the transfected DCs to induce the presentation of the mRNA encoded antigen and subsequently the activation of OVA-specific CD8+ T-lymphocytes (LTs).

Results Using different ratios of CPPs/mRNA, we observed a transfection efficiency reaching 50% of GFP+ cells for both the RAW264.7 and DC2.4 cell lines with a total absence of cytotoxicity using the 5MoU-modified mRNA. When a long double-stranded RNA (dsRNA) or a short 5'ppp hairpin RNA (hpRNA) was added to our formulations as an adjuvant, a 3-fold increase in the expression of maturation markers was observed on both cell lines. Next, we found that up to 50% of OVA-mRNA transfected DC2.4 cells presented the OVA antigen on MHC class I molecules. Interestingly, the addition of dsRNA and hpRNA, although inducing the maturation of the cells, made the percentage of presenting DC2.4 cells drop to 20% and 30%, respectively. When co-cultured with OVA-specific CD8+ hybridoma cell line B3Z, OVA-mRNA transfected DC2.4 were able to induce a 20-fold increase of activation independently of the presence of an adjuvant. However, when these DC2.4 were put in co-cultures with primary CD8+ LTs of OVA-specific mice OT-I, only the adjuvant-supplemented formulations were able to induce the proliferation of the LTs.

Conclusions We were able to identify CPP-based formulations capable of efficiently transfecting mRNA into APCs. The addition of an RNA-based adjuvant induced DC maturation and could represent an additional benefit as it leads towards a cellular immune response, as shown by the ability of these cells to induce the proliferation of CD8+ LTs. We now aim to test the ability of our formulations to induce immune reactions *in vivo*, specifically as therapeutic anti-cancer vaccines.

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P03.03 ABSTRACT WITHDRAWN