SYSTEMIC LEVELS OF THE SOLUBLE CO-INHIBITORY AND CO-STIMULATORY IMMUNE CHECKPOINT MOLECULES IN BASAL CELL CARCINOMA


1University of Pretoria, Pretoria, South Africa; 2The Medical Oncology Centre of Rosebank, Johannesburg, South Africa

Background
Although co-inhibitory immune checkpoint proteins are primarily involved in promoting inhibitory cell-cell interactions in adaptive immunity, especially tumor immunity, the soluble cell-free variants of these molecules are also detectable in the circulation of cancer patients where they retain immunosuppressive activity. Nevertheless, little is known about the systemic levels of these soluble co-inhibitory immune checkpoints in patients with various subtypes of basal cell carcinoma (BCC), which is the most invasive and treatment-resistant type of this most commonly occurring malignancy.

Methods
We have measured the systemic concentrations of five prominent co-inhibitory immune checkpoints, namely CTLA-4, LAG-3, PD-1/PD-L1, and TIM-3, as well as those of C-reactive protein (CRP) and vitamin D (VD), in a cohort of patients (n = 40) with BCC, relative to those of a group of control participants (n = 20), using the combination of multiplex bead array, laser nephelometry, and ELISA technologies, respectively. Additionally, in the subsequent study, we measured co-stimulatory checkpoints (CD27, CD28, CD40, ICOS, GITR, GITRL, CD8-6, and CD80), co-inhibitory checkpoints (PD-1, PD-L1, CTLA-4, TIM-3, LAG-3, BTLA-4) and dual checkpoints (TRL-2 and HVEM).

Results
The median systemic concentrations of CRP and VD were comparable between the two groups; however, those of all five immune checkpoints were significantly elevated (P = 0.0184 – P < 0.00001), with those of CTLA-4 and PD-1 being highly correlated (r = 0.87; P < 0.00001) (table 1). The levels of CD27, CD28, CD40, and other immune checkpoint levels will be presented at the time of the meeting as this study is ongoing.

Conclusions
This novel finding identifies the existence of systemic dysregulation in BCC and underscores the therapeutic promise of immune checkpoint targeted therapy, as well as the potential of these immune checkpoint molecules to serve as prognostic/predictive biomarkers in BCC.

Ethics Approval
Ethics approval was granted by The Research Ethics Committee, Faculty of Health Sciences, University of Pretoria (Ethics Committee Approval Numbers 326/2016, 251/2019 and 510/2020).

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Comparing the median levels of systemic soluble immune checkpoints in basal cell carcinoma patients with those of healthy controls