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

[1]Nonkululeko Z Malinga, [1]Bernardo Rapoport*, [1]Siwele Shalete, [1]Helen Steel, [1]Luyanda Kwofie, [1]Pieter Meyer, [1]Ronald Anderson, [1]Mahlatse Kgokolo, [2]Teresa Smit. *[1]University of Pretoria, Pretoria, South Africa; [2]The 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).

Abstract 84 Table 1 Comparing the median levels of systemic soluble immune checkpoints in basal cell carcinoma patients with those of healthy controls

Table 1: Comparing the median levels of systemic soluble immune checkpoints in basal cell carcinoma patients with those of healthy controls.

	ICM		BCC (n=40) Median pg/ml (95%CI)	Controls (n=20) Median pg/ml (95%CI)	p value
Co-stimulatory	CD27	UP	3360,665 (2363,64 - 4970,73)	1410,54 (1259,16 - 2172,74)	0,0002
	CD28	UP	17047,05 (8487,16 - 30677,1)	11314,17 (7236,45 - 14883,36)	0,2523
	CD40	UP	1308,5 (968,17 - 1779,77)	1222,255 (769,43 - 1349,26)	0,4148
	ICOS	UP	15359,79 (7591,11 - 20308,75)	12902,86 (7980,59 - 15316,53)	0,3428
	GITR	UP	1217,4 (664,31 - 1795,54)	698,205 (228,01 - 1222,24)	0,0538
	GITRL	UP	2527,32 (1470,48 - 3599,4)	2107,325 (1784,1 - 2724,34)	0,3799
	CD86	UP	2215,865 (793,93 - 3292,67)	1636,65 (781,54 - 2144,3)	0,2427
	CD80	UP	1450,26 (863,6 - 2161,26)	1212,29 (781,71 - 1590,1)	0,3428
Co-inhibitory	PD-1	UP	10978,21 (5714,49 - 14351,17)	2524,69 (1832,95 - 3038,34)	0,0000
	PD-L1	UP	1740,25 (773,982 - 1980,649)	228,67 (139,61 - 274,66)	0,0000
	PD-L2	UP	14705,27 (13102,68 - 16375,87)	12008,07 (10670,4 - 14023,9)	0,0011
	CTLA-4	UP	744,92 (422,08 - 1129,16)	126,49 (56,24 - 241,25)	0,0000
	TIM-3	UP	7519,74 (6619,886 - 8157,926)	12008,07 (10670,4 - 14023,9)	0,0000
	LAG-3	UP	388288,90 (243248,3 - 540480,6)	11106,96 (6595,67 - 15093,31)	0,0000
	BTLA	DOWN	12284,97 (8754,07 - 19151,59)	25439,74 (17274,69 - 32427,56)	0,0061
Dual	TLR-2	UP	17696,28 (10473,49 - 24211,18)	15731,88 (12262,72 - 19913,19)	0,6437
	HVEM	UP	2052,45 (1894,5 - 2317,55)	1299,11 (1263,46 - 1458,94)	0,0000
Other	Arginase		25,52 (25,52 - 29,8505)	25,52 (25,52 - 72,15)	0,2897
	RANTES	UP	131,46 (97,25 - 174,9144)	90,83 (70,78 - 148,71)	0,2097
	TGF-β1	UP	7,54 (4,549417 - 10,79543)	5,83 (4,18 - 6,83)	0,1469
	FAP	UP	115,67 (94,02 - 130,19)	109,04 (70,83 - 127,33)	0,2425

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