Presence of PD-L1(+) CTCs is significantly associated with T/N stage and lymphovascular invasion in colorectal cancer patients

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Liquid Biopsy 2 Session
4/16, 8:00:00 AM – 12:00 PM
Poster Section 26

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Background

PD-L1 biomarker assessment on tumor tissue is an important predictive marker for anti-PD-1 treatments, and is approved by the FDA as a companion diagnostic test for immuno-checkpoint antagonists. However, these tests remain challenging because of the dynamic nature and heterogeneity of PD-L1 expression, and the lack of availability of tumor tissue. Liquid biopsy tests for circulating tumor cells provide a great source of non-invasive and real-time tumor cells. Here, we isolated CTCs, analyzed their PD-L1 expression, and investigated their correlation with clinicopathological parameters in various stages of colorectal cancer patients.

Methods

- CRC patients who underwent curative surgical resection at Taipei Veterans General Hospital (VGHTPE)
- All patients provided written informed consent and followed the protocols approved by the Internal Review Board of VGHTPE
- Mesenteric vein blood (MVB) samples were collected into K_2EDTA vacationer tubes and analyzed by the MiSelect R system
- CTCs are defined as EpCAM+, Cytokeratin+ and CD45- with intact nuclei. PD-L1 was measured by an anti-PD-L1 primary antibody
- Cochran-Armitage Trend (CA test) and Chi-square tests were used for statistical analysis

Results

Clinicopathological characteristics of CRC patients

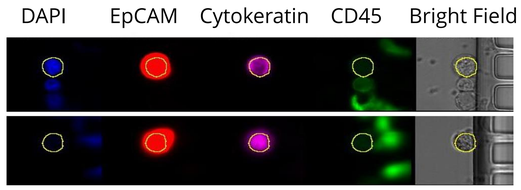
	Stage I (n=24)	Stage II (n=38)	Stage III (n=42)	Stage IV (n=12)
Age, median (range)	64 (37-79)	68 (38-92)	64 (37-84)	59 (47-90)
Gender				
Male	10	28	22	8
Female	14	10	20	4
Tumor location				
Colon	20	27	29	9
Rectum	4	11	13	3
T stage				
T1	14	0	3	0
T2	10	0	5	1
T3	0	24	21	4
T4	0	14	13	7
N stage				
N0	24	38	0	3
N1	0	0	31	3
N2	0	0	11	6
CEA (≥ 5 ng/mL)	3	17	17	10
CA 19-9 (≥ 37 ng/mL)	1	7	8	5

Conclusion

PD-L1 was heterogeneously expressed on CTCs in CRC patients. PD-L1 expression increased with disease progression, which may indicate tumors that escape from immune surveillance. Furthermore, the expression of PD-L1 on CTCs is highly correlated with blood and lymphatic vascular invasion, which may be a mechanism for local and distal metastasis. Further investigation is warranted to better understand the clinical significances of PD-L1 expression on CTCs and its potential clinical utility for cancer immunotherapy.

Isolation and analysis of CTCs from MVB

CTCs on the MiSelect R System



The presence of CTCs in MVB is positively correlated with tumor staging

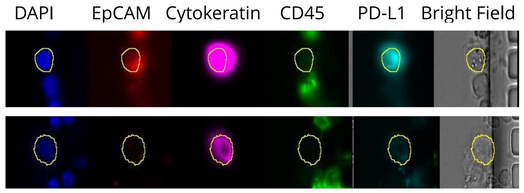
	Percentage of patients with CTCs	Range of CTC count in 8 mL
Stage I	20.8% (5/24)	0-9
Stage II	42.1% (16/38)	0-20
Stage III	45.2% (19/42)	0-515
Stage IV	58.3% (7/12)	0-20
P-value = 0.0298		

The presence of CTCs is positively correlated with T stage and CEA

Clinicopathological variables	CTCs present	CTCs absent	P value
T stage T1/T2 (n = 33) T3/T4 (n = 83)	18% 49%	82% 51%	0.003
N stage N0 (n = 65) N(+) (n = 51)	34% 49%	66% 51%	0.128
CEA ≥ 5mg/mL (n = 47) < 5mg/mL (n = 68)	51% 32%	49% 68%	0.05
CA-199 ≥ 37mg/mL (n = 21) < 37mg/mL (n = 92)	52% 38%	48% 62%	0.32
Blood Vascular Invasion (+) (n=26) (-) (n = 84)	54% 39%	46% 61%	0.68
Lymphovascular Invasion (+) (n = 30) (-) (n = 80)	50% 32%	50% 68%	0.28

Analysis of PD-L1 expression on isolated CTCs

Heterogeneous expression of PD-L1 in CTCs



The presence of PD-L1(+) CTCs is positively correlated with tumor staging

	Percentage of all patients with PD-L1(+) CTCs (N = 116)	Percentage of CTC positive patients with PD-L1(+) cells (N = 47)
Stage I	8.3% (2/24)	40.0% (2/5)
Stage II	21.1% (8/38)	50.0% (8/16)
Stage III	35.7% (15/42	78.9% (15/19)
Stage IV	50.0% (6/12)	85.7% (6/7)
	P-value = 0.0017	P-value = 0.0178

The presence of PD-L1(+) CTCs is significantly correlated with CEA and lymphovascular invasion

Clinicopathological variables	PD-L1(+) CTCs present	PD-L1(+) CTCs absent	P value
T stage T1/T2 (n = 33) T3/T4 (n = 83)	6% 48%	94% 52%	0.016
N stage N0 (n = 65) N(+) (n = 51)	12% 33%	88% 67%	0.013
CEA ≥ 5mg/mL (n = 47) < 5mg/mL (n = 68)	36% 10%	64% 90%	0.002
CA-199 ≥ 37mg/mL (n = 21) < 37mg/mL (n = 92)	33% 17%	67% 83%	0.13
Blood Vascular Invasion (+) (n=26) (-) (n = 84)	42% 17%	58% 83%	0.014
Lymphovascular Invasion (+) (n = 30) (-) (n = 80)	36% 18%	64% 82%	0.004