Using a clinicopathologic and gene expression model to identify melanoma patients at high risk for disease relapse

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Background:

- ~50% of deaths occur in patients initially diagnosed with stage I/II melanoma,[1,2] however, there is no tool to identify these high-risk patients who currently have no access to adjuvant therapy.
- This study assessed whether the recently developed CP-GEP model could identify melanoma patients at high risk for disease relapse.
- CP-GEP model combines Breslow thickness, patient age and the expression of 8 genes in primary diagnostic biopsy tissue.[3]

Methods:

- 837 consecutive melanoma patients who had a sentinel lymph node biopsy (SLNB) performed within 90 days of their diagnosis at Mayo Clinic (Table 1).
- Patients were stratified according to their risk of relapse: CP-GEP High Risk or CP-GEP Low Risk. Main clinical endpoint of this study was five-year relapse free survival (RFS).

Table 1. Patient and tumor clinicopathologic characteristics based on AJCC 8th edition.

AJCC stage (8th edition)	Unknown (n = 2)	IA (n = 186)	IB (n = 253)	IIA (n = 141)	IIB (n = 49)	IIC (n = 6)	III (n = 200)	Overall (n = 837)
Gender, n (%)								
Female	1 (50.0%)	72 (38.7%)	97 (38.3%)	46 (32.6%)	17 (34.7%)	3 (50.0%)	75 (37.5%)	311 (37.2%)
Male	1 (50.0%)	114 (61.3%)	156 (61.7%)	95 (67.4%)	32 (65.3%)	3 (50.0%)	125 (62.5%)	526 (62.8%)
Age at SLNB (years)								
Mean (SD)	57.0 (9.90)	57.5 (16.6)	60.8 (16.2)	63.1 (13.6)	63.5 (15.6)	75.7 (7.28)	53.4 (17.0)	58.9 (16.4)
Median	57.0	60.0	63.0	64.0	66.0	76.0	55.0	60.0
[Min, Max]	[50.0, 64.0]	[17.0, 85.0]	[16.0, 89.0]	[21.0, 88.0]	[20.0, 87.0]	[64.0, 85.0]	[15.0, 86.0]	[15.0, 89.0]
Ulceration, n (%)								
Yes	0 (0%)	14 (7.5%)	0 (0%)	55 (39.0%)	45 (91.8%)	6 (100%)	72 (36.0%)	192 (22.9%)
No	0 (0%)	170 (91.4%)	253 (100%)	86 (61.0%)	4 (8.2%)	0 (0%)	126 (63.0%)	639 (76.3%)
ND	2 (100%)	2 (1.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.0%)	6 (0.7%)
Mitotic rate, n (%)								
Absent	0 (0%)	27 (14.5%)	54 (21.3%)	11 (7.8%)	1 (2.0%)	0 (0%)	7 (3.5%)	100 (11.9%)
1 – 6	1 (50.0%)	155 (83.3%)	168 (66.4%)	89 (63.1%)	20 (40.8%)	2 (33.3%)	136 (68.0%)	571 (68.2%)
> 6	1 (50.0%)	4 (2.2%)	28 (11.1%)	41 (29.1%)	28 (57.1%)	4 (66.7%)	54 (27.0%)	160 (19.1%)
ND	0 (0%)	0 (0%)	3 (1.2%)	0 (0%)	0 (0%)	0 (0%)	3 (1.5%)	6 (0.7%)
SLNB status, n (%)								
Negative	2 (100%)	186 (100%)	253 (100%)	141 (100%)	49 (100%)	6 (100%)	0 (0%)	637 (76.1%)
Positive	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	200 (100%)	200 (23.9%)

Results:

- Stratification based on SLNB status and CP-GEP classification demonstrated the discriminative effect of both (Figure 1 and Figure 2).
- 51% of SLNB negative patients were classified as CP-GEP High Risk. The prognosis of these CP-GEP High Risk patients is similar to stage IIC/IIIA melanoma patients with a reported RFS ranging from 63% to 77%.[4,5] This confirms heterogeneity in prognosis among patients with stage I/II melanoma (Figure 3).

Main conclusions

The **CP-GEP** model can be successfully used to stratify patients based on their **risk of disease relapse.**

SLNB negative patients with CP-GEP High Risk results **may benefit from therapeutic interventions**.

Future directions for research

Independent **validation studies are ongoing** to validate the CP-GEP model in various patient populations.

References

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Figure 1. Kaplan-Meier analysis of the entire 837 cohort, stratification by SLNB status.

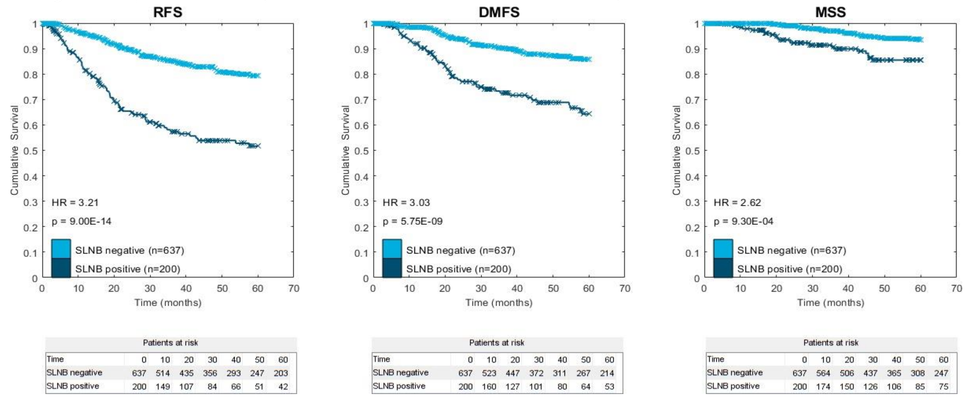

Figure 2. Kaplan-Meier analysis of the entire 837 cohort, stratification by CP-GEP classification.

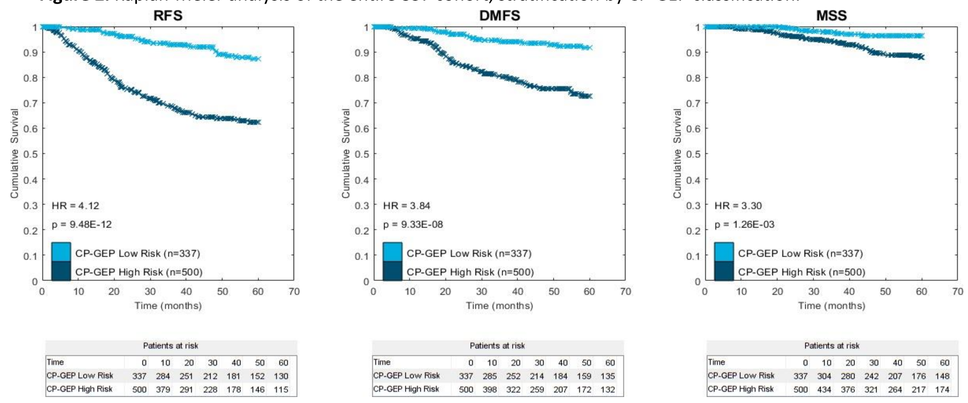

Figure 3. Kaplan-Meier analysis of the 637 SLNB negative patients, stratification by CP-GEP classification.