Supporting Information

Appendix S1. Protocol for P-STAT5 Immunohistochemistry

Antibody: Abcam ab32364, purified rabbit anti-p-STAT5 (clone: E208) 220ug/ml

Species reactivity: Human, mouse and rat

Positive control tissue: skin - normal or carcinoma, placental trophoblasts, breast carcinoma

Positive control block: Multi tissue TMA, placenta or breast carcinoma x2128

Staining pattern: Nuclear

- Sections (3-µm) were affixed to Menzel Superfrost Plus adhesive slides and air-dried overnight at 37^{O}C.
- Sections were dewaxed and rehydrated through descending graded alcohols to phosphate-buffered saline (PBS), pH 7.4, using standard protocol.
- Sections were transferred to EDTA pH 9.0, and subjected to 20 minutes heat antigen retrieval at 95^{O}C using the Biocare Medical decloaking chamber. Following completion of the cool down cycle, sections were removed and allow to cool for a further 20 minutes before transferring back to TBS.
- Sections were washed in 3 cycles of TBS.
- Endogenous peroxidase activity was blocked by incubating the sections in 3.0% H_2O_2 in TBS for 10 minutes.
- Sections were washed in 3 cycles of TBS for 5 minutes each.
- Biocare Medical Background Sniper was applied for 30 minutes.
- Excess Sniper was removed and 10% normal goat serum was applied for 30 minutes.
- Excess normal serum was decanted from the sections.
- The primary antibody was diluted 1:150 in Biocare Medical Da Vinci Green, applied overnight at room temperature.
- Sections were washed in three changes of TBS for 5 minutes each, with the first buffer change containing 0.5% (v/v) Triton X-100.
- Biocare Medical MACH2 anti-rabbit HRP was applied for 60 minutes at RT.

- Sections were washed in three changes of TBS for 5 minutes each.
- Control slide signals were developed in vector NovaRed for 5 minutes.
- Sections were washed in gently running tap water for 5-10 minutes to remove excess chromogen.
- Sections were lightly counterstained in Mayers' haematoxylin (program 6), then dehydrated through ascending graded alcohols, cleared in xylene, and mounted using DePeX or similar.

Supplementary Table 1: Multivariate subdistribution hazard regression model for selected clinicopathologic factors, SLN status, and pSTAT5 detection on melanoma-specific death and death due to other causes in a cohort of 189 patients with primary cutaneous melanoma

	Melanoma-specific death (n = 32)		**Death due to other causes (n = 19)**	
Factor	**Sub-HR (95% CI)**	***p***	**Sub-HR (95% CI)**	***p***
High pSTAT5 (≥31)	0.19 (0.04 - 0.89)	0.036	1.11 (0.33 - 3.77)	0.870
SLN status	3.46 (1.30 - 9.22)	0.013	0.76 (0.22 - 2.58)	0.656
Sex (female)	0.57 (0.26 - 1.27)	0.169	1.16 (0.48 - 2.80)	0.734
Age (per year)	0.99 (0.96 - 1.02)	0.509	1.09 (1.03 - 1.14)	0.001
Breslow thickness (per mm)	1.18 (1.00 - 1.40)	0.047	0.99 (0.81 - 1.22)	0.937
Head or neck location	2.06 (0.78 - 5.41)	0.143	0.67 (0.10 - 4.66)	0.689
Ulceration	1.29 (0.46 - 3.63)	0.632	1.73 (0.71 - 4.20)	0.224

Analysis conducted using subdistribution hazard regression modelling. Multivariate adjustment performed including each of the listed variables.

Abbreviations: pSTAT5, phosphorylated signal transducer and activator of transcription 5; SLN, sentinel lymph node; Sub-HR, subdistribution hazard ratio; CI, confidence interval

Supplementary Table 2: Association between pSTAT5 detection in selected cellular compartments with melanoma-specific survival in primary cutaneous melanoma, including adjustment for SLN status

	Unadjusted		Adjusted[a]	
Factor	**HR (95% CI)**	***p***	**HR (95% CI)**	***p***
pSTAT5 detection				
High melanocytic pSTAT5 (≥84%)	0.65 (0.15 - 2.71)	0.551	0.35 (0.08 – 1.61)	0.178
High lymphocytic pSTAT5 (≥54%)	0.37 (0.05 - 2.72)	0.328	0.26 (0.03 – 2.29)	0.224
High vascular pSTAT5 (≥73%)	0.32 (0.04 - 2.31)	0.256	0.18 (0.02 – 1.50)	0.112
SLN status	4.47 (2.21 - 9.01)	<0.001		
Sex (female)	0.61 (0.29 - 1.27)	0.185		
Age (per year)	1.00 (0.97 - 1.03)	0.962		
Breslow thickness (per mm)	1.15 (1.03 - 1.29)	0.016		
Head or neck location	2.45 (0.94 - 6.38)	0.067		
Ulceration	1.76 (0.85 - 3.62)	0.127		

Analysis conducted using Cox proportional hazards regression modelling. [a]Multivariate adjustment performed for each pSTAT5 subset with adjustment for all remaining variables.

Abbreviations: pSTAT5, phosphorylated signal transducer and activator of transcription 5; SLN, sentinel lymph node; HR, hazard ratio; CI, confidence interval

Supplementary Table 3: Association between pSTAT5 detection in selected cellular compartments with melanoma-specific survival in primary cutaneous melanoma, excluding adjustment for SLN status

	Unadjusted		Adjusted[a]	
Factor	**HR (95% CI)**	***p***	**HR (95% CI)**	***p***
pSTAT5 detection				
High melanocytic pSTAT5 (≥84%)	0.65 (0.15 - 2.71)	0.551	0.40 (0.09 - 1.81)	0.237
High lymphocytic pSTAT5 (≥54%)	0.37 (0.05 - 2.72)	0.328	0.14 (0.02 - 1.21)	0.075
High vascular pSTAT5 (≥73%)	0.32 (0.04 - 2.31)	0.256	0.13 (0.02 - 1.18)	0.070
Sex (female)	0.61 (0.29 - 1.27)	0.185		
Age (per year)	1.00 (0.97 - 1.03)	0.962		
Breslow thickness (per mm)	1.15 (1.03 - 1.29)	0.016		
Head or neck location	2.45 (0.94 - 6.38)	0.067		
Ulceration	1.76 (0.85 - 3.62)	0.127		

Analysis conducted using Cox proportional hazards regression modelling. [a]Multivariate adjustment performed for each pSTAT5 subset with adjustment for all remaining variables.

Abbreviations: pSTAT5, phosphorylated signal transducer and activator of transcription 5; HR, hazard ratio; CI, confidence interval