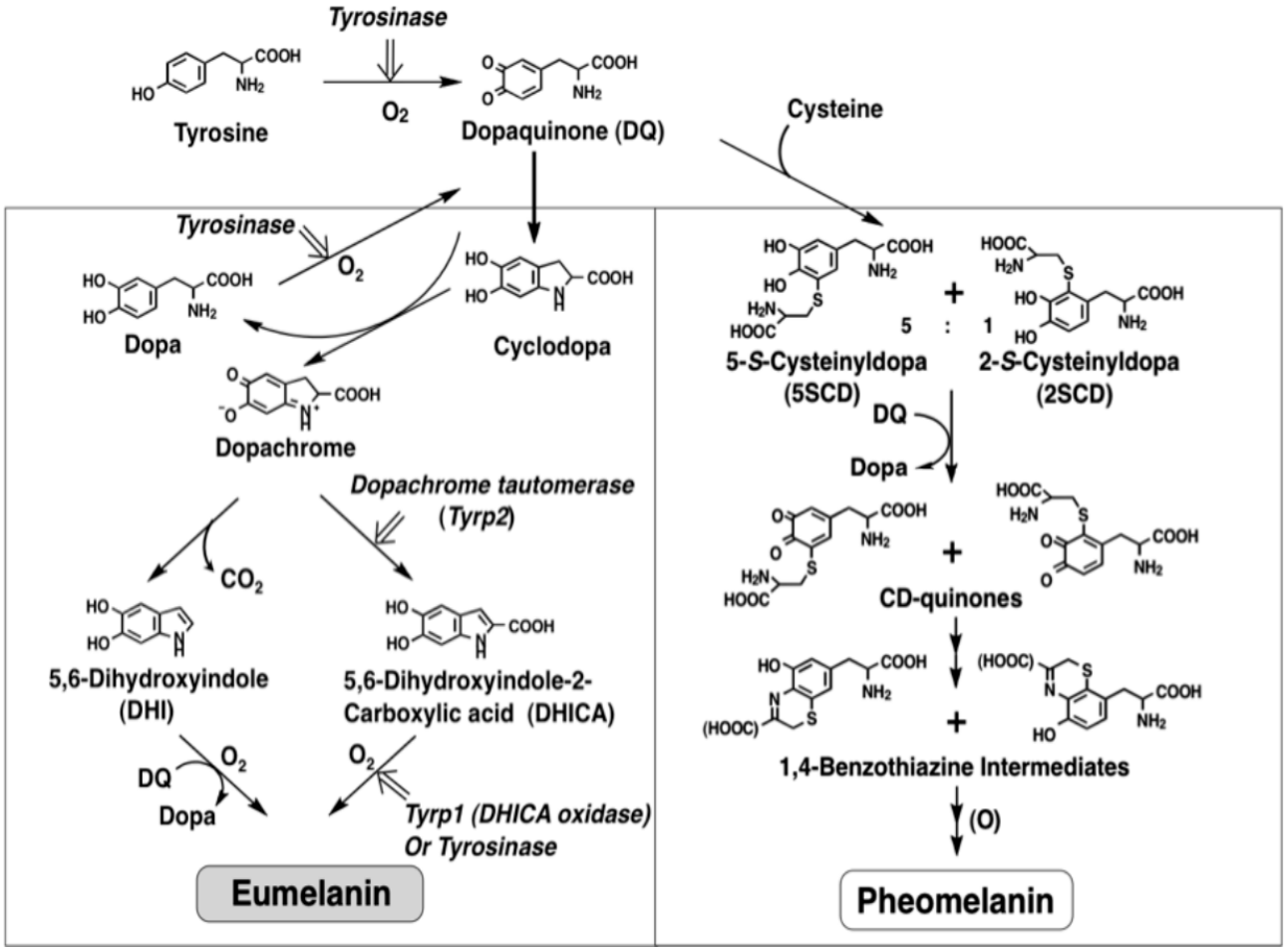

Supplemental Figure S1. Biosynthesis pathway of eumelanin and pheomelanin.

Supplemental Table S1. Serum and urinary biomarkers for melanoma.

Biomarker	Functions	References
VEGF (Vascular endothelial growth factor)	VEGF receptor ligand	12
FGF	FGF receptor ligand	13
EGF	EGF receptor ligand	14
Placental growth factor	Neuropilin-1 and -2 receptor ligand	15
TNF	G-protein-coupled receptor ligand	16
IL-8	G-protein-coupled receptor ligand	17
Laminin-5	Laminin receptor	18
Osteopontin	Integrin avb3 ligand	19
Tyrosinase	Essential enzyme in melanin synthesis	20
Gp100/pmel-17	Melanin synthesis-associated melanosomal matrix glycoprotein	21
S100 proteins (S100B)	Cell division and differentiation-associated acidic calcium-binding protein	22
Serum amyloid A (SAA)	A superfamily of acute-phase proteins and proinflammatory adipokine	23
C reactive protein (CRP)	Tumor-associated inflammatory response	24
MIA	A small soluble protein	25
L-dopa/L-tyrosine	Precursors of melanin	26
TA-90	Potential immunostimulatory or antineoplastic activator	27
Survivin	Apoptosis inhibition	28
Cytoplasmic/high-molecular-weight melanoma-associated antigen (CYT-MAA/HMW-MAA)	Melanoma progression	29
Galectin-3	B-galactoside-binding protein	30
Gangliosides	Interactions between melanoma cells	31
Circulating-tumor DNA (ctDNA)	DNA methylation pattern	32
Micro-RNAs (miR)	Regulation of gene expression	33
Long non-coding RNAs	Regulation of gene expression	34
IL-1	Survival or proliferation-associated factor	35
IL-4	Survival or proliferation-associated factor	36
IL-6	Survival or proliferation-associated factor	37
IL-10	Survival or proliferation-associated factor	38
IL-12	Survival or proliferation-associated factor	39
YKL-40	Survival or proliferation-associated factor	40
Circulating melanoma cells (CMC)	Cancer cells released by tumor	41
Lactate dehydrogenase (LDH)	An indicator for liver metastasis	42
Glypican-3	Survival or proliferation-associated factor	43
SPARC (Secreted protein acidic and rich in cysteine)	Matricellular protein	44
PKCa	Survival or proliferation-associated factor	45
5SCD	Precursor of melanin	46
6H5MI2C	Precursor of melanin	47

Supplemental Table S2. Patient characteristics

Total number of patients	218	
Sex		
Male	112	(51.4%)
Female	106	(48.6%)
Age[a]		
Mean ± SD	54.8 ± 15.3 years	
Range	12-88 years	
Diagnosis		
Acral lentiginous melanoma	101	(46.3%)
Nodular melanoma	45	(20.6%)
Superficial spreading melanoma	43	(19.7%)
Lentigo maligna melanoma	11	(5.0%)
Mucosal melanoma	6	(2.8%)
Uveal melanoma	3	(1.4%)
Unknown	9	(4.1%)
Site		
Head and neck	19	(8.7%)
Trunk	28	(12.8%)
Leg	30	(13.8%)
Arm	19	(8.7%)
Foot	103	(47.2%)
Hand	6	(2.8%)
Mucous	6	(2.8%)
Ocular	3	(1.4%)
Unknown	4	(1.8%)
Stage		
I	25	(11.5%)
II	63	(28.9%)
III	112	(51.4%)
IV	18	(8.3%)
Pigment production[b]		
Melanotic	158	(72.5%)
Amelanotic	12	(5.5%)
Unknown	48	(22.0%)

[a]At the initial visit.
[b]In primary lesion.

Adapted from Wakamatsu et al. (46)

Supplemental Table S3. Frequency of elevated levels of serum 5SCD according to the presence or

absence of metastasis.

	No.	%
With distant metastasis (n = 62)		
5SCD all ≦ 10 nmol/L	4	6
5SCD once > 10 nmol/L	1	2
5SCD multiple > 10 nmol/L	57	92
With recurrence/local metastasis (n = 13)		
5SCD all ≦ 10 nmol/L	8	62
5SCD once > 10 nmol/L	4	31
5SCD multiple > 10 nmol/L	1	7
Without recurrence/metastasis (n = 143)		
5SCD all ≦ 10 nmol/L	95	66
5SCD once > 10 nmol/L	32	22
5SCD multiple > 10 nmol/L	16	11

Adapted from Wakamatsu et al. (46)