

SUPPLEMENTARY MATERIAL

Petanin Potentiated JNK Phosphorylation to Negatively Regulate the ERK/CREB/MITF Signaling Pathway for Anti-Melanogenesis in Zebrafish

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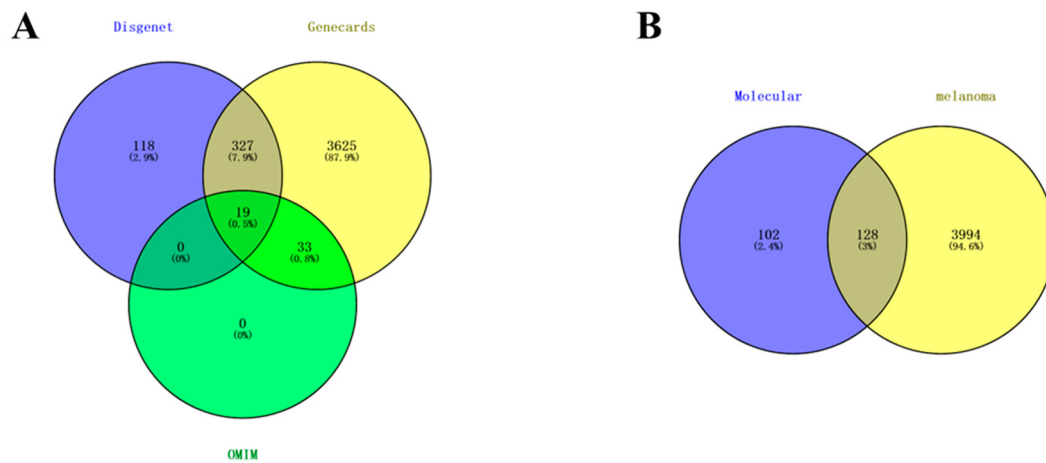


Figure S1. Venn diagram of intersection of targets related to melanin and compounds((**A**) Screening of OMIM targets, (**B**) Intersection of compound targets and melanin targets)

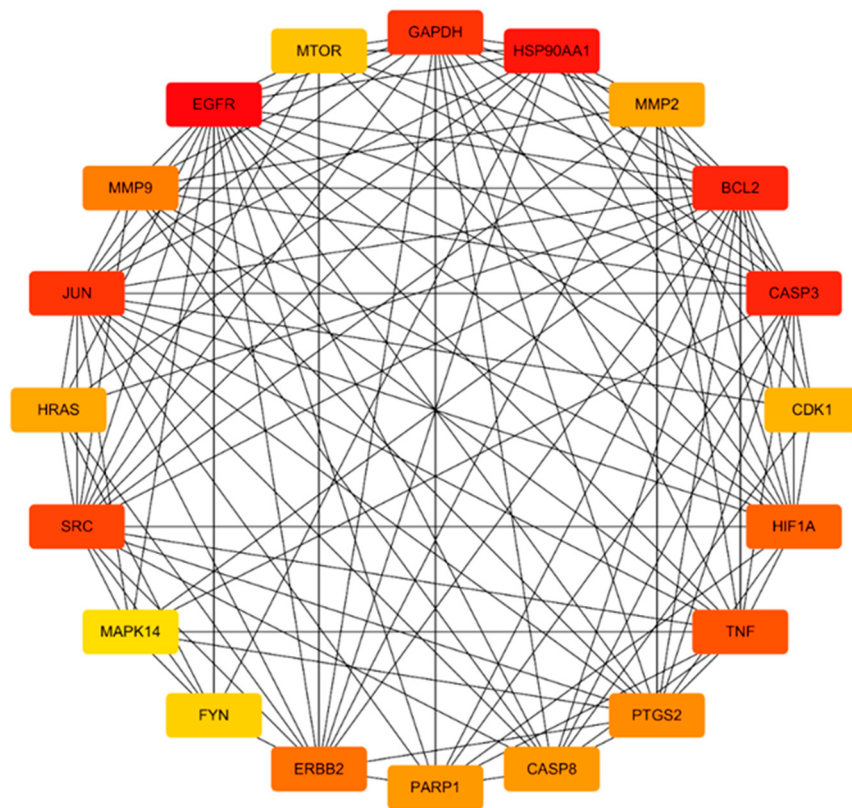


Figure S2. Top 20 of Melanogenesis related targets intersect with targets of compounds

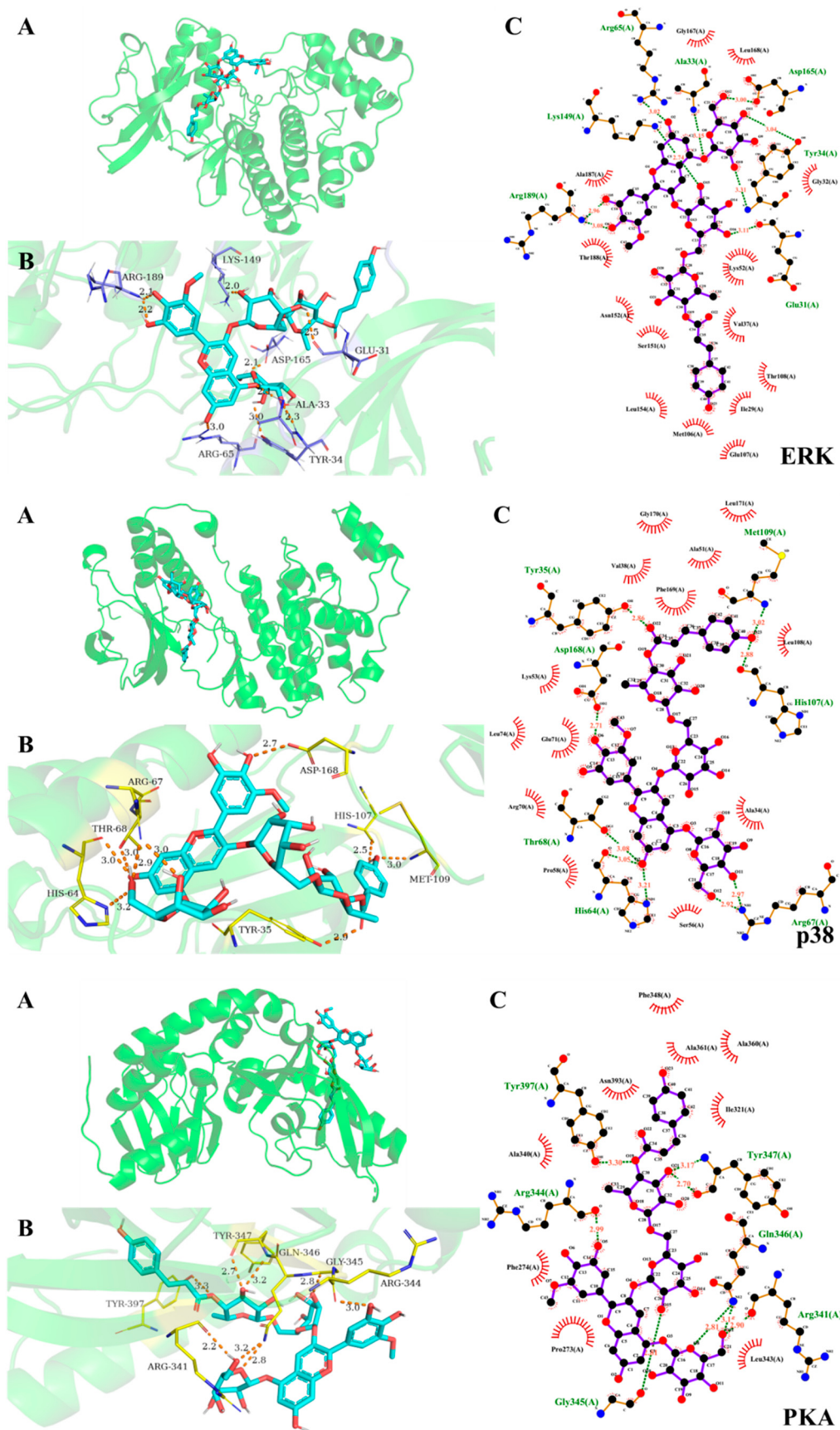


Figure S3. Molecular docking of petanin with ERK, p38 and PKA ((A) 3D structure), (B) 3D diagram of hydrogen bonds), (C) 2D diagram of hydrogen bonds).

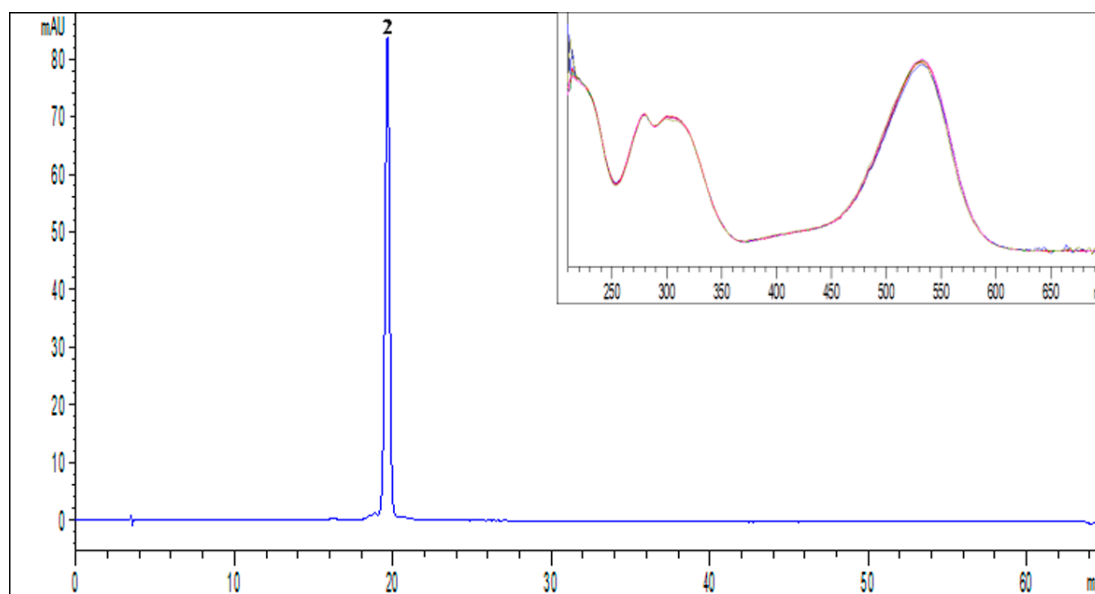


Figure S4. HPLC and spectrogram of petanin (purity $\geq 99.43\%$)

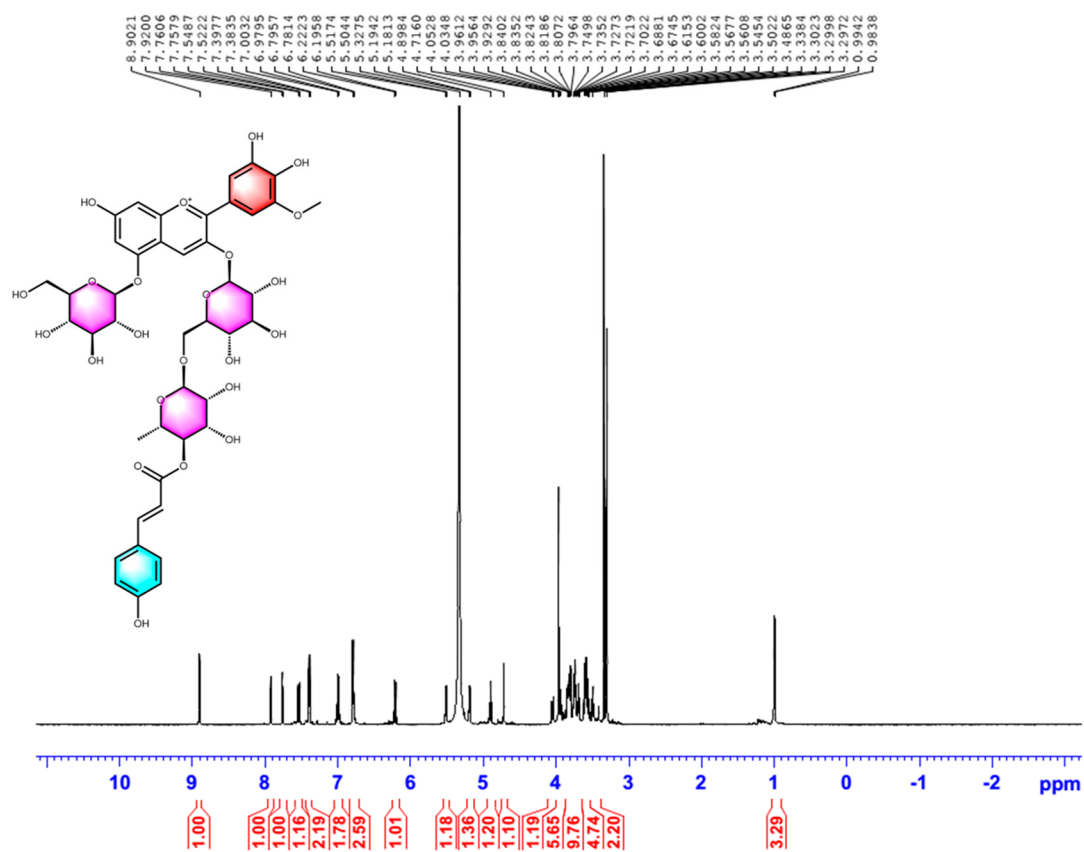


Figure S5. ^1H NMR and structure of petanin

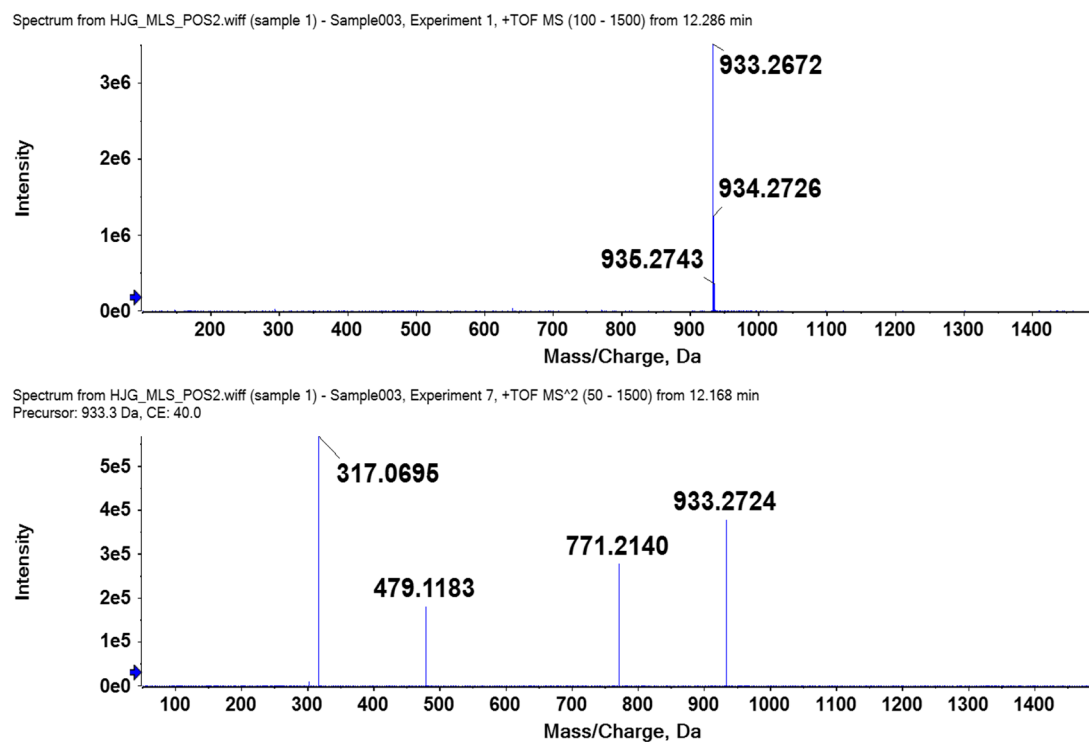


Figure S6. Mass spectrum of petanin from liquid chromatography-mass spectrometry

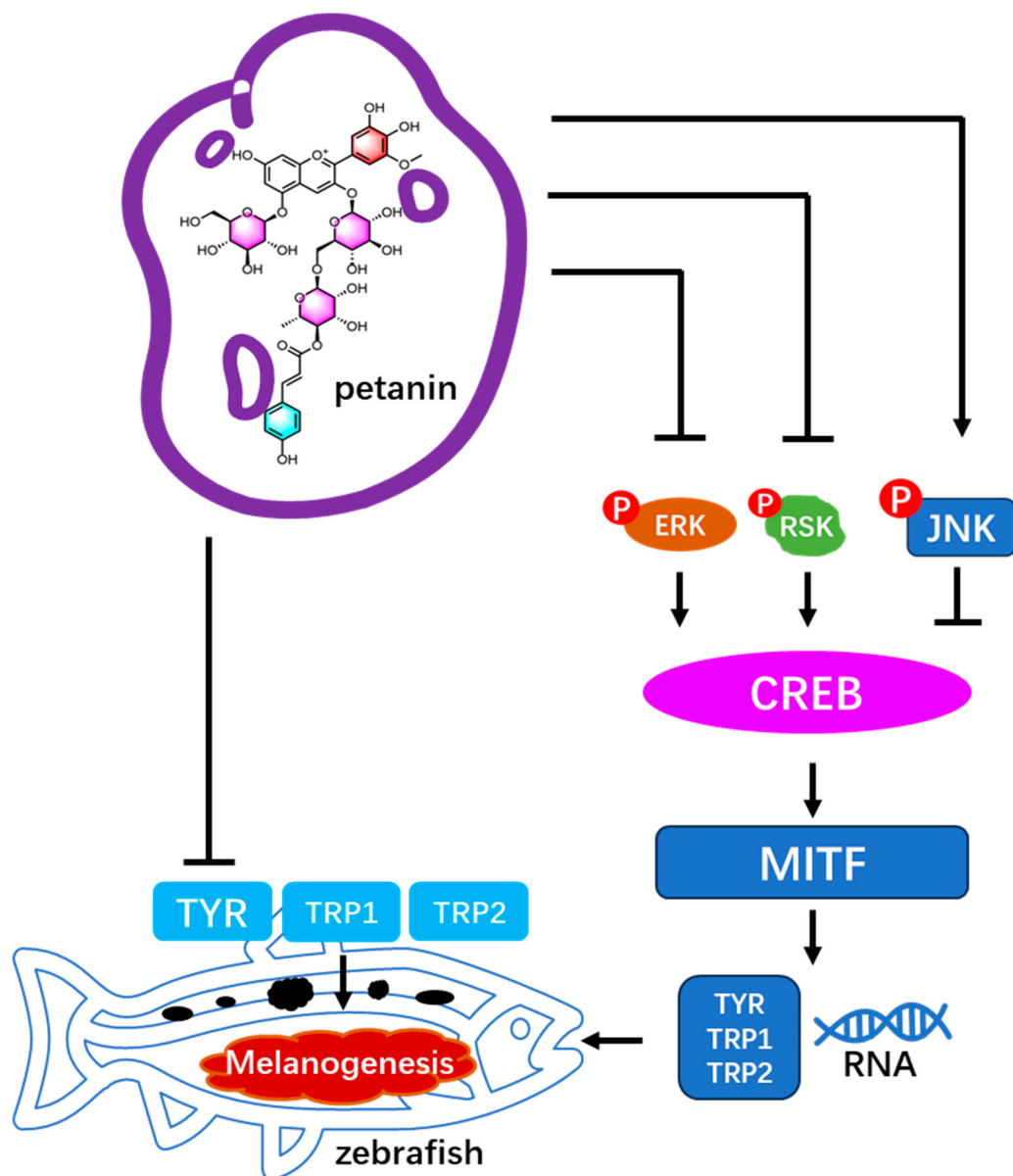


Figure S7. Effect of petanin on ERK/CREB/MITF signaling pathway

Table S1. Molecules docking of Petanin binding energy and hydrogen bonds with key signaling pathway protein

Compound	Protein	PDB ID	Amino acid	Distance (Å)	Affinity (kcal/mol)
Petanin	ERK	5KE0	ARG189	2.1/2.2	-9.8
			LYS149	2.0	
			GLU31	2.5	
			ALA33	2.1	
			TYR34	2.3/3.0	
			ARG65	3.0	
			ASP165	2.1	
	p38	3ZS5	ASP168	2.7	-9.4
			HIS107	2.5	
			MET109	3.0	
			TYR35	2.9	
			HIS64	3.2/3.0	
			THR68	3.0	
			ARG67	2.9/3.0	
	PKA	1CX4	TYR347	2.7/3.2	-8.4
			GLN346	3.2/2.8	
			GLY345	2.8	
			ARG344	3.0	
			ARG341	2.2	
			TYR397	3.3	
	JNK	3PZE	SER179	3.0	-10
			ARRG69	2.8/3.3	
			GLN37	3.2	
			GLY38	2.8	
			SER34	2.8/2.0/3.0/3/5	
			ILE32	2.0/3.0/2.8	
			MET111	2.8	

Table S2. Primers for mRNA associated with melanogenesis in zebrafish

Gene name	Primer
<i>gadph</i>	F: ACAGCAACACAGAAGACCGT R: ATACCAGCACCAGCGTCAAA
<i>α-MSH (pomca)</i>	F: GCCCCTGAACAGATAGAGCC R: CTTGATGGGTCTGCGTTTGC
<i>mclr</i>	F: TCATCTTGGTGGTGTGGCTTGC R: AAGAACGGTCCCCAGCAGAGG
<i>creb</i>	F: GCCATGTTCACTTACCATTGAG R: TTGTAAGAGGCATGTGAGATGG
<i>mitf</i>	F: TGTACAGCAATCATGCTCTTCC R: GTCCCCAGCTCCTTAATTCTGTC
<i>trp1α</i>	F: CTCATCATCGTCGCCATC R: GAACCTCCTGAAGAACACA
<i>trp2</i>	F: TGGACAGTAAACCCTGGGGA R: CCGGCAAAGTTTCCAAAGCA
<i>tyr</i>	F: GATCCAGGTCAGCGGTTTGT R: ACCGATGCGATTATTCCTGCT
<i>MAPK1 (ERK-2)</i>	F: TCCACTCCGCAAACGTTCTT R: CATACTCCGTCAGGAAGCCG
<i>rsk</i>	F: CAGCATACTCCAGTCCCACC R: TACCGCAGCAGGATCTCAAC
<i>p38α</i>	F: TGGACATTTGGTCAGTGGGC R: CTGATGTAAGTACGAGCCTCATGG
<i>MAPK8 (JNK1)</i>	F: TCGCTAGTTGGCATCGTTTATG R: CGGAGGTTCTGAAGACGATCA