

Figure S1. The scheme of animal experiment design.

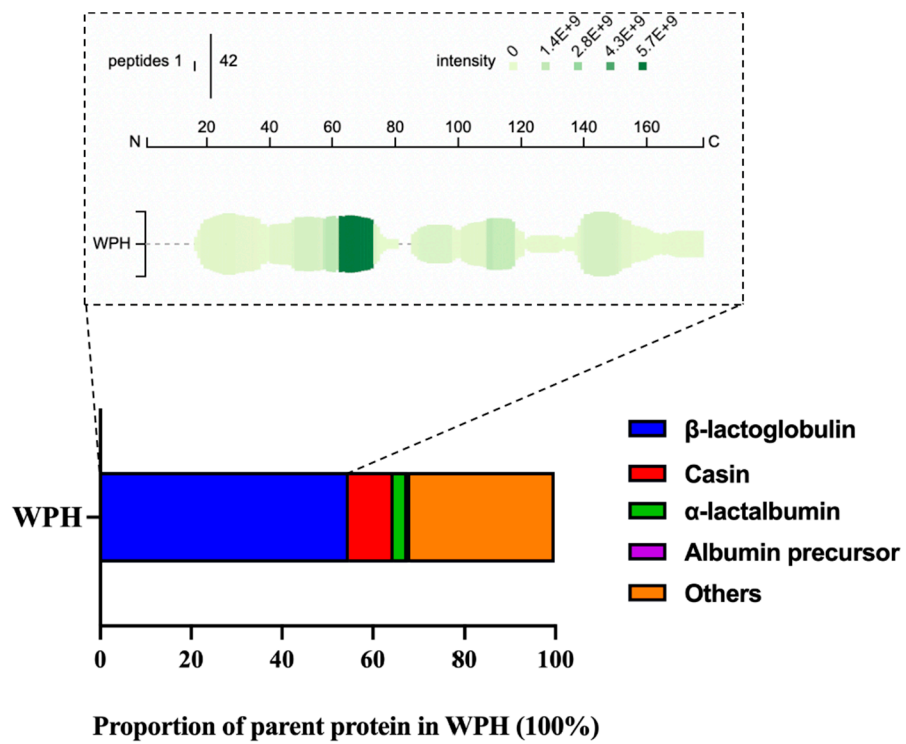
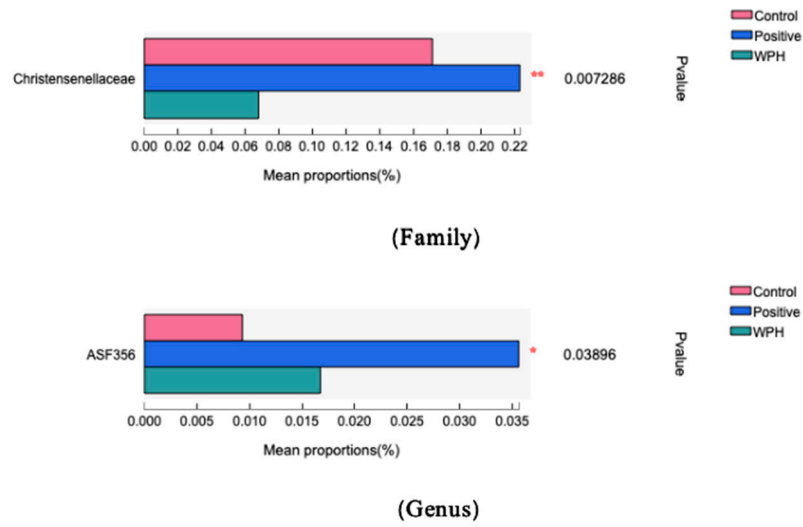


Figure S2. The proportion of parent protein for WPH and the peptide profile of β -Lactoglobulin in WPH.

A



B

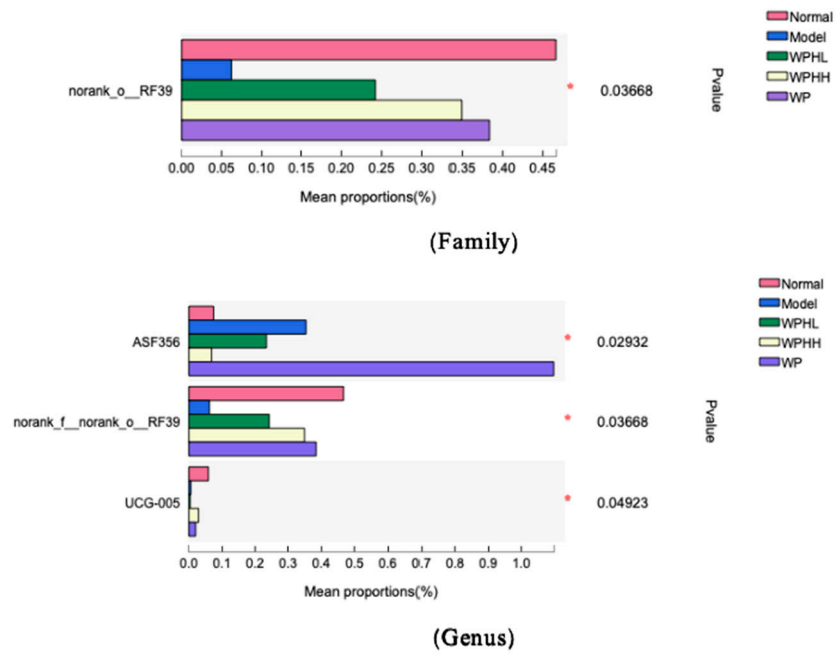


Figure S3. Relative abundances of genera that showed significant differences among groups at different taxonomic levels were obtained by one-way ANOVA. A represents scopolamine-induced ICR mice; B represents old-aged C57BL/6J mice. * and ** mean $p < 0.05$ and $p < 0.01$ compared to the model group.

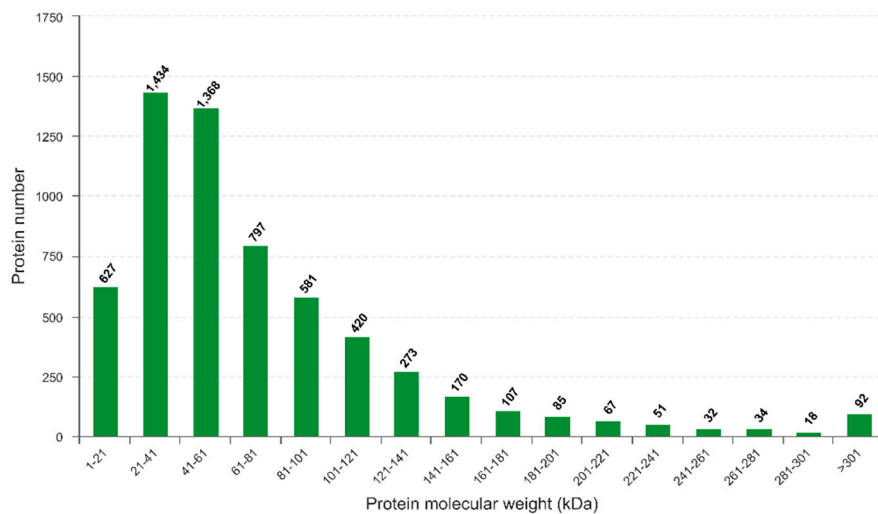
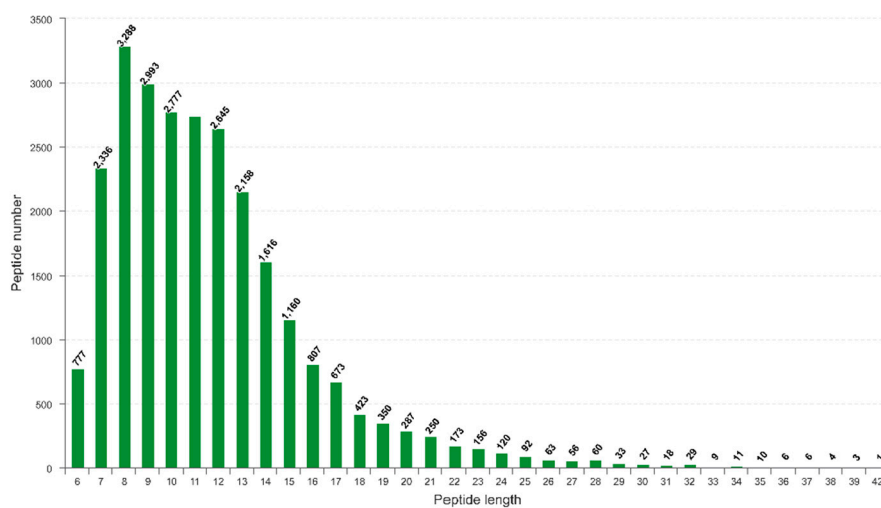
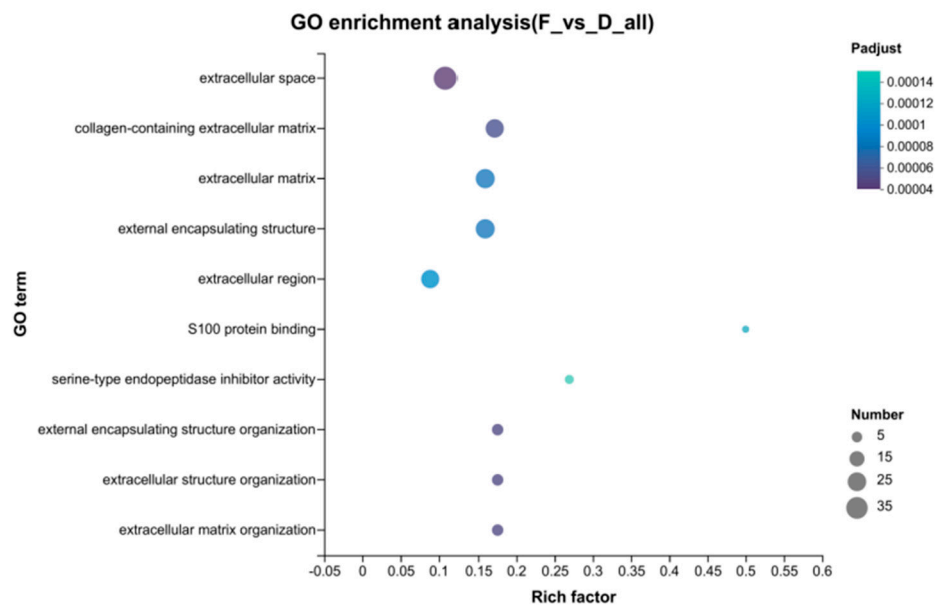
A**B**

Figure S4. Protein molecular weight distribution (A) and peptide length distribution (B) in identified protein.

A



B

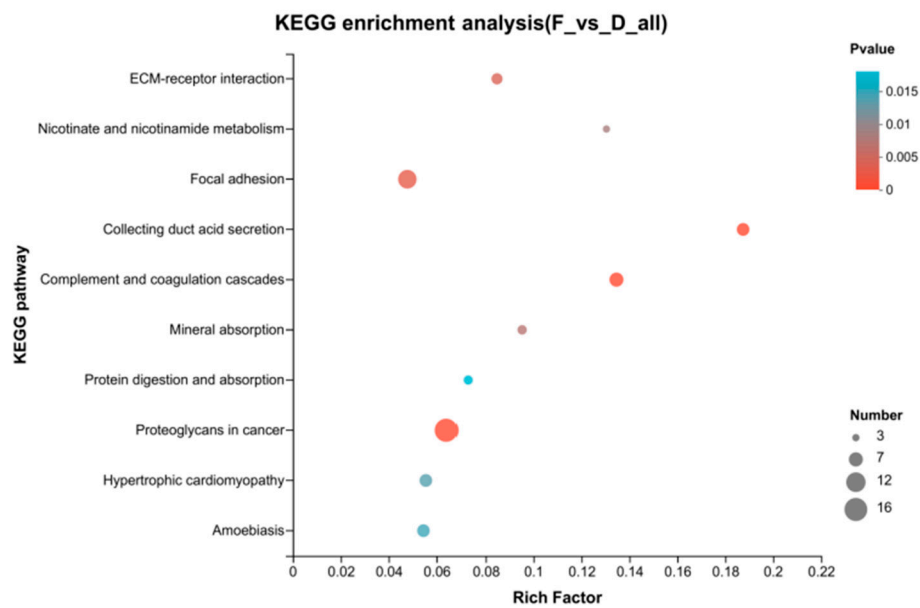


Figure S5. Bubble chart of differentially expressed proteins in GO enrichment analysis (A) and KEGG enrichment analysis (B).

Table S1. The mobile phase gradient of LC-MS/MS analysis

Time	Flow Rate (μL/min)	Solvent A (%)	Solvent B (%)
0	180	95	5
5	180	95	5
45	180	65	35
50	180	0	100
54	180	0	100
55	180	95	5
70	180	95	5

Table S2. The Gene Ontology (GO) enrichment information of WPH group and model group

GO ID	GO Term	Category	<i>p</i> -Value	Count
GO:0005615	extracellular space	CC	0.000040535	35
GO:0045229	external encapsulating structure organization	BP	0.000049409	10
GO:0043062	extracellular structure organization	BP	0.000049409	10
GO:0030198	extracellular matrix organization	BP	0.000049409	10
GO:0062023	collagen-containing extracellular matrix	CC	0.000055591	23
GO:0031012	extracellular matrix	CC	0.000083263	25
GO:0030312	external encapsulating structure	CC	0.000083263	25
GO:0005576	extracellular region	CC	0.000099324	23
GO:0044548	S100 protein binding	MF	0.000122701	5
GO:0004867	serine-type endopeptidase inhibitor activity	MF	0.000145004	7
GO:0005201	extracellular matrix structural constituent	MF	0.000153598	5
GO:0050840	extracellular matrix binding	MF	0.000165506	6
GO:0004866	endopeptidase inhibitor activity	MF	0.000225268	8
GO:0030414	peptidase inhibitor activity	MF	0.000240522	8
GO:0061135	endopeptidase regulator activity	MF	0.00035769	8
GO:0002020	protease binding	MF	0.00035769	8
GO:0005604	basement membrane	CC	0.000370521	7
GO:0061134	peptidase regulator activity	MF	0.000817873	8
GO:0031214	biomineral tissue development	BP	0.000893933	5
GO:0110148	biomineralization	BP	0.000893933	5

Table S3. The KEGG pathway of differentially expressed proteins (DEPs)

KEGG Description	Pathway ID	DEPs Number	<i>p</i> -Value
Proteoglycans in cancer	mmu05205	16	0.000008589
Collecting duct acid secretion	mmu04966	6	0.000018824
Complement and coagulation cascades	mmu04610	7	0.000035606
Focal adhesion	mmu04510	11	0.00277315
ECM-receptor interaction	mmu04512	5	0.004074328
Mineral absorption	mmu04978	4	0.006696747
Nicotinate and nicotinamide metabolism	mmu00760	3	0.007851817
Hypertrophic cardiomyopathy	mmu05410	6	0.01315984
Amoebiasis	mmu05146	6	0.014311603
Protein digestion and absorption	mmu04974	4	0.017071603