Proteomic Analysis of the Serum of Patients with Stable Vitiligo and Progressive Vitiligo

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To the Editor: Vitiligo is not a fatal disease; however, it can have strong social and psychological impacts on the patients. Genetic susceptibility, autoimmunity, neural dysregulation, melanin self-destruction, and oxidative stress may be involved in the pathogenesis of vitiligo. Based on its clinical development, vitiligo can be divided into the progressive vitiligo (PV) or the stable vitiligo (SV). To date, at least 50 susceptible genes had been found in vitiligo.[1] However, only a few genes presented a clear association with the high inherent risk of vitiligo and the protein levels of these genes were scarce. Recently, combination methods had been introduced in order to obtain better results. Nevertheless, no validated tool could confirm on the stage of vitiligo. Proteomics is a useful tool for large-scale screening of disease-related proteins. It could provide a better understanding of the biological and molecular events for this disease. Isobaric tag for relative and absolute quantitation (iTRAQ) is a systematic protein quantitative analytical method. It has the highest flux, the smallest system error, and the most powerful function for diagnosis, treatment, and prognosis. In this study, we identified differentially expressed proteins using iTRAQ-based proteomic technology and constructed an interaction network for SV and PV with the aim to identify potential group proteins as markers to distinguish between SV and PV.

All the patients and healthy controls were enrolled at the Dermatological Outpatient Clinic of the First Hospital of China Medical University from 2015 to 2016. Vitiligo was diagnosed clinically by experienced dermatologists. Staging of the disease was performed according to the Vitiligo Disease Activity Score (VIDA) in the *Consensus of Vitiligo Diagnosis and Treatment* (2014 edition) issued by the Dermatology Committee of Pigmentary Disease of the Chinese Association of Integrative Medicine. Patients with PV (VIDA score over 2 points) showed emergence of new skin lesions expansion of the original skin lesions or occurrence of the Koebner phenomenon within three months. Patients with SV were defined as those with stable lesions for at least one year. The sites and progression of the lesions and the extent of cutaneous involvement were documented.

Clinical information of the patients with PV and SV are presented in Supplementary Tables 1 and 2. Ten serum samples from each group were pooled together for proteomic experiments. The remaining 20 serum samples were used in Western blotting experiments for verification of results.

Pooled serum samples from each group were prepared before proteomic analysis. The ProteoPrep Blue Albumin and IgG Depletion kit (Sigma-Aldrich, Co., St. Louis, MO, USA) were used to remove albumin, and IgG protein concentration was estimated using the BCA Protein Assay Kit (Thermo Scientific, Rockford, California, USA). Total proteins of each group were analyzed by iTRAQ (AB Sciex, Framingham, Massachusetts, USA), liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS). Protein samples (100 μg) were reduced, alkylated, and subjected to tryptic hydrolysis. iTRAQ labeling was performed using iTRAQ Reagents manufacturer's protocol. Each sample was labeled with the respective iTRAQ tags. All the labeled peptides were merged and evaporated to dryness in a vacuum centrifuge.

The iTRAQ labelled samples were firstly diluted to 100 μl with H2O buffer (NH_3•H_2O, pH=10) before high performance liquid chromatography on a Dionex Ultimate 3000 system (Dionex, Sunnyvale, CA, USA) at 25˚C on a Gemini NX 3u C18 110A; 150.0 mm × 2.0 mm Phenomenex column, and Gemini 3u C6 Phenyl 110A; 100.0 mm × 2.0 mm column (all from Phenomenex, Torrance, CA, USA). The flow rate used for reversed-phase column separation was 0.2 ml/min with H_2O (mobile Phase A) and 80% ACN (mobile Phase B). A solvent gradient system was used: 0–15 min, 5–10% B; 15–48 min, 15–25% B; 48–60 min, 25–37% B; 60–65 min, 37–95% B; and 65–70 min, 95% B. The elution was monitored by absorbance at 214/280 nm, and fractions were collected every 50 s. In total, 10 fractions were combined and dried.

Peptides were separated by a linear gradient according to the manufacture's instruction. MS analysis was performed on a Q

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Exactive system (Thermo Fisher Scientific, California, USA) in information-dependent mode. MS spectra were acquired across the mass range of 350–1800 m/z in high-resolution mode (>35,000); a maximum of 20 precursors per cycle were chosen for fragmentation from each MS spectrum with a 120-ms minimum accumulation time for each precursor and dynamic exclusion for 10s. The tandem mass spectra were recorded in high-sensitivity mode (resolution >175,000) with rolling collision energy and iTRAQ reagent collision energy adjustments.

Proteins extracted from the serum samples of 20 patients with SV, 20 patients with PV, and 20 healthy controls were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (11–15% acrylamide). After transferring the blots onto PVDF membranes and blocking overnight (5% skim milk and 0.05% Tween-20 in PBS), the primary antibody was added for 1 h, followed by PBS washing, addition of a secondary HRP-conjugated antibody, and development with a chemiluminescence detection system (ECL, Pierce, USA). Anti-plasma serine protease inhibitor (SERPINA5), hepatocyte growth factor activator (HGFAC), anti-leucine zipper protein 4 (LUZP4), and anti-phosphoinositide phospholipase C (PLCH2) were used (Abcam, USA).

The interaction network of differentially expressed proteins was constructed by the Cytoscape (National Institute of General Medical Sciences, USA), which is an open source software platform for visualizing molecular interaction networks and biological pathways and integrating these networks with annotations. The differentially expressed proteins involved in biological processes, molecular functions, cell components, and pathway enrichment were evaluated using the Cytoscape platform based on Gene Ontology (GO) terms. The corresponding *P* value analysis was simultaneously obtained using ReactomeFIViz (National Institute of General Medical Sciences).

The peptide data were analyzed with Protein Pilot Software 5.0 using the Paragon protein database search algorithm (AB Sciex, Framingham, Massachusetts, USA). The resulting MS/MS spectra were searched against the International Protein Index human sequence database (version 3.83). The parameters for the analysis were set as follows: Cys alkylation with methyl methanethiosulfonate, digestion with trypsin, and allowance of up to one missed trypsin cleavage. The false discovery rate (FDR) analysis was also performed using the integrated tools (FDR ≤0.01).

All the data were analyzed using Statistical Package for the Social Sciences Software (SPSS Inc., Chicago, IL, USA) version 16.0. The significant difference was analyzed by one-way analysis of variance (ANOVA). The gray value ratio of each band compared between the groups (SV or PV compared to control) was used to calculate the significant difference by least significant difference as a *post hoc* test. A value of $P < 0.05$ was considered statistically significant.

In total, 171 differentially expressed proteins were identified through iTRAQ. Compared with the control group, there were 80 (42 upregulated and 38 downregulated) and 89 (56 upregulated and 33 downregulated) differentially expressed proteins in the SV and PV groups, respectively [Supplementary Tables 3 and 4]. Among these differentially expressed proteins, 39 showed similar changes in both the SV and PV groups. Among them, the differentially expressed upregulated and downregulated proteins were 19 and 20. When the progressive stage was compared with the stable stage of vitiligo, 71 (23 upregulated and 48 downregulated) proteins were found to be differentially expressed [Supplementary Table 5].

The differentially expressed proteins in the SV and PV groups were analyzed based on their GO clustering using the Cytoscape platform [Supplementary Figures 1 and 2]. The significance of the first 15 annotated functions was ranked according to the *P* values. The differently expressed proteins were categorized based on their molecular function, biological process, pathway enrichment, and cell component.

In the SV group, molecular function of the differentially expressed proteins included immunoglobulin (Ig) receptor binding, antigen binding, phosphatidylcholine binding, serine-type endopeptidase inhibitor activity, endopeptidase inhibitor activity, Ig binding, protease binding, complement component C1q binding, serine-type endopeptidase activity, oxygen transporter activity, glycoprotein binding, heparin binding, proteoglycan binding, low-density lipoprotein particle binding, and laminin binding proteins, as compared to the controls. PV group expressed the above proteins similar to those in the SV group, except that had no differential expression of complement component C1q binding, proteoglycan binding, low-density lipoprotein particle binding, and laminin binding. In addition, hemoglobin binding, haptoglobin binding, arachidonic acid binding, Toll-like receptor 4 binding, peptidoglycan binding, and heme binding proteins were also differentially expressed in the PV group.

Enrichment in pathway showed that differentially expressed proteins for both the vitiligo stages were involved in complement cascade, clotting cascade, sequestering of ions, and reverse cholesterol transport. However, amb2 integrin signaling and retinoid metabolism pathway were only identified in the progressive stage. The differentially expressed proteins in the biological process were those involved in complement activation, B cell and phagocytosis recognition, and innate immune response of both the vitiligo groups. Differentially expressed proteins related to responses to bacterium and the acute-phase process were detected in PV. The differentially expressed proteins related to cell components included proteins involved in extracellular components such as exosomes, Ig complexes, and the related matrix, in both the vitiligo groups. Functional proteins involved in the acute-phase response, such as the sequestering of ions, reverse lipid transport, and oxygen transport, were markedly highly expressed in the PV group, indicating that these proteins and their molecular functions and pathways may play primary roles in the pathogenesis of vitiligo.

Based on the results obtained from the iTRAQ-based proteomic analyses, the four most prominent differentially expressed proteins were reexamined by Western blotting. The two proteins (SERPINA5 and HGFAC) were upregulated in both the stages of vitiligo. SERPINA5 expression was significantly different in both the stages of vitiligo (SV vs. control, $P < 0.05$; PV vs. control, $P < 0.05$). In addition, PLCH2 expression was upregulated in the SV (SV vs. control, $P < 0.05$) and LUZP4 was significantly downregulated in the PV (PV vs. control, $P < 0.01$) [Figure 1].

To better understand the mechanism underlying the pathogenesis of vitiligo, a protein interaction network for the differentially expressed proteins identified in the SV and PV groups was constructed using Cytoscape. The proteins marked with circles and different colors were identified in our analysis, and those marked with boxes are the linker proteins added by the Cytoscape platform [Supplementary Figure 3].

Vitiligo is a common chronic acquired disease characterized by depigmentation. Currently, no specific curative therapy and no satisfactory method are available to predict or control the progression of the disease. Proteomics is a feasible approach for large-scale screening of vitiligo-related proteins to elucidate its pathogenesis. The present study employed iTRAQ-based quantitative proteomic

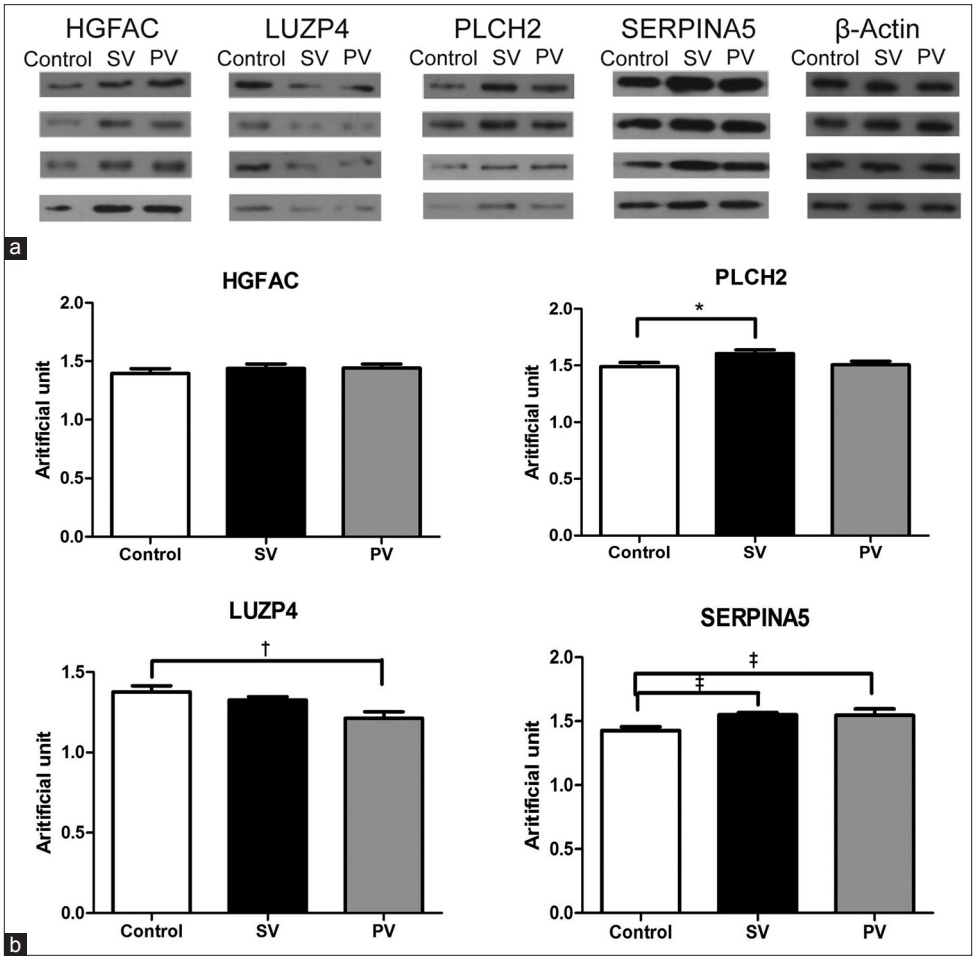

Figure 1: The differential expression of four proteins in the different stages of vitiligo and controls. (a) Each column represents one group, and the groups were as follows: controls, patients with stable, and those with progressive patients. Beta-actin was used as the loading control. (b) The gray value ratio of each band compared between the groups (SV or PV compared with control) was used to calculate the significant differences by one-way analysis of variance. *Represents that the difference is statistically significant in PLCH2 ($P < 0.05$, SV vs. control); †represents that the difference is statistically significant in LUZP4 ($P < 0.01$, PV vs. control); ‡represents that the difference is statistically significant in SERPINA5 ($P < 0.05$, SV vs. control and PV vs. control). SV: Stable vitiligo; PV: Progressive vitiligo; HGFAC: Hepatocyte growth factor activator; LUZP4: Leucine zipper protein 4; PLCH2: Phosphoinositide phospholipase C; SERPINA5: Plasma serine protease inhibitor.

tools to identify vitiligo-related proteins in the serum of patients with vitiligo. Disadvantage of this method is that the differentially expressed proteins identified might not fully represent the differentially expressed proteins in the independent sample. However, we generally choose the intersection of different proteins identified in the mixed samples and then selected individual samples to validate the proteomic results by Western blotting experiment. This method has also been proved to be reasonable and feasible in several reports. Our results revealed differentially expressed proteins in the vitiligo samples. Among them, 39 differentially expressed proteins were detected in both the vitiligo groups.

Autoimmunity is believed to be the primary cause of vitiligo. In our study, we identified many Ig heavy chain V proteins and Ig chain C proteins that were differentially expressed in SV and PV compared with the controls. We also identified the IgA complex significantly differentially expressed in both the stages of vitiligo compared to the controls from the cell component analysis. Therefore, the increased or decreased plasma levels of Ig heavy chain V or chain C might be potential group proteins requiring further investigation. Our proteomic analysis also showed increased levels of apolipoproteins (i.e., apolipoprotein A1, apolipoprotein A2, and apolipoprotein B) and decreased levels of serum paraoxonase/arylesterase 1 (PON1). These proteins were also analyzed to relate with lipid digestion, mobilization, and transport pathway. Pietrzak *et al*.[2] reported that lipid metabolism was disrupted in vitiligo-affected children, possibly resulting from disrupted metabolic processes in the adipose tissue as well as oxidative stress. In our study, we found that PON1 levels were decreased in SV but not in PV. This finding indicates that PON1 may decrease when patients are in a stable condition.

Zinc-alpha-2-glycoprotein, an essential component of numerous proteins involved in biological defense mechanisms and functioning against oxidative stress, is differentially expressed in patients with SV. Some of these identified proteins are $Zn^{(2+)}$ dependent, such as the plasma protein histidine-rich glycoprotein.[3] Thus, we propose that zinc ion-binding proteins may play a role in the pathogenesis of vitiligo. In addition to the proteins involved in zinc ion binding, some of the identified proteins were involved in calcium ion binding, such as PLCH2 and vitamin D-binding protein. The results of Western blotting test revealed that PLCH2 levels were increased in both the stages of vitiligo, especially in SV. These results showed that proteins with functions related to sequestering calcium ions

and reverse cholesterol transport were expressed at markedly high levels in the PV group. There are reports in the literature that polymorphisms in the vitamin D receptor are associated with vitiligo.[4] Clinical trials have also shown that the plasma levels of 25-hydroxy vitamin D and calcium are significantly decreased in patients with vitiligo. Ongoing studies continue to uncover potential roles for the components of the neurosensory system in the skin homeostasis and disease states.

In addition, interestingly, proteins involved in other pathways were identified and further verified through Western blotting. SERPINA5 protein, a negative regulator of the Toll pathway, was increased in both SV and PV. It seemed to be associated with micropapillary growth and the invasive phenotype of serious vitiligo that had protease inhibitor-independent activity. The expression and role of serine-type endopeptidase inhibitors in the differentiation of human skin pigmentation remains elusive. Some studies have identified a serine-type protease inhibitor related to palmitoyltransferase that has an effect on melanogenesis.[5] Among other known serine protease inhibitors (SERPINs), the enhanced stability of PAI-1 might play a role in the development of autoimmune disease and the pathophysiology of vitiligo.

Moreover, another protein HGFAC was identified and validated in the serum of patients with vitiligo. This protein has serine-type endopeptidase activity and was found to play a role in malignant melanoma progression. Interestingly, LUZP4 levels were found to be decreased in both the vitiligo stages compared to those in the controls. Although LUZP4 was not associated with vitiligo, it has been frequently reported to be activated in melanoma, where it is required for growth.[6] LUZP4 may function to promote the export of mRNAs, which would normally function to export proteins. Thus, it is possible that LUZP4 could also affect melanocyte cell growth.

In conclusion, our findings indicated that the autoimmunity proteins, lipid metabolism, oxidative stress proteins (Ig heavy chain V and C, HBB, HBG1, and HBA1), ion-dependent proteins (zinc-alpha-2-glycoprotein, PLCH2, and vitamin D-binding protein), and serine-type inhibitor proteins (increases in SERPINA5 and decreases in LUZP4) might be involved in the pathogenesis of vitiligo. Even though the sample size was small, the differentially expressed proteins that were identified might provide useful information for the diagnosis of early-stage vitiligo prior to the appearance of severe symptoms or for the elucidation of the pathophysiological mechanism.

Declaration of patient consent

We certify that we have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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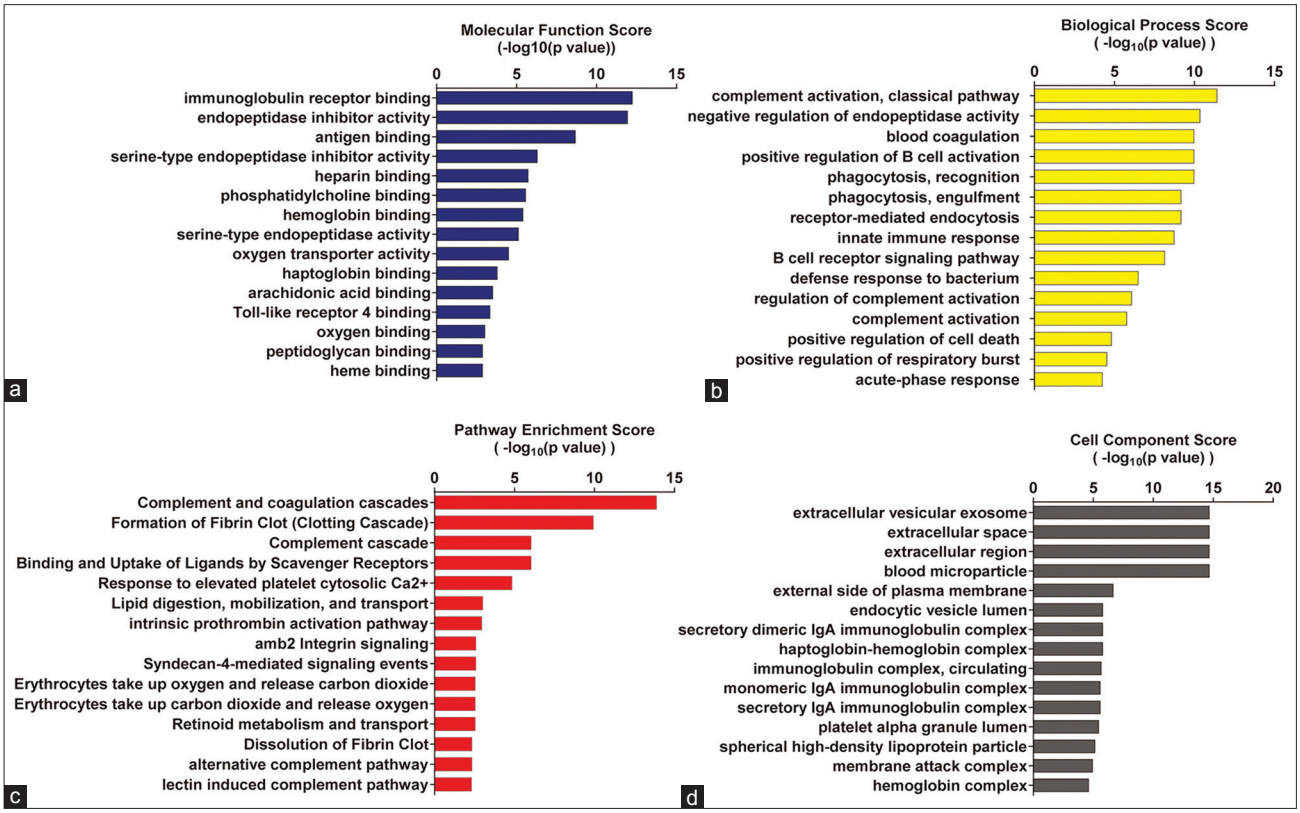
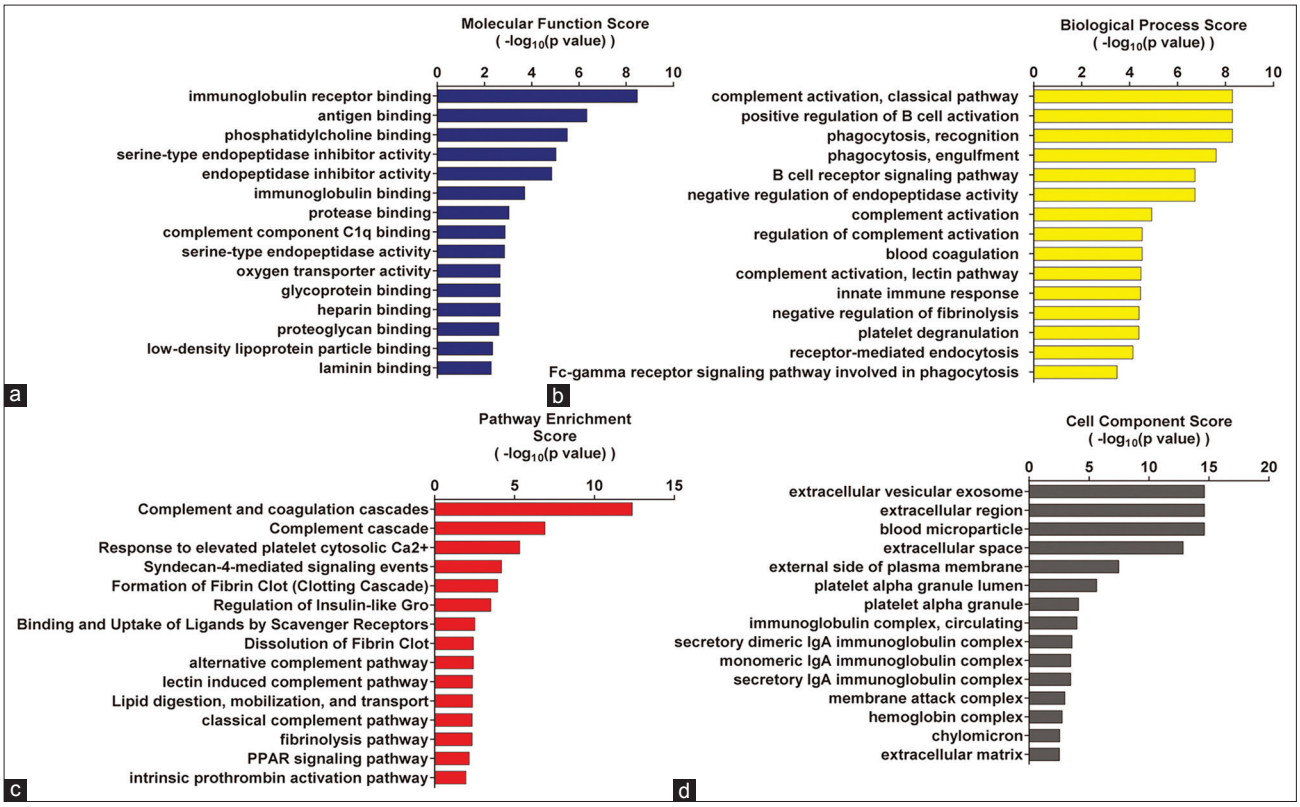
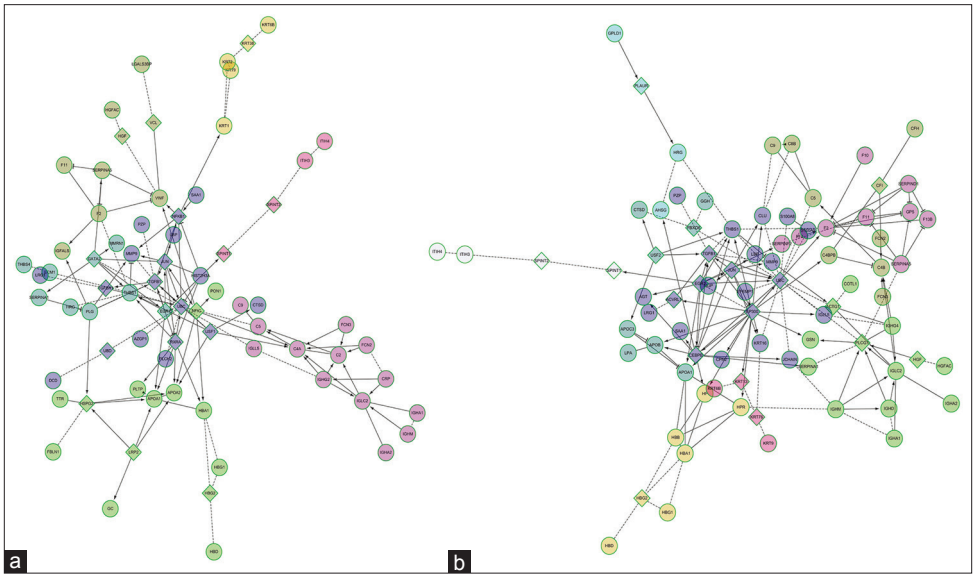


Supplementary Figure 1: Categorization of differentially expressed proteins of progressive vitiligo compared to control. (a) The top 15 proteins with molecular function. (b) The top 15 proteins involved in biological processes. (c) The top 15 proteins in pathway enrichment. (d) The top 15 proteins of cell component. The log-transformed enrichment scores for molecular function, biological process, pathway enrichment, and cell component are indicated on the x axis.



Supplementary Figure 2: Categorization of differentially expressed proteins of stable vitiligo compared to control. (a) The top 15 proteins with molecular function. (b) The top 15 proteins involved in biological processes. (c) The top 15 proteins in pathway enrichment. (d) The top 15 proteins of cell component. The log-transformed enrichment scores for molecular function, biological process, pathway enrichment and cell component are indicated on the x axis.



Supplementary Figure 3: Protein interaction network of vitiligo. (a) Protein interaction network in stable vitiligo; (b) protein interaction network of progressive vitiligo. The proteins marked with circles and different colors were identified, and those marked with boxes are the linker proteins added by the Cytoscape platform.

Supplementary Table 1: Characteristics of patients with PV

Number	Gender	Age (years)	Time of new-onset	Site	Koebner phenomenon	Family history
Patient 1	Male	17	Nearly 1 month	e, f, k, l	Yes	No
Patient 2	Male	29	Nearly 3 months	a, b, c, e, f	Yes	Yes
Patient 3	Female	33	Nearly 1 month	a, b, c, e, f, g, j, k, l	Yes	No
Patient 4	Female	24	Nearly 1 month	e, f, k, l	Yes	No
Patient 5	Female	19	Nearly 1 month	a, b, c, f, k, l	No	Yes
Patient 6	Male	41	Nearly 4 months	a, b, c, g, k, l	Yes	No
Patient 7	Female	38	Nearly 2 months	a, b, d, e, f, k, l	Yes	No
Patient 8	Male	29	Nearly 1 month	g, i, j	No	No
Patient 9	Female	33	Nearly 3 months	a, b, c, d, e, f, g, k, l	Yes	No
Patient 10	Male	26	Nearly 6 months	e, f, k, l	Yes	No

The VIDA integral: Nearly 6 weeks appear new lesions or lesions expand (+4), nearly 3 months appear new lesions or lesions expand (+3), nearly 6 months appear new lesions or lesions expand (+2); nearly 1 year appear new lesions or lesions expand (+1). Score >1 points is progression, >4 points for the rapid progression. All patients have no autoimmune disease. Vitiligo in the progressive stage included 12 cases of sporadic vitiligo (40.0%), 10 cases of acrofacial (33.3%), and 8 cases of universal (26.7%), they are 5 males and 5 females. a: Head (3%); b: Face (3%); c: Neck (3%); d: Upperarm (7%); e: Forearm (6%); f: Hands (5%); g: Trunk (26%); h: Perineum (1%); i: Hip (5%); j: Thigh (21%); k: Shin (13%); l: Feet (7%). VIDA: Vitiligo Disease Activity Score; PV: Progressive vitiligo.

Supplementary Table 2: Characteristics of patients with SV

Number	Gender	Age	Time of stable phase (years)	Site	Koebner phenomenon	Family history
Patient 11	Male	27	>10	e, f, k, l	No	Yes
Patient 12	Female	38	>10	a, b, c, e, f, g, i, j, k, l	No	No
Patient 13	Female	43	>20	a, b, c, e, f, l	No	No
Patient 14	Female	20	>4	a, b, c, e, f	No	No
Patient 15	Female	16	>5	a, b, c, f, k, l	No	No
Patient 16	Male	33	>10	a, b, c, e, f, k, l	No	No
Patient 17	Male	47	>10	a, b, c, d, e, f, g, k, l	No	No
Patient 18	Female	34	>20	g, i, j	No	Yes
Patient 19	Female	26	>10	g, i, j, k, l	No	No
Patient 20	Male	29	>10	a, b, c, e, f, k, l	No	No

The evaluation of the criterion in SV is set by disease activity score (VIDA). Depigmentation phase was stable for >1 year (0 score), at the same time, there is spontaneous pigment regeneration (−1). All patients have no autoimmune disease. Vitiligo in the stable stage included 14 cases of sporadic vitiligo (46.7%), 8 cases of acrofacial (26.7%), 8 cases of universal (26.7%), they are 4 males and 6 females. a: Head (3%); b: Face (3%); c: Neck (3%); d: Upperarm (7%); e: Forearm (6%); f: Hands (5%); g: Trunk (26%); h: Perineum (1%); i: Hip (5%); j: Thigh (21%); k: Shin (13%); l: Feet (7%). VIDA: Vitiligo disease activity score; SV: Stable vitiligo.

Supplementary Table 3: Identification of differentially expressed proteins of SV samples versus control samples

Accession number	Protein name	Gene name	Mw	pI	Coverage (%)	Peptides (95%)	Unused protscore	SV ratio
B9DI82	Phosphoinositide phospholipase C (fragment)	*PLCH2*	134,778.10	7.64	3.15	1	1.8	5.73
P05154	Plasma serine protease inhibitor	*SERPINA5*	45,674.14	9.30	21.92	7	11.73	10.07
A0A0B4J2B7	Protein IGHV3-30 (fragment)	*IGHV3-30*	12,946.63	9.10	84.62	39	4	5.29
P23083	Ig heavy chain V-I region V35	N/A	13,008.57	9.59	73.50	28	6.08	3.27
P06331	Ig heavy chain V-II region ARH-77	N/A	16,228.27	8.45	26.71	29	2	3.56
A0A0C4DH31	Protein IGHV1-18 (fragment)	*IGHV1-18*	12,820.29	8.98	55.56	20	6.01	2.82
P01876	Ig alpha-1 chain C region	*IGHA1*	37,654.23	6.08	79.04	191	35.61	4.23
A0A075B6K4	HCG2043238 (fragment)	*IGLV3-10*	12,628.89	4.72	59.83	17	10.2	2.37
A0A0B4J2H0	Protein IGHV1-69-2 (fragment)	*IGHV1-69-2*	12,660.18	8.64	59.83	33	4	1.80
Q15485	Ficolin-2	*FCN2*	34,000.76	6.31	24.60	9	8.1	2.59
A0A075B6K9	Ig lambda-2 chain C regions (fragment)	*IGLC2*	11,236.38	6.91	99.06	84	20.51	3.40
A0A0B4J1V0	Protein IGHV3-15 (fragment)	*IGHV3-15*	12,925.64	8.84	78.15	20	8.1	1.98
A0A0C4DH67	Protein IGKV1-8 (fragment)	*IGKV1-8*	12,537.18	9.21	58.26	18	4.27	1.83
A0A075B6N7	Ig alpha-2 chain C region (fragment)	*IGHA2*	36,590.95	5.86	67.35	72	10.04	2.33
D6RF35	Vitamin D-binding protein	*GC*	53,020.02	5.38	84.45	81	4.01	1.81
P06319	Ig lambda chain V-VI region EB4	N/A	14,146.57	4.85	39.69	10	4.87	1.69
P81605	Dermcidin	*DCD*	11,283.74	6.09	20.91	1	2.04	1.51
Q08380	Galectin-3-binding protein	*LGALS3BP*	65,330.25	5.13	29.06	10	14.59	1.88
Q04756	Hepatocyte growth factor activator	*HGFAC*	70,681.11	6.99	20.00	14	16.16	1.82
P03951	Coagulation factor XI	*F11*	70,108.40	8.47	17.76	8	8.34	1.75
P01709	Ig lambda chain V-II region MGC	N/A	11,557.43	5.12	42.34	2	2	1.92
P06316	Ig lambda chain V-I region BL2	N/A	13,564.07	7.64	62.31	12	4.11	1.85
P35908	Keratin, type II cytoskeletal 2 epidermal	*KRT2*	65,432.11	8.07	24.10	13	17.64	1.65
A0A0B4J231	Immunoglobulin lambda-like polypeptide 5	*IGLL5*	23,150.06	9.08	55.35	63	4.32	2.09
A0A0C4DH41	Protein IGHV4-61 (fragment)	*IGHV4-61*	13,065.75	9.36	55.93	35	13.04	1.57
A0A0G2JN06	Ig gamma-2 chain C region (fragment)	*IGHG2*	35,900.23	7.66	79.75	142	14.68	1.51
A0A0C4DH38	Protein IGHV5-51 (fragment)	*IGHV5-51*	12,674.41	8.45	70.09	25	8.07	1.57
Q71DI3	Histone H3.2	*HIST2H3A*	15,387.84	11.27	34.56	3	3.9	1.74
A0A0B4J1U2	Protein IGLV7-43 (fragment)	*IGLV7-43*	12,450.88	6.52	16.24	5	3.06	1.57
B4E1Z4	Uncharacterized protein	N/A	140,941.20	6.82	54.58	104	101.59	1.57
P00734	Prothrombin	*F2*	70,036.12	5.64	72.19	69	56.96	1.70
P02042	Hemoglobin subunit delta	*HBD*	16,055.28	7.84	90.48	33	11.89	1.64
P01780	Ig heavy chain V-III region JON	N/A	12,319.98	9.39	60.87	10	2	1.70
A0A087WYJ9	Ig mu chain C region	*IGHM*	65,700.17	6.52	66.44	118	55.83	1.55
P02766	Transthyretin	*TTR*	15,886.83	5.52	72.11	23	18.87	1.58

Contd...

Supplementary Table 3: Contd...

Accession number	Protein name	Gene name	Mw	pI	Coverage (%)	Peptides (95%)	Unused protscore	SV ratio
P01703	Ig lambda chain V-I region NEWM	N/A	10,904.07	9.39	78.64	22	2.01	1.96
P04196	Histidine-rich glycoprotein	*HRG*	59,577.63	7.09	46.67	24	24.58	1.59
P00747	Plasminogen	*PLG*	90,568.09	7.04	62.35	94	74.79	1.67
P01031	Complement C5	*C5*	188,303.00	6.11	44.93	66	91.04	1.57
P14780	Matrix metalloproteinase-9	*MMP9*	78,457.32	5.69	12.31	6	10.76	1.58
A0A0C4DH68	Protein IGKV2-24 (Fragment)	*IGKV2-24*	13,078.87	8.74	55.83	20	4.71	1.63
P69905	Hemoglobin subunit alpha	*HBA1*	15,257.36	8.72	60.56	24	9.73	1.54
Q9P127	Leucine zipper protein 4	*LUZP4*	35,936.42	9.47	3.83	2	2	−4.09
P35527	Keratin, type I cytoskeletal 9	*KRT9*	62,063.62	5.14	19.90	13	14.49	−4.10
P02763	Alpha-1-acid glycoprotein 1	*ORM1*	23,511.27	4.93	53.73	57	22.45	−2.98
P69891	Hemoglobin subunit gamma-1	*HBG1*	16,140.27	6.64	45.58	14	4.7	−3.12
P19827	Inter-alpha-trypsin inhibitor heavy chain H1	*ITIH1*	101,387.90	6.31	50.27	87	53.78	−1.84
P0C0L4	Complement C4-A	*C4A*	192,783.20	6.66	71.90	219	181.76	−1.66
P27169	Serum paraoxonase/ arylesterase 1	*PON1*	39,730.81	5.08	62.82	40	23.94	−2.23
P02748	Complement component C9	*C9*	63,172.73	5.43	49.37	32	35.29	−2.69
O75636	Ficolin-3	*FCN3*	32,902.61	6.20	36.12	15	13.22	−3.20
P35858	Insulin-like growth factor-binding protein complex acid labile subunit	*IGFALS*	66,034.20	6.33	30.08	13	23.34	−2.03
P02750	Leucine-rich alpha-2-glycoprotein	*LRG1*	38,177.44	6.45	37.46	15	17.79	−2.02
P07996	Thrombospondin-1	*THBS1*	129,381.40	4.71	30.94	37	50.97	−2.17
P04259	Keratin, type II cytoskeletal 6B	*KRT6B*	60,066.25	8.09	23.05	10	8.03	−2.16
P19652	Alpha-1-acid glycoprotein 2	*ORM2*	23,602.35	5.03	54.23	33	9.59	−2.20
P0DJI8	Serum amyloid A-1 protein	*SAA1*	13,531.86	6.28	63.11	6	2.91	−2.19
P20742	Pregnancy zone protein	*PZP*	16,3861.00	5.97	37.52	119	31.65	−2.34
P02741	C-reactive protein	*CRP*	25,038.26	5.45	23.66	3	3.3	−2.07
P18428	Lipopolysaccharide-binding protein	*LBP*	53,382.97	6.23	18.09	9	12.92	−2.20
A0A0A6YYG9	Protein ARPC4-TTLL3	*ARPC4-TTLL3*	71,718.39	5.59	6.40	2	2	−1.57
Q14624	Inter-alpha-trypsin inhibitor heavy chain H4	*ITIH4*	103,356.20	6.51	65.59	110	85.05	−1.77
Q13201	Multimerin-1	*MMRN1*	138,108.60	8.15	8.63	5	5.48	−1.93
P01011	Alpha-1-antichymotrypsin	*SERPINA3*	47,650.31	5.33	66.19	86	43.42	−1.63
P04264	Keratin, type II cytoskeletal 1	*KRT1*	66,037.95	8.15	29.35	21	26.61	−1.82
A0A075B6K3	Protein IGLV2-11 (fragment)	*IGLV2-11*	12,643.88	6.69	51.26	5	4	−1.84
P23142	Fibulin-1	*FBLN1*	77,213.47	5.07	29.16	16	21.44	−1.89
Q16610	Extracellular matrix protein 1	*ECM1*	60,673.46	6.25	34.44	12	19.14	−1.68
P04275	von Willebrand factor	*VWF*	309,262.00	5.29	16.74	27	50.73	−1.57
P02647	Apolipoprotein A-I	*APOA1*	30,777.44	5.56	88.39	228	77.72	−1.53
E7ES19	Thrombospondin-4	*THBS4*	96,004.91	4.39	10.46	4	3.04	−1.62
P19823	Inter-alpha-trypsin inhibitor heavy chain H2	*ITIH2*	106,462.20	6.40	49.79	90	49.73	−1.58
P06681	Complement C2	*C2*	83,266.95	7.23	41.09	30	10.01	−1.73
P01009	Alpha-1-antitrypsin	*SERPINA1*	46,735.98	5.37	88.28	240	91.91	−1.49
P25311	Zinc-alpha-2-glycoprotein	*AZGP1*	34,258.30	5.71	64.09	35	37.02	−1.73

Contd...

Supplementary Table 3: Contd...

Accession number	Protein name	Gene name	Mw	pI	Coverage (%)	Peptides (95%)	Unused protscore	SV ratio
V9GYM3	Apolipoprotein A-II	*APOA2*	14,914.10	8.43	63.16	52	28.49	−1.62
A0A087WXI2	IgGFc-binding protein	*FCGBP*	44,5207.00	5.16	7.45	10	18.84	−1.63
P07339	Cathepsin D	*CTSD*	44,551.72	6.10	11.89	2	2.02	−1.61
Q06033	Inter-alpha-trypsin inhibitor heavy chain H3	*ITIH3*	99,848.02	5.49	38.20	24	22.37	−1.52
P55058	Phospholipid transfer protein	*PLTP*	54,738.80	6.53	31.03	10	15.38	−1.61

Mw: Molecular weight; PV: Progressive vitiligo; SV: Stable vitiligo; N/A: Not applicable; pI: Isoelectric point.

Supplementary Table 4: Identification of differentially expressed proteins of PV samples versus control samples

Accession number	Protein name	Gene name	Mw	pI	Coverage (%)	Peptides (95%)	Unused protscore	PV ratio
A0A024R6I7	Alpha-1-antitrypsin	*SERPINA1*	46,707.93	5.37	87.80	230	2	39.25
P05154	Plasma serine protease inhibitor	*SERPINA5*	45,674.14	9.30	21.92	7	11.73	10.53
Q04756	Hepatocyte growth factor activator	*HGFAC*	70,681.11	6.99	20.00	14	16.16	2.55
P00739	Haptoglobin-related protein	*HPR*	39,029.11	6.63	81.03	100	14.38	2.41
P08779	Keratin, type I cytoskeletal 16	*KRT16*	51,267.25	4.98	27.27	9	9.89	2.91
P69905	Hemoglobin subunit alpha	*HBA1*	15,257.36	8.72	60.56	24	9.73	2.73
P03951	Coagulation factor XI	*F11*	70,108.40	8.47	17.76	8	8.34	2.08
Q15485	Ficolin-2	*FCN2*	34,000.76	6.31	24.60	9	8.1	2.89
A0A0B4J2H0	Protein IGHV1-69-2 (fragment)	*IGHV1*-69-2	12,660.18	8.64	59.83	33	4	1.70
P01876	Ig alpha-1 chain C region	*IGHA1*	37,654.23	6.08	79.04	191	35.61	4.58
P80108	Phosphatidylinositol-glycan-specific phospholipase D	*GPLD1*	92,335.35	5.91	28.45	17	30.27	1.84
P04114	Apolipoprotein B-100	*APOB*	515,598.30	6.58	66.10	550	468.39	1.89
K7ER74	Protein APOC4-APOC2	*APOC4-APOC2*	20,049.07	6.36	51.69	21	16	2.17
P06331	Ig heavy chain V-II region ARH-77	N/A	16,228.27	8.45	26.71	29	2	2.45
A0A0B4J231	Immunoglobulin lambda-like polypeptide 5	*IGLL5*	23,150.06	9.08	55.35	63	4.32	2.55
B0YIW2	Apolipoprotein C-III	*APOC3*	12,815.43	7.90	47.01	36	12.61	2.47
P02042	Hemoglobin subunit delta	*HBD*	16,055.28	7.84	90.48	33	11.89	2.10
P23083	Ig heavy chain V-I region V35	N/A	13,008.57	9.59	73.50	28	6.08	1.94
P0C0L5	Complement C4-B	*C4B*	192,749.20	6.89	71.56	220	8.82	2.77
P55056	Apolipoprotein C-IV	*APOC4*	14,552.90	9.19	49.61	6	5.38	2.10
P08697	Alpha-2-antiplasmin	*SERPINF2*	54,565.11	5.87	43.79	29	19.89	1.58
P06396	Gelsolin	*GSN*	85,696.47	5.90	53.07	53	47.75	2.02
A0A075B6N7	Ig alpha-2 chain C region (fragment)	*IGHA2*	36,590.95	5.86	67.35	72	10.04	2.24
P00734	Prothrombin	*F2*	70,036.12	5.64	72.19	69	56.96	1.81
P68871	Hemoglobin subunit beta	*HBB*	15,998.21	6.74	82.31	43	24.33	2.09
P10909	Clusterin	*CLU*	52,494.01	5.89	51.22	63	34.68	1.65
P04196	Histidine-rich glycoprotein	*HRG*	59,577.63	7.09	46.67	24	24.58	2.17
B4E1Z4	Uncharacterized protein	N/A	140,941.20	6.82	54.58	104	101.59	2.14
P19652	Alpha-1-acid glycoprotein 2	*ORM2*	23,602.35	5.03	54.23	33	9.59	1.77
F5H7G1	Complement component C8 beta chain	*C8B*	61,230.52	7.86	30.61	9	18.49	2.48
P00742	Coagulation factor X	*F10*	54,731.14	5.68	37.50	13	23.06	1.73
A0A0C4DH41	Protein IGHV4-61 (fragment)	*IGHV4-61*	13,065.75	9.36	55.93	35	13.04	1.60
P08519	Apolipoprotein (a)	*LPA*	501,314.20	5.58	39.78	20	29.93	1.56
A0A075B6K9	Ig lambda-2 chain C regions (fragment)	*IGLC2*	11,236.38	6.91	99.06	84	20.51	2.01

Contd...

Supplementary Table 4: Contd...

Accession number	Protein name	Gene name	Mw	pI	Coverage (%)	Peptides (95%)	Unused protscore	PV ratio
P08603	Complement factor H	*CFH*	139,095.00	6.21	59.38	138	120.45	1.76
P04259	Keratin, type II cytoskeletal 6B	*KRT6B*	60,066.25	8.09	23.05	10	8.03	1.55
Q12805	EGF-containing fibulin-like extracellular matrix protein 1	*EFEMP1*	54,640.10	4.95	14.81	5	8.01	1.69
E9PHK0	Tetranectin	*CLEC3B*	17,793.93	4.96	66.25	15	10.07	1.59
P08493	Matrix Gla protein	*MGP*	12,353.06	9.71	14.56	1	2	1.50
P43652	Afamin	*AFM*	69,068.41	5.64	58.93	46	52.35	1.99
O00391	Sulfhydryl oxidase 1	*QSOX1*	82,576.74	9.13	14.59	4	7.52	1.77
P20851	C4b-binding protein beta chain	*C4BPB*	28,357.18	5.05	38.89	7	9.3	1.68
P01031	Complement C5	*C5*	188,303.00	6.11	44.93	66	91.04	1.94
A0A087WTM7	Apolipoprotein B-100	*APOB*	489,827.10	6.69	67.61	536	2	1.61
P01011	Alpha-1-antichymotrypsin	*SERPINA3*	47,650.31	5.33	66.19	86	43.42	1.53
A0A075B6K4	HCG2043238 (fragment)	*IGLV3-10*	12,628.89	4.72	59.83	17	10.2	1.58
P14780	Matrix metalloproteinase-9	*MMP9*	78,457.32	5.69	12.31	6	10.76	1.66
P05546	Heparin cofactor 2	*SERPIND1*	57,069.95	6.41	58.72	52	41.5	1.75
P02765	Alpha-2-HS-glycoprotein	*AHSG*	39,324.24	5.43	64.31	72	35.09	1.73
P01019	Angiotensinogen	*AGT*	53,153.57	5.87	41.24	32	21.65	1.67
Q14624	Inter-alpha-trypsin inhibitor heavy chain H4	*ITIH4*	103,356.20	6.51	65.59	110	85.05	1.73
P19827	Inter-alpha-trypsin inhibitor heavy chain H1	*ITIH1*	101,387.90	6.31	50.27	87	53.78	1.62
A0A0C4DH68	Protein IGKV2-24 (fragment)	*IGKV2-24*	13,078.87	8.74	55.83	20	4.71	1.59
P02647	Apolipoprotein A-I	*APOA1*	30,777.44	5.56	88.39	228	77.72	1.56
P05160	Coagulation factor XIII B chain	*F13B*	75,509.92	6.01	50.08	31	42	1.53
P06316	Ig lambda chain V-I region BL2	N/A	13,564.07	7.64	62.31	12	4.11	1.66
Q14019	Coactosin-like protein	*COTL1*	15,944.79	5.54	11.27	1	2	−14.79
A0A087WYJ9	Ig mu chain C region	*IGHM*	65,700.17	6.52	66.44	118	55.83	−9.37
P01591	Immunoglobulin J chain	*JCHAIN*	18,098.40	5.12	70.44	15	9.66	−5.02
Q92820	Gamma-glutamyl hydrolase	*GGH*	35,963.95	6.66	29.25	4	6.3	−2.55
O43866	CD5 antigen-like	*CD5L*	38,087.45	5.28	44.96	18	21.83	−2.96
Q9P127	Leucine zipper protein 4	*LUZP4*	35,936.42	9.47	3.83	2	2	−3.96
P04278	Sex hormone-binding globulin	*SHBG*	43,778.68	6.22	34.33	10	13.7	−2.67
A0A0C4DH43	Uncharacterized protein (fragment)	N/A	13,312.31	8.50	35.29	2	2.07	−3.28
A0A0G2JPD4	Ig gamma-4 chain C region (fragment)	*IGHG4*	35,940.14	7.18	73.09	175	6.07	−2.35
P02750	Leucine-rich alpha-2-glycoprotein	*LRG1*	38,177.44	6.45	37.46	15	17.79	−2.36
A0A0B4J1X5	Protein IGHV3-74 (fragment)	*IGHV3-74*	12,839.47	8.91	83.76	104	3.38	−4.07
P05109	Protein S100-A8	*S100A8*	10,834.38	6.51	39.78	6	8.75	−2.39
P07996	Thrombospondin-1	*THBS1*	129,381.40	4.71	30.94	37	50.97	−2.06
P00738	Haptoglobin	*HP*	45,204.78	6.13	88.18	235	70.99	−1.85
P06702	Protein S100-A9	*S100A9*	13,241.85	5.71	49.12	4	7.05	−2.00
A0A0C4DH67	Protein IGKV1-8 (fragment)	*IGKV1-8*	12,537.18	9.21	58.26	18	4.27	−1.84
P40197	Platelet glycoprotein V	*GP5*	60,958.46	9.73	12.86	4	4.72	−1.92
Q06033	Inter-alpha-trypsin inhibitor heavy chain H3	*ITIH3*	99,848.02	5.49	38.20	24	22.37	−2.05
Q8IVF4	Dynein heavy chain 10, axonemal	*DNAH10*	514,834.70	5.64	6.15	3	2.03	−2.03
A0A087WUS7	Ig delta chain C region	*IGHD*	42,352.35	8.38	42.71	16	11.8	−2.75
P07339	Cathepsin D	*CTSD*	44,551.72	6.10	11.89	2	2.02	−2.02
O75636	Ficolin-3	*FCN3*	32,902.61	6.20	36.12	15	13.22	−1.64
P35527	Keratin, type I cytoskeletal 9	*KRT9*	62,063.62	5.14	19.90	13	14.49	−1.71
P02776	Platelet factor 4	*PF4*	10,844.83	8.93	29.70	2	4	−1.80
P02748	Complement component C9	*C9*	63,172.73	5.43	49.37	32	35.29	−1.50
P69891	Hemoglobin subunit gamma-1	*HBG1*	16,140.27	6.64	45.58	14	4.7	−1.52

Contd...

Supplementary Table 4: Contd...

Accession number	Protein name	Gene name	Mw	pI	Coverage (%)	Peptides (95%)	Unused protscore	PV ratio
P83593	Ig kappa chain V-IV region STH (fragment)	N/A	12,060.29	7.94	71.56	16	2.01	−1.77
P0DJI8	Serum amyloid A-1 protein	*SAA1*	13,531.86	6.28	63.11	6	2.91	−1.70
P18428	Lipopolysaccharide-binding protein	*LBP*	53,382.97	6.23	18.09	9	12.92	−1.51
P22792	Carboxypeptidase N subunit 2	*CPN2*	60,555.93	5.63	26.61	15	14.3	−1.70
P20742	Pregnancy zone protein	*PZP*	163,861.00	5.97	37.52	119	31.65	−1.53
P01770	Ig heavy chain V-III region NIE	N/A	12,898.45	9.75	54.62	24	6.02	−1.69
P06313	Ig kappa chain V-IV region JI	N/A	14,632.35	6.15	71.43	51	13.34	−1.60

Mw: Molecular weight; PV: Progressive vitiligo; N/A: Not applicable; pI: Isoelectric point.

Supplementary Table 5: Differentially expressed proteins occurring in PV compared with SV

Accession number	Protein name	Gene name	Mw	Coverage (%)	Peptides (95%)	Unused protscore	PV/SV ratio
A0A087WYJ9	Ig mu chain C region	*IGHM*	65,700.17	66.44	118	55.83	12.47
Q14019	Coactosin-like protein	*COTL1*	15,944.79	11.27	1	2	19.41
A0A0B4J1X5	Protein IGHV3-74 (fragment)	*IGHV3-74*	12,839.47	83.76	104	3.38	5.97
P01591	Immunoglobulin J chain	*JCHAIN*	18,098.40	70.44	15	9.66	4.83
A0A087WUS7	Ig delta chain C region	*IGHD*	42,352.35	42.71	16	11.8	4.66
A0A0C4DH67	Protein IGKV1-8 (fragment)	*IGKV1-8*	12,537.18	58.26	18	4.27	2.78
O43866	CD5 antigen-like	*CD5L*	38,087.45	44.96	18	21.83	2.65
P04278	Sex hormone-binding globulin	*SHBG*	43,778.68	34.33	10	13.7	2.23
A0A0C4DH31	Protein IGHV1-18 (fragment)	*IGHV1-18*	12,820.29	55.56	20	6.01	2.75
P01770	Ig heavy chain V-III region NIE	*IGHA1*	12,898.45	54.62	24	6.02	2.09
D6RF35	Vitamin D-binding protein	*GC*	53,020.02	84.45	81	4.01	1.66
O43866	CD5 antigen-like	*CD5L*	38,087.45	44.96	18	21.83	2.65
P04278	Sex hormone-binding globulin	*SHBG*	43,778.68	34.33	10	13.7	2.23
A0A0C4DH43	Uncharacterized protein (fragment)	*N/A*	13,312.31	35.29	2	2.07	3.70
A0A087WUS7	Ig delta chain C region	*IGHD*	42,352.35	42.71	16	11.8	4.66
P05109	Protein S100-A8	*S100A8*	10,834.38	39.78	6	8.75	1.91
P01709	Ig lambda chain V-II region MGC	N/A	11,557.43	42.34	2	2	1.85
P23083	Ig heavy chain V-I region V35	N/A	13,008.57	73.50	28	6.08	1.58
P01780	Ig heavy chain V-III region JON	N/A	12,319.98	60.87	10	2	1.67
A0A0C4DH31	Protein IGHV1-18 (fragment)	*IGHV1-18*	12,820	55.56	45	6.01	2.75
P06702	Protein S100-A9	*S100A9*	13,241.85	49.12	4	7.05	1.54
P60709	Actin, cytoplasmic 1	*ACTB*	41,737	6	31	35.33	1.63
A0A075B6K9	Ig lambda-2 chain C regions (fragment)	*IGLC2*	11,236.38	99.06	84	20.51	1.91
A0A024R6I7	Alpha-1-antitrypsin	*SERPINA1*	46,707.93	87.80	230	2	−51.52
P0C0L5	Complement C4-B	*C4B*	19,2749.20	71.56	220	8.82	−2.86
P02763	Alpha-1-acid glycoprotein 1	*ORM1*	23,511.27	53.73	57	22.45	−3.94

Contd...

Supplementary Table 5: Contd...

Accession number	Protein name	Gene name	Mw	Coverage (%)	Peptides (95%)	Unused protscore	PV/SV ratio
P0C0L4	Complement C4-A	*C4A*	192,783.20	71.90	219	181.76	−1.82
P19652	Alpha-1-acid glycoprotein 2	*ORM2*	23,602.35	54.23	33	9.59	−3.91
P33908	Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA	*MAN1A1*	72,969	13.17	4	6.27	−3.53
P04259	Keratin, type II cytoskeletal 6B	*KRT6B*	60,066.25	23.05	10	8.03	−2.99
P19827	Inter-alpha-trypsin inhibitor heavy chain H1	*ITIH1*	101,387.90	50.27	87	53.78	−2.58
P01011	Alpha-1-antichymotrypsin	*SERPINA3*	47,650.31	66.19	86	43.42	−2.13
P27169	Serum paraoxonase/ arylesterase 1	*PON1*	39,730.81	62.82	40	23.94	−2.58
Q14624	Inter-alpha-trypsin inhibitor heavy chain H4	*ITIH4*	103,356.20	65.59	110	85.05	−3.49
F5H7G1	Complement component C8 beta chain	*C8B*	61,230.52	30.61	9	18.49	−3.162
P23142	Fibulin-1	*FBLN1*	77,213.47	29.16	16	21.44	−1.74
P04275	von Willebrand factor	*VWF*	309,262.00	16.74	27	50.73	−1.91
P08779	Keratin, type I cytoskeletal 16	*KRT16*	51,267.25	27.27	9	9.89	−3.22
P02741	C-reactive protein	*CRP*	25,038.26	23.66	3	3.3	−2.88
P69891	Hemoglobin subunit gamma-1	*HBG1*	16,140.27	45.58	14	4.7	−1.87
P08519	Apolipoprotein (a)	*LPA*	501,314.20	39.78	20	29.93	−1.82
P68871	Hemoglobin subunit beta	*HBB*	15,998.21	82.31	43	24.33	−1.87
P35527	Keratin, type I cytoskeletal 9	*KRT9*	62,063.62	19.90	13	14.49	−2.81
P19823	Inter-alpha-trypsin inhibitor heavy chain H2	*ITIH2*	106,462.20	49.79	90	49.73	−1.91
P36980	Complement factor H-related protein 2	*CFHR2*	30,651	41.85	7	6	−1.91
Q16610	Extracellular matrix protein 1	*ECM1*	60,673.46	34.44	12	19.14	−2.07
P04264	Keratin, type II cytoskeletal 1	*KRT1*	66,037.95	29.35	21	26.61	−2.29
P02647	Apolipoprotein A-I	*APOA1*	30,777.44	88.39	228	77.72	−2.94
P05546	Heparin cofactor 2	*SERPIND1*	57,069.95	58.72	52	41.5	−1.61
P06732	Creatine kinase M-type	*CKM*	43,101	5.512	1	2	−1.50
P55056	Apolipoprotein C-IV	*APOC4*	14,552.90	49.61	6	5.38	−1.80
Q9UHG3	Prenylcysteine oxidase 1	*PCYOX1*	56,640	15.45	5	8.78	−1.63
P01042	Kininogen-1	*KNG1*	71,957	55.12	106	54.98	−2.33
P06396	Gelsolin	*GSN*	85,696.47	53.07	53	47.75	−1.51
P02748	Complement component C9	*C9*	63,172.73	49.37	32	35.29	−1.91
A0A0A0MR46	RNA-binding protein 44	*RBM44*	118,116	4.848	2	2	−1.54
P29622	Kallistatin	*SERPINA4*	48,542	49.65	24	27.74	−1.74
P36955	Pigment epithelium-derived factor	*SERPINF1*	46,312	57.89	17	26.25	−1.85
B0YIW2	Apolipoprotein C-III	*APOC3*	12,815.43	47.01	36	12.61	−1.82
C9JF17	Apolipoprotein D (fragment)	*APOD*	24,158	33.49	25	16.88	−3.25
P00450	Ceruloplasmin	*CP*	12,2205	69.86	169	102.07	−1.89

Contd...

Supplementary Table 5: Contd...

Accession number	Protein name	Gene name	Mw	Coverage (%)	Peptides (95%)	Unused protscore	PV/SV ratio
P05155	Plasma protease C1 inhibitor	*SERPING1*	55,154	55.6	49	36.17	−1.54
P06727	Apolipoprotein A-IV	*APOA4*	45,399	78.79	71	53.32	−1.54
P20742	Pregnancy zone protein	*PZP*	163,861.00	37.52	119	31.65	−1.57
P01009	Alpha-1-antitrypsin	*SERPINA1*	46,735.98	88.28	240	91.91	−2.00
P05160	Coagulation factor XIII B chain	*F13B*	75,509.92	50.08	31	42	−2.27
O00391	Sulfhydryl oxidase 1	*QSOX1*	82,576.74	14.59	4	7.52	−1.53
O75636	Ficolin-3	*FCN3*	32,902.61	36.12	15	13.22	−2.70
P02751	Fibronectin	*FN1*	26,2625	55.28	186	151.63	−2.07
P02649	Apolipoprotein E	*APOE*	36,154	50.08	31	42	−2.05
P00739	Haptoglobin-related protein	*HPR*	39,029.11	81.03	100	14.38	−2.01

Mw: Molecular weight; PV: Progressive vitiligo; SV: Stable vitiligo; N/A: Not applicable.