**Material and Methods**

**Subjects**

Skin tissue samples were collected from 6 psoriatic patients (age range 17–61 years, mean age 31 years) and 6 healthy volunteers (age range 21–54 years, mean age 38 years) from September 2017 to July 2019. Patients’ Psoriasis Area and Severity Index (PASI) scores were between 9 and 15.51, with an average score of 13.37 ± 3.34. The healthy volunteers were from the Urology and Plastic Surgery Department, without immune disorders. The diagnosis of psoriasis vulgaris was made based on both the clinical and pathological features. All subjects had not used corticosteroids, retinoic acid, and immunosuppressants either topically or systemically 3 months prior to collection of skin samples. All participants gave informed consent. The research procedure was approved by the Medical Ethics Committee of Taiyuan Central Hospital.

**Isolation, Culture and Expansion of DMSCs**

For isolation of DMSCs, the skin specimens were minced and digested with 0.25% dispase enzymeII (Sigma Aldrich, St Louis, MO) overnight at 4°C. Then, the dermis was cut as small as possible and placed in DMEM-F12 (HyClone Laboratories, Losan, UT) medium containing 10% FBS. The single-cell suspension was filtered through a 70-μm cell strainer (BD Labware, Shanghai, China) and centrifuged at 800 rpm for 6 min. The supernatant was discarded, and the cells were re-suspended with DMEM-F12 medium in T25 flasks (Corning, NY, USA) at 37℃ in a 5% CO2 incubator (Sheldon Manufacturing Inc). When cells were at 80% confluence, the cells were digested with trypsin and passaged.

**In vitro Co-Culture Experiment**

HaCaT cells were cultured in H-DMEM (Gibco, USA) supplemented with 10% FBS and 1% penicillin/streptomycin (all from Thermo Fisher) at 37°C in a 5% CO2 humidified atmosphere. A co-culture transwell chamber (12-well plate, 0.4-μm pore size; Corning, NY, USA) was used to assess the effects of DMSCs on HaCaT cells. Briefly, HaCaT cells were seeded at density of 2 × 105 into the basal chamber in 1.5 mL of H-DMEM with 10% FBS. An equivalent number of DMSCs in 500 μl DMEM-F12 were seeded into the apical chamber of a transwell insert. After co-culture for 72 h, the HaCaT cells were collected to evaluate the differentiation and proliferation. The experiment included three groups: HaCaT cell culture alone, HaCaT cells co-cultured with either normal (HaCaT + n-DMSCs) or psoriatic DMSCs (HaCaT + p-DMSCs). In some experiments, HaCaT cells were treated with the PI3K inhibitor LY294002 (50 μM) (MCE, USA) for 24 h, followed by co-culture with DMSCs. After incubation for 48 h, the cells were collected for the measurement of protein and mRNA level.

**Analysis of Cell Proliferation in vitro**

Cell Counting Kit-8 (CCK-8, Boster Biological Technology, Wuhan, China) was used to assess cell viability, while cell proliferation was assessed using 5-Ethynyl-2′- deoxyuridine (EDU) incorporation assay (RiboBio, Guangzhou, China). For CCK-8 assay, 5×103 cells were seeded in a 96-well plate and cultured overnight, followed by incubation with 10 μL of CCK-8 reagents per each well for additional 3 h at 37°C. Cell viability was evaluated by measuring the absorbance at a 450-nm wavelength using a microplate spectrophotometer (BioRad, USA). For EDU assay, HaCaT cells were cultured at a density of 4 × 103 cells per well in a 96-well plate overnight. Afterwards, cells were incubated with 50 μM EdU for 2 h, followed by fixation with paraformaldehyde. After sequential staining with Apollo reaction solution and Hoechst 33342 (5 mg/mL), cells were washed with 100 μL of PBS for 3 times and photographed under a fluorescence microscope (Olympus, Tokyo, Japan). Five random fields were taken from each slide to count the EdU positive cells. Rates of EdU-positive cells were calculated by (EdU add-in cells/Hoechst stained cells) × 100%.

**Quantitative RT-PCR**

Total RNA was isolated using Trizol (Takara, Ohtsu, Japan), then first strand of cDNA synthesis was carried out using a PrimeScript TM RT Master Mix Kit (Takara, Ohtsu, Japan) according to the manufacturer’s instructions. The reaction was performed at 37°C for 15 min and terminated by heating at 85°C for 5 s. Quantitative RT-PCR was performed in a LightCycler 480 Real-Time PCR system (Roche, Indianapolis, IN, USA), and the PCR conditions were 40 cycles of amplification (95°C, 15 s; 60°C, 1 min; and 72°C, 2 min).The relative amount of mRNA was calculated using the 2-ΔΔCt method with glyceraldehyde 3-phosphate dehydrogenase (GAPDH) as an internal control. Primer sequences are shown in Table 1.

**Simple Western Analysis**

The total protein was extracted from HaCaT cells, using RIPA lysis containing 1% PMSF and phosphatase inhibitor (DSL, Webster, USA). Protein concentrations were measured using a BCA Protein Assay kit (Sigma, USA). A Wes system (12–230 kDa separation module; ProteinSimple, Silicon Valley, USA) was used to measure expression levels of respective proteins. After heating a mixture containing 1 part of 5× fluorescent master mix and 4 parts diluted lysate at 95°C for 5 min, the mixture together with primary antibody, secondary conjugate, strepavidin-HRP or NIR and Luminol-Peroxide Mix were added to a 25-well plate. The concentrations of Primary antibodies were phospho-PI3K (1:500; Abcam), PI3K (1:1,000; Abcam), phospho-AKT (S473) (1:1,000; Abcam), AKT (1:2,000; Abcam), and β-actin (1:1,000; Abcam). Western blot bands were analyzed using Compass software (ProteinSimple). β-Actin served as a loading control.

**In vitro Scratch-Wound-Closure Assay**

After co-culture of DMSCs with HaCaTcells for 72 h, HaCaT cells were seeded into 6-well dishes at a density of 2 × 105 cells per well. When the cells reached 100% confluence, the monolayers were scratched using a sterile 200 μL pipette tip, followed by gently washing twice with PBS to remove cell debris. Subsequently, the cells were incubated with serum-free medium at 37°C in a 5% CO2 air atmosphere for 48 h. Images were taken at 0 h, 24 h, and 48 h time points, and the migration area of HaCaT cells were measured using Image J software.

### Transwell Cell Migration Assays

Transwell chamber (6.5-mm diameter, 8-μm pore size) was used to assess cell migration. After co-culture of DMSCs with HaCaTcells for 72 h, 200 µl HaCaT cell suspension (1 × 105) prepared in serum-free medium was added into the upper chamber, whereas 500 µL DMEM-F12 supplemented with 10% FBS was added into the lower chamber. After a 24-h incubation at 37 °C, cotton swab cells were used to remove the non-migrating cells. The migratory cells on the lower side of membrane were fixed in 4% paraformaldehyde and stained with 0.5% crystal violet solution. The cell number in five random fields was counted under a microscope (Olympus, Tokyo, Japan) and the average number was calculated.

**Enzyme-Linked Immunosorbent Assay**

The concentrations of stem cell factor (SCF), epidermal growth factor (EGF) and interleukin 11 (IL-11) in the cell co-culture supernatants were measured using Quantikine enzyme-linked immunosorbent assay kits for EGF, SCF, and IL-11, respectively, according to the manufacturer’s instructions. All results were normalized to the total protein content.

**Statistical Analysis**

Data were presented as the mean ± standard error of mean (SEM) of 6 separate experiments. Statistical analyses were performed using Student’s *t* test or one-way analysis of variance (ANOVA). *p* values < 0.05 were considered statistically significant.