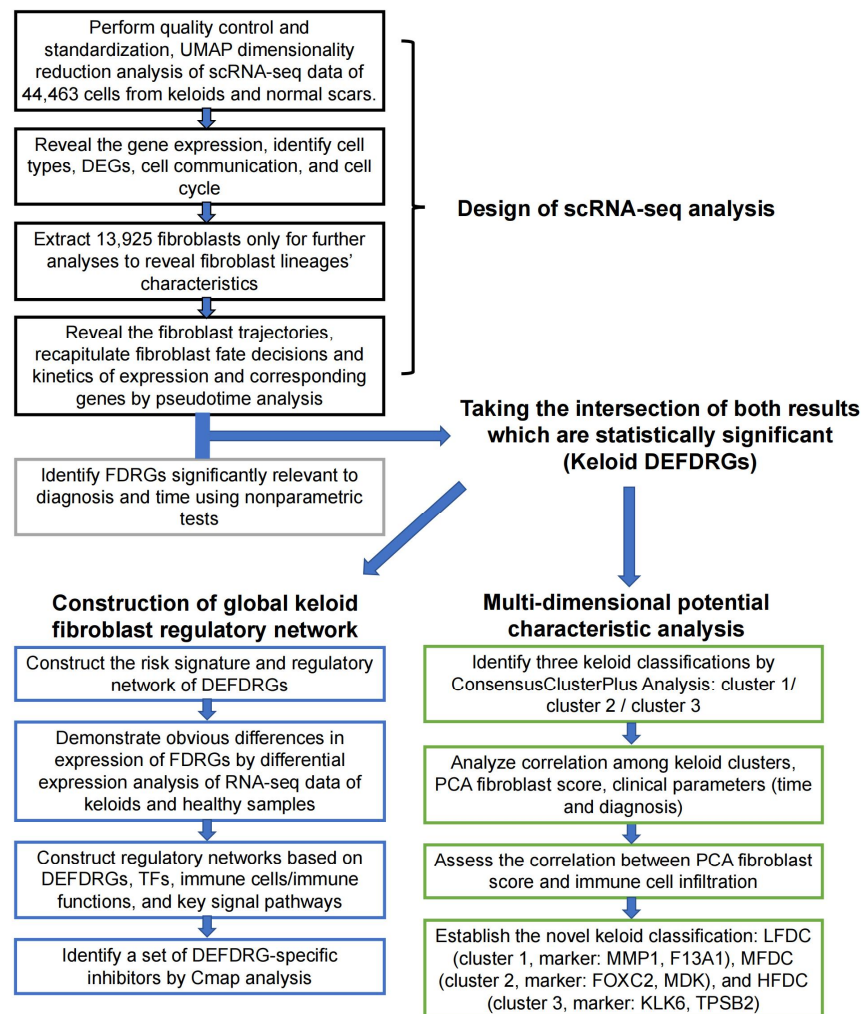
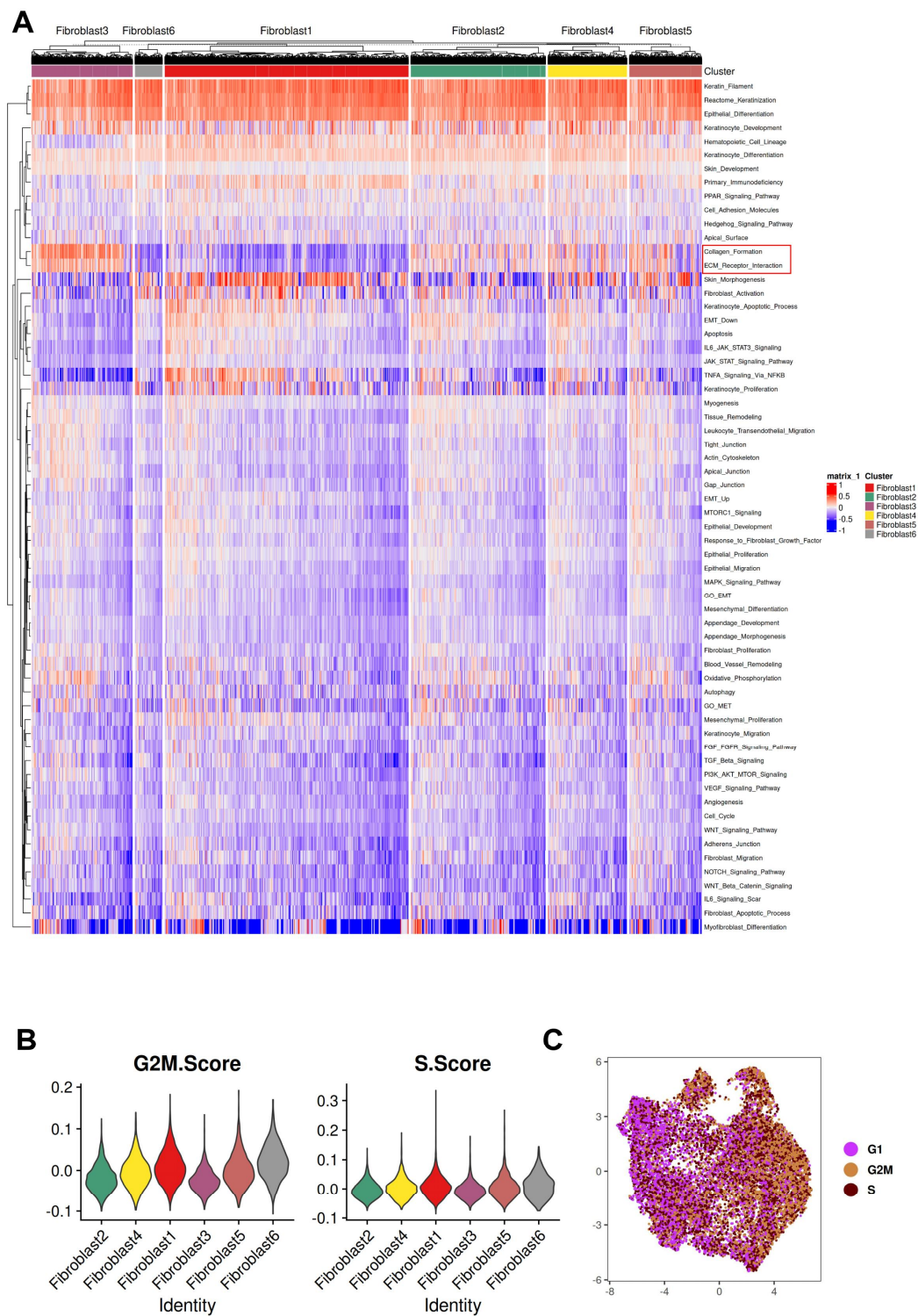


Supplementary Materials

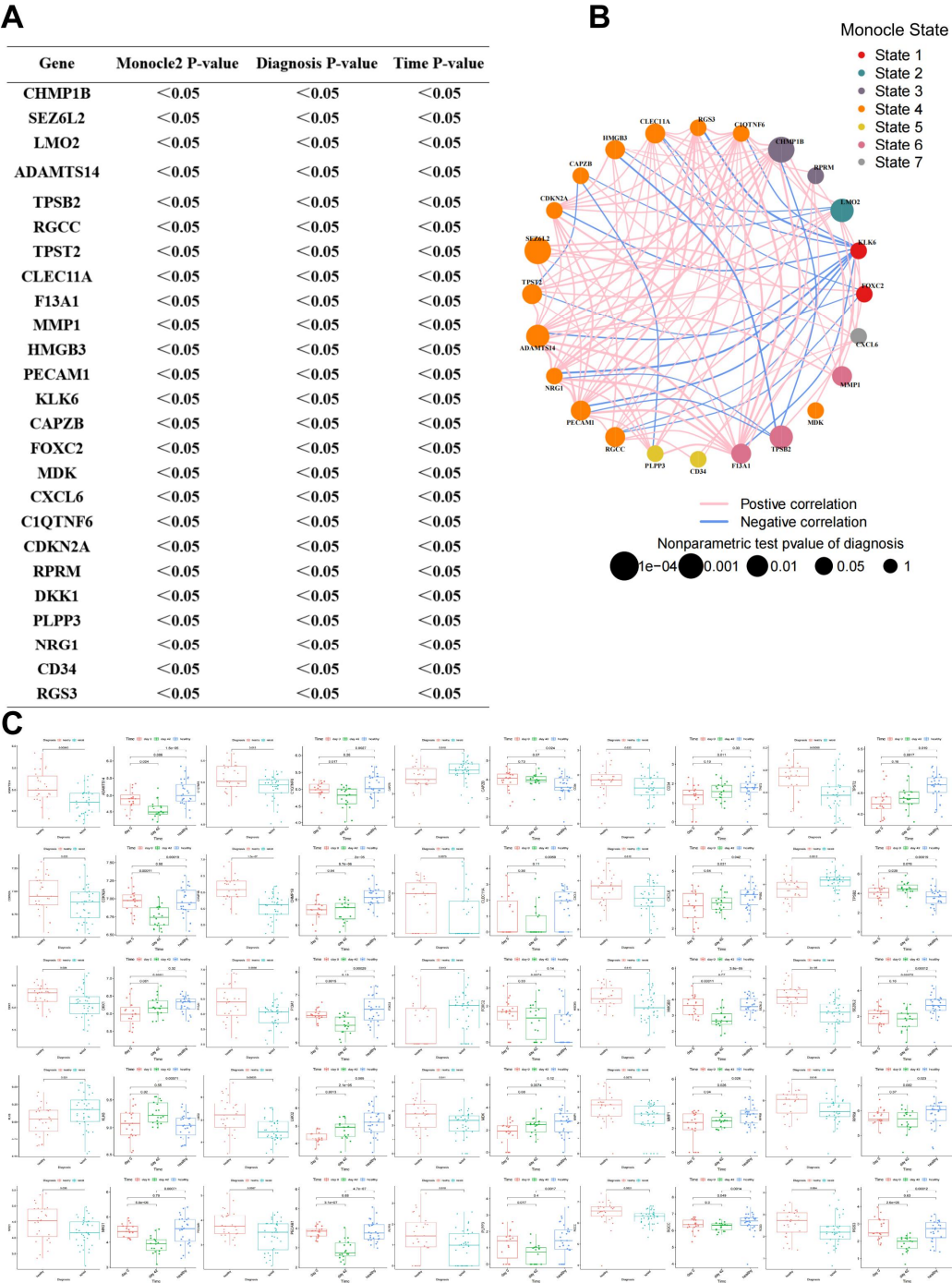


Supplementary Figure 1. The flow chart of the study (related to Figure 1A). (LFDC: Low Fibroblast Differentiation Classification; MFDC: Moderate Fibroblast Differentiation Classification; HFDC: High Fibroblast Differentiation Classification; PCA: principal component analysis; DEFDRGs: Differentially Expressed Fibroblast-Differentiation-Related Genes; UMAP: Uniform Manifold Approximation and Projection; DEGs: Differentially Expressed Genes; scRNA-seq: single-cell RNA sequencing)

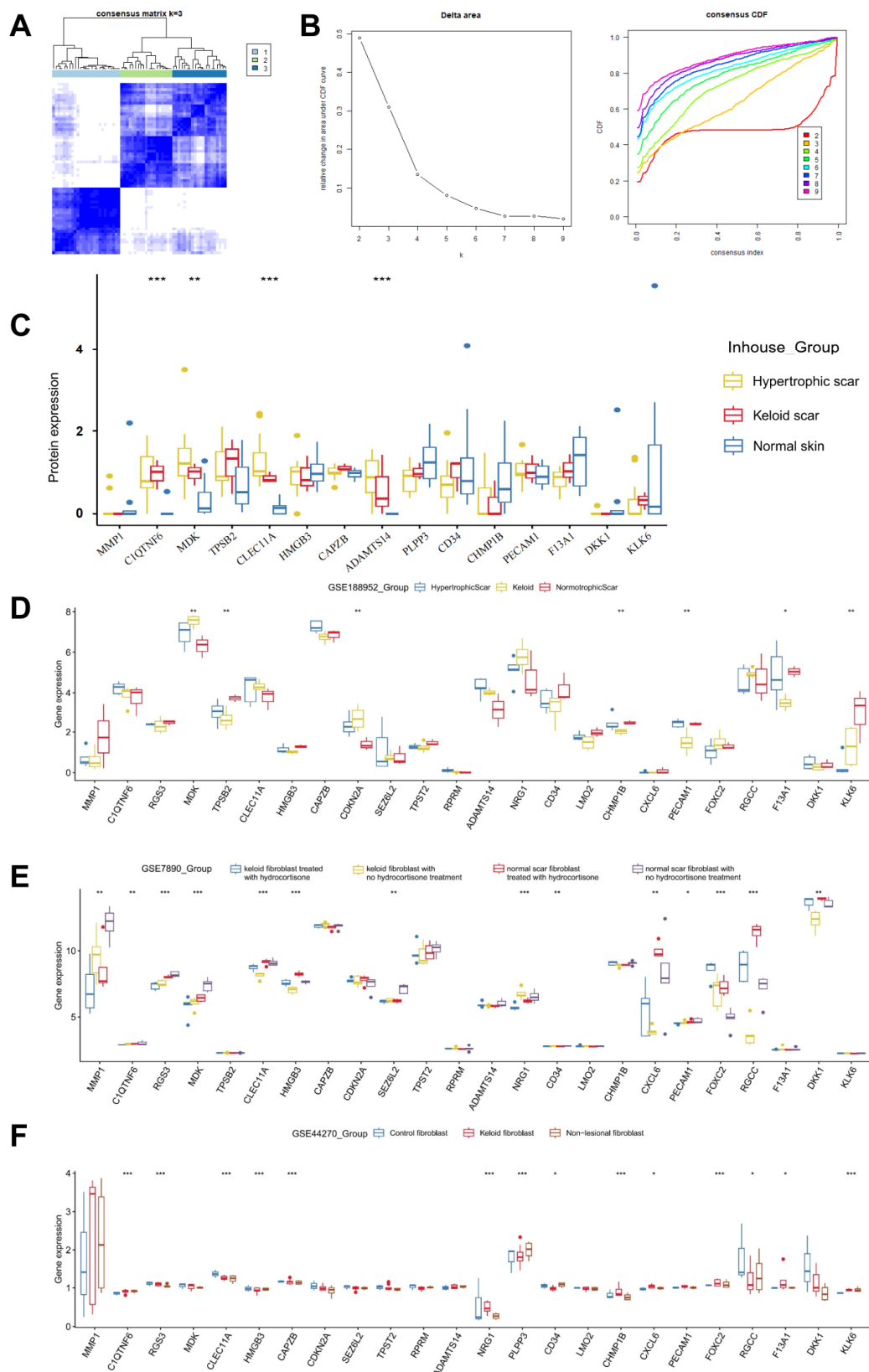
patterns of canonical genes (*DCN*, *KRT1*, *PTPRC*, *VWF*) across distinct cell types; adjacent histograms quantify the proportional distribution of each cell type in different samples. (D) The incoming and outgoing interaction strength of different cells. (DEGs: Differentially Expressed Genes; KL: Keloid; NS: Normal Skin)



Supplementary Figure 3. Signaling pathway enrichment and cell cycle analysis in fibroblast subtypes (related to Figure 2) (A) Hallmark signaling pathway enrichment in fibroblast clusters, showing collagen formation and ECM-receptor interaction as significantly enriched pathways in Fibroblast 3. (B-C) Distribution of cell cycle phases (G1, S, G2/M) across fibroblast subpopulations. (ECM: Extracellular Matrix)

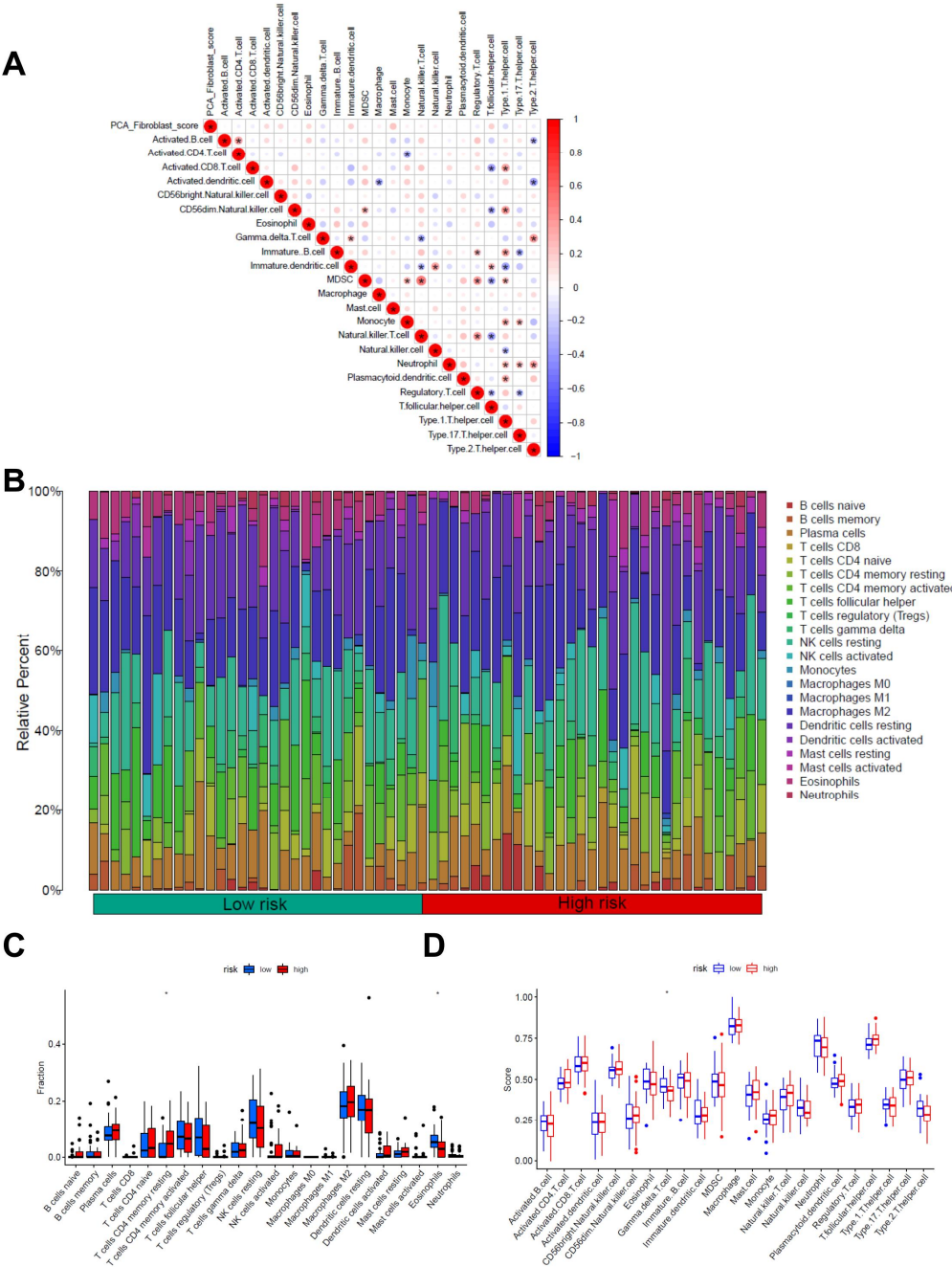


Supplementary Figure 4. Identification of DEFDRGs (related to Figure 3). (A) The list of 25 DEFDRGs. (B) Regulatory network for 25 DEFDRGs. Pink curve: positive correlation. Blue curve: negative correlation. (C) Differential expression analysis of 25 DEFDRGs across clinical diagnosis groups and time points. (DEFDRGs: Differentially Expressed Fibroblast-Differentiation-Related Genes)



Supplementary Figure 5. Consensus clustering and verification in public databases (related to Figure 4). (A) Consensus clustering of samples based on 25 DEFRG expression profiles. (B) Clustering validity assessment demonstrating optimal specificity at

$k = 3$. (C) Differential expression of DEFDRG-encoded proteins across normal skin, hypertrophic scars, and keloids. (D-F) Validation of DEFDRG expression using public sequencing datasets, showing significant differential expression for the majority of 25 DEFDRGs across three independent cohorts. (DEFDRG: Differentially Expressed Fibroblast-Differentiation-Related Gene)



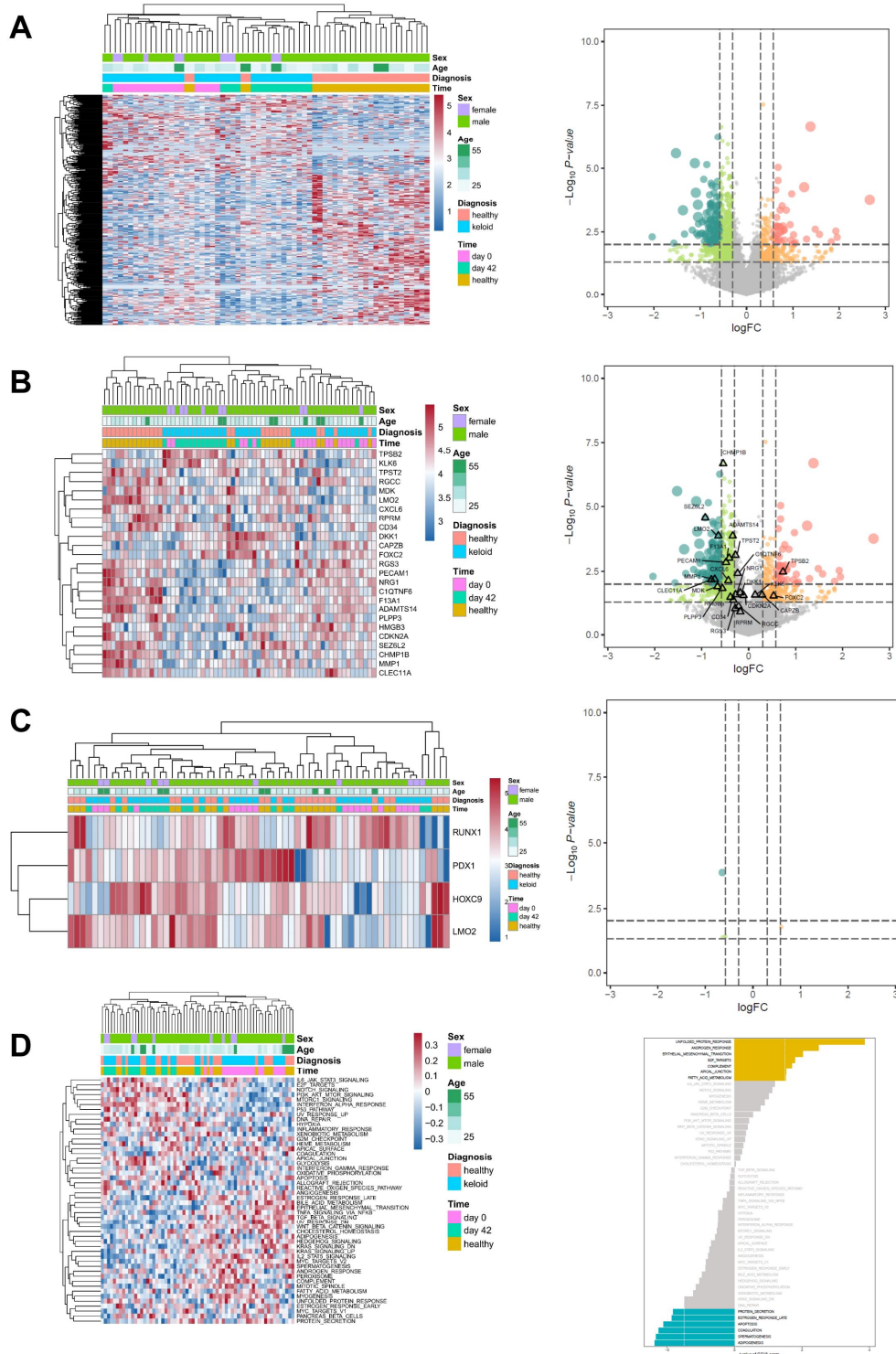
Supplementary Figure 6. Immune cell infiltration analysis in keloid risk groups. (A)

Co-expression heatmap depicting correlations between PCA-derived fibroblast scores and

immune cell. (B) Relative proportions of immune cell subtypes in high- vs. low-risk groups.

(C-D) Quantification of immune cell infiltration levels and functional scores, comparing

high-risk versus low-risk keloid subgroups. (PCA: principal component analysis)



Supplementary Figure 7. Identification of DEGs, DETFs, and signaling pathways. (A) Expression profiles of DEGs across clusters stratified by sex, age, diagnosis, and time. (B) Expression patterns of 25 DETDRGs in clusters categorized by sex, age, diagnosis, and time. (C) Differential expression of DETFs across clusters defined by clinical parameters (sex, age, diagnosis, time). (D) GSVA-based pathway scoring of 50 hallmark signaling

pathways in clusters stratified by sex, age, diagnosis, and time, with bar plots depicting pathway enrichment scores. DEGs: Differentially Expressed Genes; DETFs: Differentially Expressed Transcription Factors; GSVA: Gene Set Variation Analysis)

Supplementary Table 1. Baseline characteristics of patients with clinical keloids, hypertrophic scars, and normal skin.

Sample-ID	Group	Age	Sex	Location
SC211-9	Hypertrophic scar	6	male	lower extremity
SC117-7	Hypertrophic scar	54	male	lower extremity
SC116-7	Hypertrophic scar	54	male	perioral area
SC144-5	Hypertrophic scar	60	male	upper extremity
SC168-4	Hypertrophic scar	8	male	lower abdomen
SC154-2	Hypertrophic scar	25	male	upper extremity
SC158-3	Hypertrophic scar	22	female	lower extremity
SC55-4	Hypertrophic scar	57	female	lower extremity
SC70-6	Hypertrophic scar	34	male	lower extremity
SC68-3	Hypertrophic scar	34	male	abdomen
SC215-4	Hypertrophic scar	18	female	lumbar and dorsal region
SC216-6	Hypertrophic scar	61	male	neck
SC171-2	Hypertrophic scar	12	male	perineum
SC66-6	Hypertrophic scar	49	female	upper extremity
SC203-3	Hypertrophic scar	44	male	upper extremity
NOR202-1	Normal skin	44	female	lower extremity
NOR208-4	Normal skin	20	male	prepuce
NOR207-2	Normal skin	51	male	prepuce
NOR197-3	Normal skin	28	male	abdomen
NOR58-12	Normal skin	88	female	lower extremity
NOR164-9	Normal skin	72	male	lower extremity
NOR164-16	Normal skin	72	male	lower extremity
NOR205-2	Normal skin	/	male	prepuce
SC167-4	keloid	73	male	chest
SC136-3	keloid	67	male	upper extremity
SC141-7	keloid	63	female	chest

Supplementary Table 2. Public database datasets for validating differential expression of 25 DEFDRGs.

GEO ID	Sequencing type	Sample number	Sample information	Detected gene of 25 DEFDRGs	DEG Number	Proportion of DEG	Reference
GSE188952	RNA sequencing	12	tissues of normotrophic scars, hypertrophic scars, and keloids	24	7	29.2%	/
GSE7890	Microarray	19	fibroblasts of normal scars and keloids	24	14	58.3%	PMID: 17989729
GSE44270	Microarray	32	fibroblasts of keloid scars, adjacent non-keloid skins, and normal skins	24	14	58.3%	PMID: 23815228

DEFDRGs: Differentially Expressed Fibroblast-Differentiation-Related Genes; DEGs: Differentially Expressed Genes