

**Table SI.** GO functional enrichment analysis of proteins interacting with TM4SF1 and DDR1.

| Ontology | ID         | Description                                                   | Adjusted P-value       | geneID                                                                                   | Count |
|----------|------------|---------------------------------------------------------------|------------------------|------------------------------------------------------------------------------------------|-------|
| BP       | GO:0043062 | Extracellular structure organization                          | 2.13x10 <sup>-9</sup>  | CDH1/COL5A2/COL1A1/COL3A1/NOTCH1/ADAM10/COL5A1/COL4A1/ITGA2/ITGB5/ITGA5/COL2A1/DDR1/APOM | 14    |
| BP       | GO:0030198 | Extracellular matrix organization                             | 3.54x10 <sup>-9</sup>  | CDH1/COL5A2/COL1A1/COL3A1/NOTCH1/ADAM10/COL5A1/COL4A1/ITGA2/ITGB5/ITGA5/COL2A1/DDR1      | 13    |
| BP       | GO:0007229 | Integrin-mediated signaling pathway                           | 3.71x10 <sup>-6</sup>  | COL3A1/PTPN11/ADAM10/ITGA2/ITGB5/ITGA5/CD63                                              | 7     |
| BP       | GO:0038065 | Collagen-activated signaling pathway                          | 1.04x10 <sup>-5</sup>  | COL1A1/COL4A1/ITGA2/DDR1                                                                 | 4     |
| BP       | GO:0030199 | Collagen fibril organization                                  | 7.86x10 <sup>-5</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL2A1                                                       | 5     |
| BP       | GO:0071230 | Cellular response to amino acid stimulus                      | 2.10x10 <sup>-4</sup>  | ZEB1/COL5A2/COL1A1/COL3A1/COL4A1                                                         | 5     |
| BP       | GO:0007492 | Endoderm development                                          | 3.15x10 <sup>-4</sup>  | COL5A2/NOTCH1/COL5A1/ITGB5/ITGA5                                                         | 5     |
| BP       | GO:0038063 | Collagen-activated tyrosine kinase receptor signaling pathway | 3.71x10 <sup>-4</sup>  | COL1A1/COL4A1/DDR1                                                                       | 3     |
| BP       | GO:0001101 | Response to acid chemical                                     | 3.75x10 <sup>-4</sup>  | ZEB1/COL5A2/COL1A1/COL3A1/COL4A1/ITGA2/PTGS2/CD9                                         | 8     |
| BP       | GO:0031589 | Cell-substrate adhesion                                       | 4.27x10 <sup>-4</sup>  | COL1A1/COL3A1/NOTCH1/ITGA2/ITGB5/ITGA5/CD63/DDR1                                         | 8     |
| CC       | GO:0098644 | Complex of collagen trimers                                   | 8.04x10 <sup>-10</sup> | COL5A2/COL1A1/COL3A1/COL5A1/COL4A1/COL2A1                                                | 6     |
| CC       | GO:0005583 | Fibrillar collagen trimer                                     | 2.07x10 <sup>-9</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL2A1                                                       | 5     |
| CC       | GO:0098643 | Banded collagen fibril                                        | 2.07x10 <sup>-9</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL2A1                                                       | 5     |
| CC       | GO:0044420 | Extracellular matrix component                                | 1.26x10 <sup>-7</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL4A1/COL2A1                                                | 6     |

|    |                |                                                                               |                        |                                                                                   |    |
|----|----------------|-------------------------------------------------------------------------------|------------------------|-----------------------------------------------------------------------------------|----|
| CC | GO:00<br>05788 | Endoplasmic reticulum<br>lumen                                                | 2.13x10 <sup>-6</sup>  | COL5A2/COL1A1/COL3A1/ADAM10/COL<br>5A1/COL4A1/CDH2/COL2A1/PTGS2                   | 9  |
| CC | GO:00<br>05581 | Collagen trimer                                                               | 2.20x10 <sup>-6</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL4<br>A1/COL2A1                                     | 6  |
| CC | GO:00<br>05925 | Focal adhesion                                                                | 1.07x10 <sup>-3</sup>  | ADAM10/CDH2/ITGA2/ITGB5/ITGA5/TSP<br>AN4/CD9                                      | 7  |
| CC | GO:00<br>62023 | Collagen-containing<br>extracellular matrix                                   | 1.07x10 <sup>-3</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL4<br>A1/CDH2/COL2A1                                | 7  |
| CC | GO:00<br>08305 | Integrin complex                                                              | 1.07x10 <sup>-3</sup>  | ITGA2/ITGB5/ITGA5                                                                 | 3  |
| CC | GO:00<br>05924 | Cell-substrate adherens<br>junction                                           | 1.07x10 <sup>-3</sup>  | ADAM10/CDH2/ITGA2/ITGB5/ITGA5/TSP<br>AN4/CD9                                      | 7  |
| MF | GO:00<br>48407 | Platelet-derived growth<br>factor binding                                     | 4.84x10 <sup>-11</sup> | COL1A1/COL3A1/COL5A1/COL4A1/COL2<br>A1                                            | 5  |
| MF | GO:00<br>05178 | Integrin binding                                                              | 5.82x10 <sup>-11</sup> | COL3A1/ADAM10/COL5A1/ITGA2/ITGB5/<br>ITGA5/TSPAN4/CD9/TSPAN8                      | 9  |
| MF | GO:00<br>30020 | Extracellular matrix<br>structural constituent<br>conferring tensile strength | 1.06x10 <sup>-9</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL4<br>A1/COL2A1                                     | 6  |
| MF | GO:00<br>50839 | Cell adhesion molecule<br>binding                                             | 4.72x10 <sup>-9</sup>  | CDH1/COL3A1/PTPN11/ADAM10/COL5A1<br>/CDH2/ITGA2/ITGB5/ITGA5/TSPAN4/CD9/<br>TSPAN8 | 12 |
| MF | GO:00<br>19838 | Growth factor binding                                                         | 1.60x10 <sup>-6</sup>  | COL1A1/COL3A1/COL5A1/COL4A1/SHC1/<br>COL2A1                                       | 6  |
| MF | GO:00<br>05201 | Extracellular matrix<br>structural constituent                                | 4.37x10 <sup>-6</sup>  | COL5A2/COL1A1/COL3A1/COL5A1/COL4<br>A1/COL2A1                                     | 6  |
| MF | GO:00<br>43394 | Proteoglycan binding                                                          | 1.18x10 <sup>-4</sup>  | COL5A1/ITGA2/COL2A1                                                               | 3  |
| MF | GO:00<br>05165 | Neurotrophin receptor<br>binding                                              | 3.06x10 <sup>-4</sup>  | FRS2/SHC1                                                                         | 2  |
| MF | GO:00<br>30898 | Actin-dependent ATPase<br>activity                                            | 4.48x10 <sup>-4</sup>  | MYO10/MYH10                                                                       | 2  |
| MF | GO:00<br>45295 | Gamma-catenin binding                                                         | 4.48x10 <sup>-4</sup>  | CDH1/CDH2                                                                         | 2  |

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The top 10 BP, CC and MF results sorted by adjusted P-value are presented. GO, Gene Ontology; TM4SF1,

transmembrane 4 L6 family member 1; DDR1, discoidin domain receptor 1; BP, biological process; CC, cellular constituent; MF, molecular function.

**Table SII.** Kyoto Encyclopedia of Genes and Genomes pathway enrichment analysis of proteins interacting with TM4SF1 and DDR1.

| ID       | Description                                            | Adjusted P-value      | Count |
|----------|--------------------------------------------------------|-----------------------|-------|
| hsa04510 | Focal adhesion                                         | $2.62 \times 10^{-5}$ | 8     |
| hsa05205 | Proteoglycans in cancer                                | $2.62 \times 10^{-5}$ | 8     |
| hsa04512 | ECM-receptor interaction                               | $2.62 \times 10^{-5}$ | 6     |
| hsa04974 | Protein digestion and absorption                       | $3.10 \times 10^{-5}$ | 6     |
| hsa05165 | Human papillomavirus infection                         | $4.47 \times 10^{-5}$ | 9     |
| hsa05412 | Arrhythmogenic right ventricular cardiomyopathy (ARVC) | $3.32 \times 10^{-3}$ | 4     |
| hsa04151 | PI3K-Akt signaling pathway                             | $4.13 \times 10^{-3}$ | 7     |
| hsa05222 | Small cell lung cancer                                 | $4.95 \times 10^{-3}$ | 4     |
| hsa04640 | Hematopoietic cell lineage                             | $5.45 \times 10^{-3}$ | 4     |
| hsa04933 | AGE-RAGE signaling pathway in diabetic complications   | $5.45 \times 10^{-3}$ | 4     |
| hsa05206 | MicroRNAs in cancer                                    | $8.72 \times 10^{-3}$ | 6     |
| hsa04926 | Relaxin signaling pathway                              | $1.18 \times 10^{-2}$ | 4     |
| hsa04145 | Phagosome                                              | $1.97 \times 10^{-2}$ | 4     |
| hsa05100 | Bacterial invasion of epithelial cells                 | $1.97 \times 10^{-2}$ | 3     |
| hsa05220 | Chronic myeloid leukemia                               | $2.07 \times 10^{-2}$ | 3     |
| hsa05410 | Hypertrophic cardiomyopathy (HCM)                      | $3.13 \times 10^{-2}$ | 3     |
| hsa05414 | Dilated cardiomyopathy (DCM)                           | $3.53 \times 10^{-2}$ | 3     |
| hsa01522 | Endocrine resistance                                   | $3.53 \times 10^{-2}$ | 3     |
| hsa05146 | Amoebiasis                                             | $3.59 \times 10^{-2}$ | 3     |
| hsa05130 | Pathogenic <i>Escherichia coli</i> infection           | $3.59 \times 10^{-2}$ | 4     |
| hsa04810 | Regulation of actin cytoskeleton                       | $4.12 \times 10^{-2}$ | 4     |
| hsa05216 | Thyroid cancer                                         | $4.25 \times 10^{-2}$ | 2     |
| hsa04722 | Neurotrophin signaling pathway                         | $4.72 \times 10^{-2}$ | 3     |
| hsa05219 | Bladder cancer                                         | $4.75 \times 10^{-2}$ | 2     |
| hsa04611 | Platelet activation                                    | $4.85 \times 10^{-2}$ | 3     |

TM4SF1, transmembrane 4 L6 family member 1; DDR1, discoidin domain receptor 1; ECM, extracellular matrix; AGE-RAGE, advanced glycation end-products-receptor for advanced glycation end-products.