Supplementary Materials and Methods

**Antibodies.** Anti-α-SMA (1A4) and anti-SDF-1 (79018) monoclonal antibodies for immunocytochemistry were purchased from R&D Systems Inc., Minneapolis, MN, USA. Anti-Pan-Keratin (C11) and anti-vimentin (R28) monoclonal antibodies were obtained from Cell Signaling Technology, Inc., Beverly, Massachusetts, USA. Anti-FAPα anti-collagen I (5D8), were obtained from Abcam Inc., Cambridge, MA, USA. Human cytokine antibody array kits were obtained from RayBiotech, Norcross, GA, USA. Rabbit anti-human Cav-1 (N-20) polyclonal antibody for Western blot and immunohistochemistry, as well as anti-β-actin (N-21) for Western blot, were obtained from Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA. Phycoerythrin (PE)-conjugated secondary antibody for flow cytometry and the Alexa Fluor secondary antibody used for immunocytochemistry were purchased from Invitrogen Corp., Carlsbad, Calif., USA.

**Indirect immunocytochemistry of cultured cells.** Cells cultured on the glass cover slips were washed thrice with PBS, fixed in 4% (weight/vol) paraformaldehyde in PBS (PFA/PBS; Sigma-Aldrich, St. Louis, MO, USA) for 10 min at room temperature, and then washed again thrice in PBS after reaching confluence. The cells were permeabilized with 0.1% (vol/vol) Triton X-100/PBS (Amresco Inc., Cleveland, Ohio, USA) for 10 min at room temperature. Afterward, the cells were washed thrice in PBS and incubated with 3% (weight/vol) bovine serum albumin (BSA)/0.3 M glycine in PBS (Sigma-Aldrich) for 2 h at room temperature to reduce the nonspecific binding of primary antibodies. Subsequently, 200 μl of the appropriate primary antibody, diluted in 3% (weight/vol) BSA/PBS, was placed on each cover slip, and then incubated overnight at 4°C. The cover slips were then washed thrice for 15 min each with PBS and were incubated with 200 μl of the secondary antibody (Alexa Fluor 488) diluted 1:2000 with 3% (weight/vol) BSA/PBS for 2 h at room temperature. Afterward, the cover slips were washed thrice for
5 min each with PBS and counter-stained with DAPI (0.1 μg/ml in PBS; Roche) for 1 min to visualize the nuclei. A final series of three 5 min washes with PBS was performed, after which, the cover slips were mounted on 1.5 μl Bio-Rad FluoroGuard™ Anti-fade Reagent (Bio-Rad, Hercules, CA, USA). The cover slips were sealed with nail polish.

**Proliferation assay.** A total of 3,000 AGS and MKN45 cells per well were seeded in 96-well plates and cultured in RPMI 1640 with 10% FCS. Then the medium was changed to serum-free RPMI for overnight incubation. Concentrated CM of the fibroblasts was added to AGS and MKN45 cells at various concentrations (0.25, 0.5, and 1.0 μg/μL), and serum-free RPMI 1640 or 10% FCS was added to the control wells. The cells were grown in a humidified atmosphere of 5% CO2 at 37°C. The cell growth of the AGS and MKN45 cell lines was each analyzed at 72 h with the CCK-8 reagent (Sigma-Aldrich) added 1 h before taking the spectrophotometric reading, according to the manufacturer's instructions

**Invasion assay.** BioCoat Matrigel-coated invasion chambers (BD Biosciences) were used to study cell invasiveness. Briefly, 1×10⁵ AGS or MKN45 cells in 500 μL serum-free medium was added to the upper chamber. The medium containing RPMI 1640, 10% FCS, or concentrated CM of the fibroblasts (0.25, 0.5, and 1.0 μg/μL) was added into the lower chamber. Serum-free medium was added to the lower chamber of the control wells. The cells were allowed to traverse the Matrigel for 72 h at 37°C in an environment with 5% CO₂. The non-invading cells on the upper surface of the membrane were removed with a cotton swab, and the filters were fixed in 0.1% glutaraldehyde and stained with 0.2% crystal violet. The number of cells that migrated to the lower side of the filter was counted under an upright microscope (Nikon Optiphot) using Image-Pro Plus 4.5 software (Media Cybernetics, Silver Spring, MD, USA). The whole area was counted per filter.
### Supplementary Table S1. Basic characteristics of 120 gastric cancer patients.

<table>
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<tr>
<th>Variables</th>
<th>Number (%)</th>
<th>5-year survival rate (%)</th>
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<tr>
<td><strong>Age (y)</strong></td>
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<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>49 (41)</td>
<td>50</td>
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<tr>
<td>≥60</td>
<td>71 (59)</td>
<td>43</td>
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<tr>
<td><strong>Sex</strong></td>
<td></td>
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<tr>
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<td>74 (68)</td>
<td>51</td>
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<tr>
<td>Female</td>
<td>36 (32)</td>
<td>30</td>
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<td><strong>H pylori infection</strong></td>
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<tr>
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<td>53 (58)</td>
<td>49</td>
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<tr>
<td>positive</td>
<td>38 (42)</td>
<td>52</td>
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<tr>
<td><strong>Size(cm)</strong></td>
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<td></td>
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<tr>
<td>&lt;5</td>
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<td>≥5</td>
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<tr>
<td><strong>Histologic type</strong></td>
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<td></td>
</tr>
<tr>
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<td>57</td>
</tr>
<tr>
<td>Poorly and others*</td>
<td>46 (38)</td>
<td>25</td>
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<td><strong>Lauren classification</strong></td>
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<td>positive</td>
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<td><strong>Depth of tumor(T)</strong></td>
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<td>T1+ T2</td>
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<td>81</td>
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<tr>
<td>T3+ T4</td>
<td>92 (77)</td>
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<td><strong>Lymph node metastasis (N)</strong></td>
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<td>57</td>
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<tr>
<td>N2+ N3</td>
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<td><strong>Distant metastasis(M)</strong></td>
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<td>M0</td>
<td>107 (89)</td>
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<td>M1</td>
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<td><strong>TNM stage</strong></td>
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Note: *H. pylori* status was determined histologically and/or serologically. GEJ: gastroesophageal junction. The TNM stage of GC was determined according to the classification system of the International Union Against Cancer (7th edition). *Other histologic types of gastric cancer mainly included mucinous adenocarcinomas and signet-ring cell carcinomas, according to the World Health Organization (WHO) classifications.
### Supplementary Table S2. Patient Characteristics of Primary Fibroblast Cultures

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<th>NO.</th>
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<th>Age (y)</th>
<th>Histological Type</th>
<th>Location</th>
<th>Lauren Classification</th>
<th>Tumor Stage</th>
<th>Adjacent Tissue</th>
<th>H. p Status</th>
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<td>1</td>
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<td>79</td>
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<td>Antrum</td>
<td>IGC</td>
<td>T4a N2 M0</td>
<td>CG with IM</td>
<td>Neg</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>61</td>
<td>P</td>
<td>Corpus</td>
<td>IGC</td>
<td>T3 N0 M0</td>
<td>CG</td>
<td>Pos</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>52</td>
<td>P</td>
<td>Antrum</td>
<td>MGC</td>
<td>T3 N3b M0</td>
<td>CG</td>
<td>Neg</td>
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<tr>
<td>4</td>
<td>Male</td>
<td>58</td>
<td>M</td>
<td>Antrum</td>
<td>DGC</td>
<td>T3 N2 M1</td>
<td>CG</td>
<td>Neg</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>54</td>
<td>M</td>
<td>Antrum</td>
<td>IGC</td>
<td>T3 N3a M0</td>
<td>CG</td>
<td>Pos</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>48</td>
<td>P</td>
<td>Corpus</td>
<td>IGC</td>
<td>T3 N0 M0</td>
<td>CG</td>
<td>ND</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>67</td>
<td>M</td>
<td>Corpus</td>
<td>DGC</td>
<td>T3 N3a M1</td>
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<td>8</td>
<td>Male</td>
<td>59</td>
<td>M</td>
<td>Antrum</td>
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<td>T4 N1 M0</td>
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<td>9</td>
<td>Male</td>
<td>84</td>
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<td>10</td>
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<td>M</td>
<td>GEJ</td>
<td>DGC</td>
<td>T2 N2 M0</td>
<td>CG</td>
<td>Neg</td>
</tr>
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</table>

Note: M-moderately differentiated; P-poorly differentiated; IGC- Intestinal gastric cancer; DGC-diffuse gastric cancer; MGC-mixed gastric cancer; T-tumor; N-lymph node; M- metastasis. IM-Intestinal metaplasia; CG-Chronic gastritis; Neg, negative; Pos, positive; ND, not determined;
### Supplementary Table S3. Expression difference of soluble mediators in the Media of GCAFs and GIAFs

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<tr>
<td>IL-2</td>
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<td>IL-3</td>
<td>1.25</td>
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<td>IL-4 *</td>
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<td>IL-5</td>
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<tr>
<td>IL-7 *</td>
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<td>interleukin 8</td>
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<td>interleukin 12A</td>
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<td>IL-12P40 *</td>
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<td>interleukin 12B</td>
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<td>IL-13</td>
<td>1.30</td>
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<td>IL-15</td>
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<td>interleukin 15</td>
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<tr>
<td>IL-1ra</td>
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<td>IL-2sRa *</td>
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<td>macrophage migration inhibitory factor</td>
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<td>TPO</td>
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<td>thrombopoietin</td>
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<td><strong>Signal Proteins</strong></td>
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<td>Protein Name</td>
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<td>---------</td>
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*GCAFs/GIAFs ratio of more than 1.3 folds; # confirmation by ELISA.
### Supplementary Table S4. Differentially Expressed Proteins in GCAFs and GIAFs by 2D-Nano-LC-ESI-MS/MS

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Forty-five up-regulated proteins in GCAFs

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| P07093 | 2     | Glia-derived nexin           | 2.78 | 2.35 | 2.46 |
| P05067 | APP | Amyloid beta A4 protein | 2.16 | 2.79 | 2.42 |
| Q9HBL0 | TNS1 | Tensin-1 | 2.29 | 2.82 | 2.74 |
| Q9Y570 | ETHE1 | Protein ETHER1, mitochondrial | 2.1 | 2.39 | 2.93 |
| P09846 | SPARC | SPARC | 2.94 | 1.62 | 1.77 |
| P07814 | 2PRCE | Bifunctional aminoacyl-tRNA synthetase | 3.13 | 2.02 | 2.47 |
| Q9Y570 | PPME1 | Protein phosphatase methylesterase 1 | 2.94 | 2.71 | 3.16 |
| Q8IYD1 | TNS1 | Tensin-1 | 2.29 | 2.82 | 2.74 |
| P61254 | RPL26 | 60S ribosomal protein L26 | 2.2 | 2.83 | 3.39 |
| P26373 | RPL13 | 60S ribosomal protein L13 | 3.42 | 2.4 | 2.43 |
| P40429 | RPL13A | 60S ribosomal protein L13a | 2.98 | 2.96 | 3.48 |
| P42677 | RPS27 | 40S ribosomal protein S27 | 3.55 | 2.2 | 2.23 |
| Q9Y5M8 | SRPRB | Signal recognition particle receptor subunit beta | 3.63 | 3.48 | 2.44 |
| P09619 | PDGFRB | Beta-type platelet-derived growth factor receptor | 2.15 | 2.33 | 3.71 |
| P56134 | ATP5J2 | ATP synthase subunit f, mitochondrial | 2.4 | 3.83 | 3.32 |
| Q16851 | UGP2 | UTP-glucose-1-phosphate uridylyltransferase | 2.11 | 2.4 | 3.94 |
| P07996 | THBS1 | Thrombospondin-1 | 3.95 | 2.47 | 2.21 |
| P62988 | RPS27A | Ubiquitin | 3.79 | 2.7 | 4.11 |
| P17301 | ITGA2 | Integrin alpha-2 | 2.39 | 4.52 | 3.04 |
| P68363 | TUBA1B | Tubulin alpha-1B chain | 2.88 | 2.15 | 4.59 |
| P54136 | RARS | Arginyl-tRNA synthetase, cytoplasmic | 4.9 | 4.94 | 4.33 |
| P12111 | COL6A3 | Collagen alpha-3(VI) chain | 4.95 | 4 | 3.33 |
| P02792 | FTL | Ferritin light chain | 3.09 | 2.29 | 5.53 |
| Q9BUT1 | BDH2 | 3-hydroxybutyrate dehydrogenase type 2 | 4.27 | 5.62 | 5.51 |
| Q14254 | FLOT2 | Flotillin-2 | 5.07 | 2.81 | 5.73 |
| SERPINE | 1 | Plasminogen activator inhibitor 1 | 2.57 | 2.42 | 5.83 |
| Q9NZO1 | GPSN2 | Synaptic glycoprotein SC2 | 3 | 3 | 5.95 |
| Q9NQW7 | XPNPEP1 | Xaa-Pro aminopeptidase 1 | 5.76 | 6.58 | 5.59 |
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| P14174 | MIF | Macrophage migration inhibitory factor | 7.19 | 2.31 | 2.75 |</p>
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Supplementary Table S6. Correlations between Cav-1 Expression and Clinical Features of GC patients

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Note: *H. pylori* status was determined histologically and/or serologically. GEJ: gastroesophageal junction. The TNM stage of GC was determined according to the classification system of the International Union Against Cancer (7th edition). *Other histologic types of gastric cancer mainly included mucinous adenocarcinomas and signet-ring cell carcinomas, according to the World Health Organization (WHO) classifications.