<table>
<thead>
<tr>
<th>Chemokine or growth factor</th>
<th>Receptor</th>
<th>Experimental evidence for chemotaxis in cancer</th>
<th>Types of cancer affected</th>
<th>Availability of drug and stage of evaluation in cancer</th>
<th>Refs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXCL12 (SDF1)</td>
<td>CXCR4</td>
<td>* Transwell or Boyden chamber * In vivo recruitment of bone-marrow derived cells * In vivo invasion assay</td>
<td>Breast, prostate, NSCLC, ovarian, pancreatic, melanoma, colorectal, renal, gastric, rhabdomyosarcoma and Ewing’s sarcoma</td>
<td>- Plerixafor (AMD3100): leukemia- Phase I/II; lymphoma- Phase I/II; Hodgkin disease- Phase I/II. - MDX-1338: leukemia-Phase I. - BTK140: multiple myeloma- Phase I/II. - CTCE-9908: ovarian- Phase I/II.</td>
<td>1-18</td>
</tr>
<tr>
<td>CCL19 and CCL21</td>
<td>CCR7</td>
<td>Transwell or Boyden chamber</td>
<td>Breast, cervical, leukemia, lung and squamous cell carcinoma</td>
<td>None</td>
<td>1, 2, 19-23</td>
</tr>
<tr>
<td>CCL22</td>
<td>CCR4</td>
<td>* Transwell or Boyden chamber</td>
<td>Breast, ovarian, leukemia and gastric</td>
<td></td>
<td>17, 24-27</td>
</tr>
<tr>
<td>CX3CL1 (fractalkine)</td>
<td>CX3CR1</td>
<td>* Transwell or Boyden chamber * In vivo recruitment of T and other immune cells</td>
<td>Pancreatic, neuroblastoma, prostate and lung</td>
<td>None</td>
<td>28-32</td>
</tr>
<tr>
<td>CCL5 (RANTES), CCL2 (MCP1), CCL3 (MIP1α) and CCL7 (MCP3)</td>
<td>CCR1</td>
<td>* Transwell or Boyden chamber * In vivo recruitment of NK cells and other immune cells</td>
<td>Colorectal, hepatocellular carcinoma and melanoma</td>
<td>- Carlumab (CNTO 888): solid tumors-Phase I; prostate- Phase II. - MLN1202: bone metastasis of solid tumors- Phase II.</td>
<td>17, 33-38</td>
</tr>
<tr>
<td>CCL25</td>
<td>CCR9</td>
<td>Transwell or Boyden chamber</td>
<td>Melanoma and leukemia</td>
<td>none</td>
<td>39-41</td>
</tr>
<tr>
<td>CXCL1, CXCL5, CXCL6 and CXCL8</td>
<td>CXCR1 and CXCR2</td>
<td>* Transwell or Boyden chamber * Wound healing assay</td>
<td>Melanoma, colorectal, head and neck, prostate and leukemia</td>
<td>none</td>
<td>42-50</td>
</tr>
<tr>
<td>EGF, TGFα, betacellulin, HBEGF, amphiregulin, heregulin, neuregulin</td>
<td>EGFR (ERBB1), ERBB2 (HER2), ERBB3 and ERBB4</td>
<td>Breast, lung, glioblastoma, colorectal, gastric, mesothelioma and neurofibromatosis</td>
<td>- <strong>Trastuzumab</strong>: breast cancer-Approved; lung, NSCLC, sarcoma, urothelial, oesophageal, gastric, head and neck, endometrial, colorectal, prostate - Phase II. - <strong>Gefitinib</strong>: NSCLC - Approved; colorectal - Phase I; ovarian - Phase I/II; breast, bladder, cervical, oesophageal, hepatocellular, gastrointestinal, prostate, renal - Phase II; lung, head and neck - Phase III. - <strong>Erlotinib</strong>: NSCLC and pancreatic - Approved; lung, head and neck, rectal - Phase I/II; breast, brain, oesophageal, pancreatic, colorectal, bladder, ovarian, sarcoma - Phase II; oral, pancreatic, colorectal, lung, esophageal, head and neck - Phase III. - <strong>Lapatinib</strong>: breast cancer - Approved; bladder, lymphoma, renal - Phase I; ovarian - Phase I/II; head and neck, prostate, neurofibromatosis, pancreatic, gastric, esophageal, melanoma - Phase II. - <strong>Cetuximab</strong>: colorectal, head and neck - Approved; cervical - Phase I/II; brain, pancreatic, gastric, ovarian, lung, rectal, breast - Phase II; NSCLC, oesophageal - Phase III. - <strong>Trastuzumab-DM1</strong>: breast - Phase I/II/III. - <strong>Pertuzumab</strong>: colorectal - Phase II; breast, ovarian, neuroendocrine, NSCLC, prostate pancreatic - Phase II. - <strong>Neratinib</strong>: breast - Phase I/II; NSCLC, lung - Phase II. - <strong>Canertinib</strong> (CI-1033): NSCLC - Phase I; lung, breast - Phase II. - <strong>Pelitinib</strong> (EKB-569): solid tumors - Phase I; NSCLC, lung, colorectal, rectal - Phase II. - <strong>Afatinib</strong> (BIBW 2992): glioblastoma - Phase I; breast, prostate, colorectal, NSCLC, head and neck, glioma - Phase II.</td>
<td>7, 51-65</td>
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</tr>
</tbody>
</table>

| FGF | FGFR1-4 | Breast, ovarian, pancreatic, glioblastoma, Ewing's sarcoma and renal | - **PEG-interferon alfa-2b**: melanoma - Phase II. - **BGJ398**: solid tumors with FGFR amplification - Phase I. - **E-3810**: solid tumors - Phase I. - **TSU-68**: hepatocellular - Phase I/II. - **Dovitinib lactate** (TKI258): solid tumors - Phase I; melanoma - Phase I/II; renal - Phase I/II; prostate, urothelial, multiple myeloma - Phase II. - **BIBF 1120**: ovarian - Phase I/II/III; | 66-73 |

* Transwell or Boyden chamber * Pipette following * Dunn chamber * 3D invasion * In vivo invasion * Intravital imaging

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<tr>
<th></th>
<th><strong>Boyden chamber</strong></th>
<th>Wound healing assay</th>
</tr>
</thead>
</table>

In format provided by Condeelis et al. (AUGUST 2011)
| PDGF | PDGFR | Breast, glioblastoma, mesothelioma and melanoma | - Imatinib (STI-571): leukemia and gastrointestinal – Approved.  
- Sunitinib (SU011248): renal and gastrointestinal - Approved; prostate, liver - Phase II.  
- Sorafenib: renal and liver - Approved; glioma, glioblastoma, astrocytoma - Phase I.  
- TSU-68*: hepatocellular - Phase I/II.  
- TKI258*: solid tumors- Phase I; melanoma- Phase I/II; renal- Phase I/II; prostate, urothelial, multiple myeloma-Phase II.  
- Motesanib (AMG 706): pancreatic, oesophageal, rectal, colorectal - Phase I; breast, lung, NSCLC - Phase I/II; thyroid, gastrointestinal, ovarian, multiple myeloma - Phase II.  
- Vatalanib (PTK787): renal, breast, NSCLC - Phase I/II; prostate, sarcoma, lymphoma, mesothelioma - Phase II; colorectal, rectal - Phase III.  
- Nilotinib: glioma - Phase II.  
- Leflunomide (SU101): glioma and sarcoma - Phase I.  
- Olaratumab (IMC-3G3): ovarian, NSCL - Phase II.  
- MEDI-575: solid tumors - Phase I.  
- Pazopanib* (GW786034): NSCLC, neuroendocrine tumors - Phase II.  
- AP 12009: melanoma, pancreatic, colorectal - Phase I; glioblastoma, astrocytoma - Phase II.  
- GC1008: renal, melanoma, mesothelioma - Phase I.  
- Lucanix: lung, bronchogenic carcinoma - Phase II.  
- IMA 12: thymoma - Phase II.  
- XL228: lymphoma, solid tumors - Phase I.  
- AXL1717: solid tumors - Phase I.  

| TGFβ | TGFβR1 and TGFβR2 | Breast, lung, squamous cell and oesophageal | - Nicotuzumab: head and neck - Phase III.  
- AP 12009: melanoma, pancreatic, colorectal - Phase I; glioblastoma, astrocytoma - Phase II.  
- GC1008: renal, melanoma, mesothelioma - Phase I.  
- Lucanix: lung, bronchogenic carcinoma - Phase II.  

| IGF1 | IGF1R | Sarcoma, breast, multiple myeloma, lymphoma, choriocarcinoma, mesothelioma and melanoma | - BII022: solid tumors, hepatocellular, NSCLC - Phase I.  
- OSI-906: advanced solid tumors - Phase I; ovarian - Phase I/II; breast - Phase II; adrenocortical - Phase III.  
- SCH 717454: colorectal, osteosarcoma - Phase II.  
- RG1507: breast, solid tumors- Phase I; sarcoma- Phase II.  
- IMA 12: thymoma - Phase II.  
- XL228: lymphoma, solid tumors - Phase I.  
- AXL1717: solid tumors - Phase I.  

Prostate, endometrial, colorectal, NSCLC, glioblastoma, hepatocellular - Phase II.  

74-82 | 83-90 | 54, 91-97
### Table 1: In vitro and in vivo invasion assays

<table>
<thead>
<tr>
<th>Assay Type</th>
<th>Model System</th>
<th>Assay Details</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Transwell</em> or <em>Boyden</em> chamber</td>
<td>Breast, ovarian, endometrial, prostate, gastric and leukemia</td>
<td></td>
<td><strong>ARRY-382</strong>: neoplasm metastasis - Phase I.  <strong>PLX3397</strong>: solid tumors - Phase I.</td>
</tr>
<tr>
<td><em>Dunn</em> chamber</td>
<td><em>3D invasion</em></td>
<td></td>
<td>7, 52, 53, 98-103</td>
</tr>
<tr>
<td><em>In vivo</em> invasion</td>
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</tr>
<tr>
<td><em>Intravital imaging</em></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>CSF1</strong> (MCSF)</td>
<td><strong>CSF1R</strong> (MCFSR or CD115)</td>
<td>* Transwell or *Boyden chamber</td>
<td>Breast, ovarian, endometrial, prostate, gastric and leukemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>* Dunn chamber</td>
<td><strong>ARRY-382</strong>: neoplasm metastasis - Phase I.  <strong>PLX3397</strong>: solid tumors - Phase I.</td>
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<td>* 3D invasion</td>
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<tr>
<td><strong>VEGFA and VEGFC</strong></td>
<td><strong>VEGFR1-3</strong></td>
<td>* Transwell or *Boyden chamber</td>
<td>Melanoma, prostate, sarcoma, meningioma and leukemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>* 3D culture</td>
<td><strong>Bevacizumab</strong>: colorectal, lung, breast, glioblastoma, kidney - Approved.  <strong>Sorafenib</strong>: renal, liver - Approved; glioma, glioblastoma, astrocytoma - Phase I.  <strong>Axitinib</strong> (AG-013736): colorectal - Phase I/II; adrenal cortex tumors, melanoma, parietal, NSCLC, thyroid - Phase II; renal - Phase III.  <strong>Vatalanib</strong> (FTK787): renal, breast, NSCLC - Phase I/II; prostate, sarcoma, lymphoma, mesothelioma - Phase II; colorectal, rectal - Phase III.  <strong>Vandetanib</strong>: breast, colon, lung, renal, adrenal, gastric, ovarian, cervical, thyroid, sarcoma - Phase I/II; NSCL - Phase III.  <strong>Ramucirumab</strong> (IMC-1121B): hepatocellular, prostate, NSCLC, colorectal, ovarian, melanoma - Phase II; gastric, breast - Phase III.  <strong>IMC-18F1</strong>: breast, colorectal - Phase II.  <strong>AMG 706</strong>: pancreatic, esophageal, rectal, colorectal - Phase I; breast, lung, NSCLC - Phase I/II; thyroid, gastrointestinal, ovarian, multiple myeloma - Phase II.  <strong>pazopanib</strong> (GW786034): NSCLC, neuroendocrine tumors - Phase II.</td>
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<td>104-111</td>
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</tbody>
</table>
Listed above are some of the major factors involved in chemotaxis in cancer. Literature search for this table was performed for each factor with the keywords “cancer and chemotaxis”.

For the clinical information, in addition to the literature, a search of the clinicaltrials.gov database was performed for current clinical trials.

#: drugs with more than one molecular target.


REFERENCES


