Stem Cells and Microenvironment: Illuminating the path to new, targeted treatments

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Seed and Soil Hypothesis

Figure 1 | **Stephen Paget.**

‘“The best work in the pathology of cancer now is done by those who…are studying the nature of the seed. They are like scientific botanists, and he who turns over the records of cases of cancer is only a ploughman, but his observations of the properties of the soil might also be useful”’.
(Stephen Paget)

Experimental model for tumor metastasis

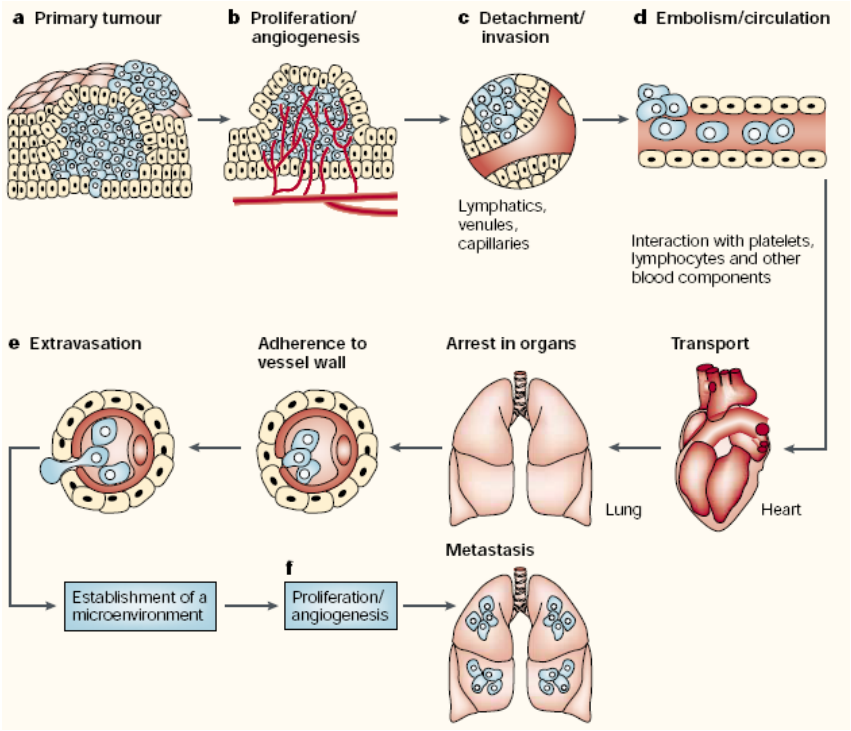
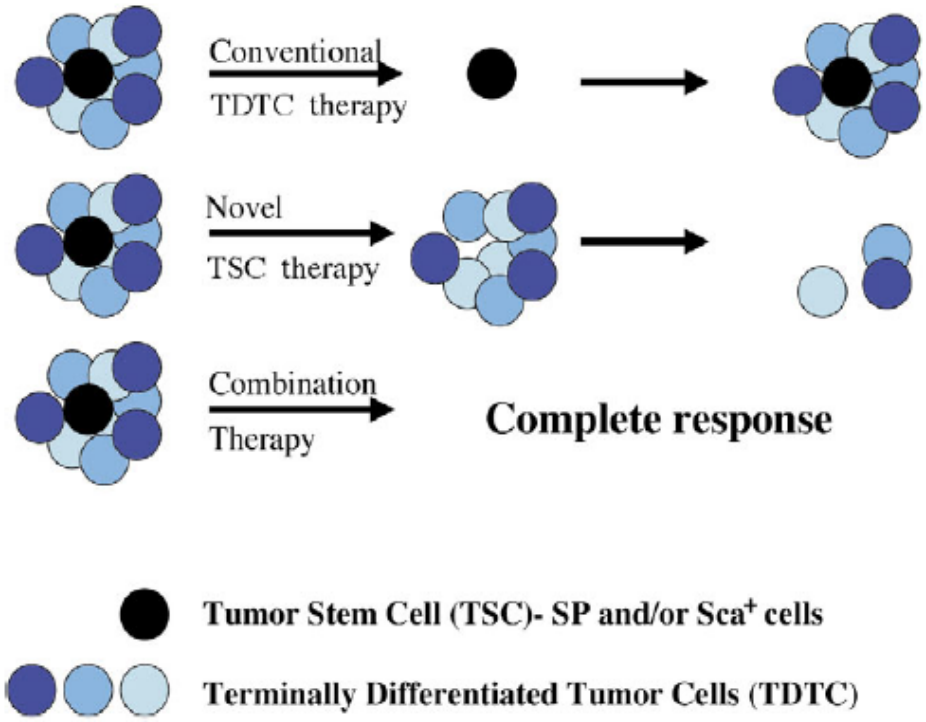


Table 1 | **Regulation of metastasis**

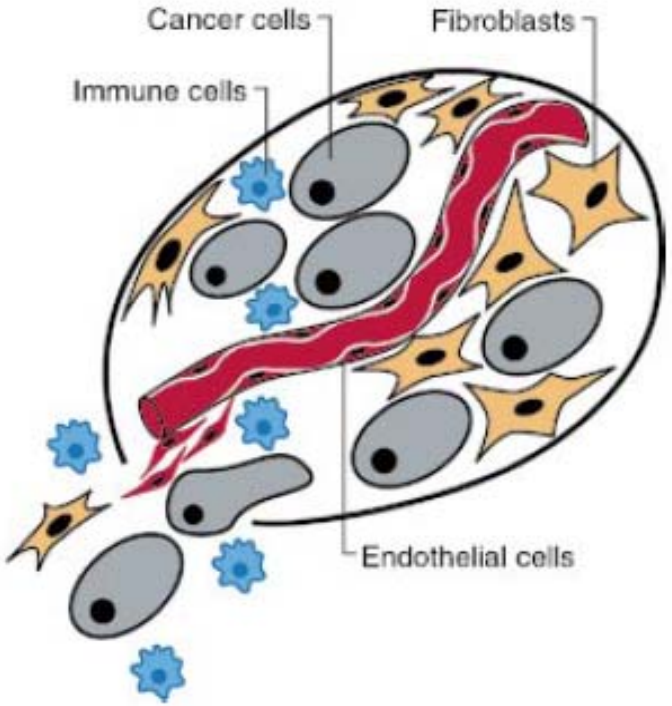
Cell type	Facilitation of metastasis	Inhibition of metastasis
Tumour cells	Production of growth factors and their receptors	Antigenicity
	Production of angiogenic factors	Inhibitors of angiogenesis
	Motility, invasiveness	Cohesion (E-cadherin)
	Aggregation, deformability	Tissue inhibitors of proteolytic enzymes
	Specific cell-surface receptors and adhesion molecules	
Host cells	Paracrine and endocrine growth factors	Tissue barriers
	Neovascularization	Blood turbulence, endothelial cells
	Platelets and their products	Tissue inhibitors of proteolytic enzymes
	Immune cells and their products	Antiproliferative factors
		Inhibitors of angiogenesis

Seed and Soil Revisited

Seed



Soil



Woodward WA, Chen MS, Behbod F, Rosen JM. On mammary stem cells. J Cell Sci 2005; 118:3585-94.

Definition of cancer stem cell and tumor microenvironment

Cancer Stem Cell

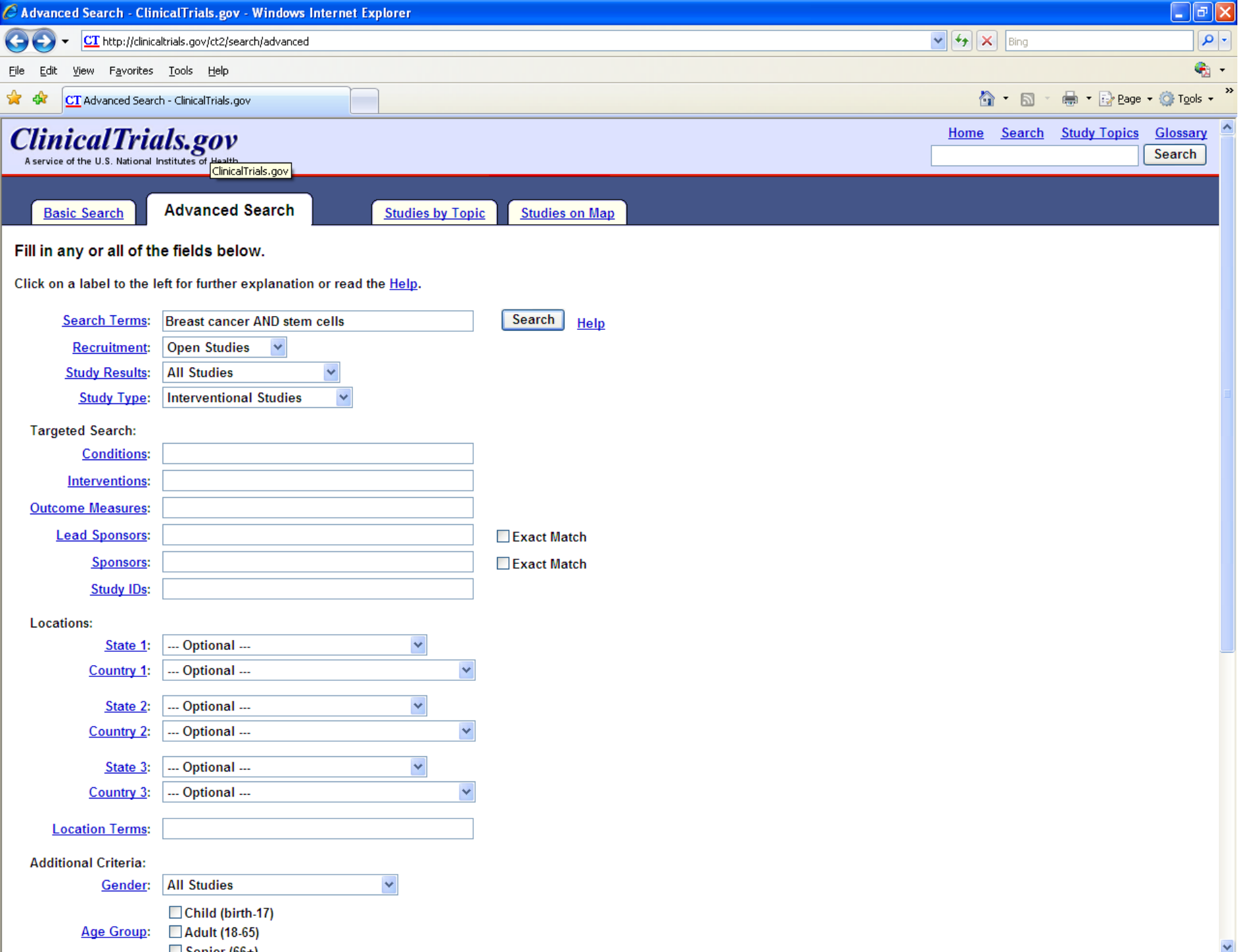
- Capable of forming tumors in immune deficient mice efficiently
- Unique cell surface markers
- Experimental breast cancer stem cell markers – CD44+/CD24-; ALDH +

Tumor microenvironment

- Provides scaffold to support cancer cell growth
- Fibroblasts/extracellular matrix
- Vasculature/lymphatics
- Immune cells

Research Questions

- Prevention – How do we define a cancer stem cell and how do we target it?
- Locally - What makes the tumor microenvironment permissive to cancer stem cell and tumor growth?
- Distant - What makes the distant metastatic site permissive to tumor growth?


Advanced Search - ClinicalTrials.gov - Windows Internet Explorer
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Home Search Study Topics Glossary
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Basic Search
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Studies on Map
Fill in any or all of the fields below.
Click on a label to the left for further explanation or read the Help.
Search Terms: Breast cancer AND stem cells
Search
Help
Recruitment: Open Studies
Study Results: All Studies
Study Type: Interventional Studies
Targeted Search:
Conditions:
Interventions:
Outcome Measures:
Lead Sponsors:
Exact Match
Sponsors:
Exact Match
Study IDs:
Locations:
State 1: --- Optional ---
Country 1: --- Optional ---
State 2: --- Optional ---
Country 2: --- Optional ---
State 3: --- Optional ---
Country 3: --- Optional ---
Location Terms:
Additional Criteria:
Gender: All Studies
Age Group:
Child (birth-17)
Adult (18-65)

Found 38 studies with search of: Breast cancer AND stem cells | Open Studies | Interventional Studies

Include studies that are not seeking new volunteers.

Display Options

Rank	Status	Study
1	Recruiting	Purged Circulating Tumor Cells (CTCs) From Metastatic Breast Cancer Condition: Breast Cancer Interventions: Drug: Carboplatin; Drug: Cyclophosphamide; Drug: Thiotepa; Procedure: Stem Cell Transplant
2	Recruiting	Combination Chemotherapy With or Without Trastuzumab Followed By an Autologous Stem Cell Transplant and Radiation Therapy in Treating Patients With Stage III or Stage IV Breast Cancer Condition: Breast Cancer Interventions: Biological: trastuzumab; Drug: carboplatin; Drug: cyclophosphamide; Drug: melphalan; Drug: thiotepa; Procedure: adjuvant therapy; Procedure: autologous-autologous tandem hematopoietic stem cell transplantation; Procedure: bone marrow ablation with stem cell support; Radiation: radiation therapy
3	Recruiting	Chemotherapy Followed by Peripheral Stem Cell Transplantation Plus Biological Therapy in Treating Women With Stage IV Breast Cancer Condition: Breast Cancer Interventions: Biological: therapeutic autologous lymphocytes; Drug: ICE regimen; Drug: carboplatin; Drug: cyclophosphamide; Drug: etoposide; Drug: high-dose chemotherapy; Drug: ifosfamide; Drug: thiotepa; Procedure: leukapheresis; Procedure: peripheral blood stem cell transplantation
4	Recruiting	Combination Chemotherapy and Radiation Therapy Followed By Cyclosporine and Mycophenolate Mofetil in Treating Patients Who Are Undergoing a Donor Stem Cell Transplant for Hematologic Cancer, Metastatic Breast Cancer, or Kidney Cancer Conditions: Breast Cancer; Chronic Myeloproliferative Disorders; Kidney Cancer; Leukemia; Lymphoma; Multiple Myeloma and Plasma Cell Neoplasm; Myelodysplastic Syndromes; Myelodysplastic/Myeloproliferative Diseases Interventions: Biological: CD4+CD25+ regulatory T cells; Biological: anti-thymocyte globulin; Drug: cyclophosphamide; Drug: cyclosporine; Drug: fludarabine phosphate; Drug: mycophenolate mofetil; Procedure: allogeneic hematopoietic stem cell transplantation; Procedure: peripheral blood stem cell transplantation; Radiation: total-body irradiation
5	Recruiting	Quantitation of Endothelial Progenitor Cells as Markers of Tumor Angiogenesis in Breast Cancer Conditions: Breast Cancer Stage IV; Breast Cancer Stage I; Breast Cancer Stage II Intervention: Procedure: Blood Draw
6	Recruiting	Ondansetron in Preventing Nausea and Vomiting in Patients Undergoing a Stem Cell Transplant Conditions: Breast Cancer; Chronic Myeloproliferative Disorders; Gestational Trophoblastic Tumor; Leukemia; Lymphoma; Multiple Myeloma and Plasma Cell Neoplasm; Myelodysplastic Syndromes; Myelodysplastic/Myeloproliferative Diseases; Nausea and Vomiting; Neuroblastoma; Ovarian Cancer; Testicular Germ Cell Tumor Interventions: Drug: ondansetron hydrochloride; Other: survey administration; Procedure: autologous hematopoietic stem cell transplantation
7	Recruiting	Phase I/II Study of MK-0752 Followed by Docetaxel in Advanced or Metastatic Breast Cancer Condition: Metastatic Breast Cancer Interventions: Drug: MK-0752 and Docetaxel; Drug: MK-0752
8	Recruiting	Moxifloxacin in Preventing Bacterial Infections in Patients Who Have Undergone Donor Stem Cell Transplant Conditions: Breast Cancer; Chronic Myeloproliferative Disorders; Gestational Trophoblastic Tumor; Infection; Leukemia; Lymphoma; Multiple Myeloma and Plasma Cell Neoplasm; Myelodysplastic Syndromes; Myelodysplastic/Myeloproliferative Diseases; Neuroblastoma; Ovarian Cancer; Testicular Germ Cell Tumor Intervention: Drug: moxifloxacin hydrochloride

Potential therapeutic agents

- MK-0752 (Notch Signaling)
- OMP-21M18 (monoclonal antibodies targeting Notch Signaling)
- Salinomycin