Cancer Therapeutics: Time to Swim Downstream?

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This figure shows a colony of fluorescent MCF-7 breast cancer cells growing on a layer of normal primary human fibroblasts. The fluorescent image is shown on the right; it is merged with the brightfield image (100 $\times$) on the left. Cancer cells require the noncancerous cells in tumors (the tumor stroma) like fish require water. The stroma, including fibroblasts, adipocytes, endothelial cells, and immune cells, has been demonstrated to provide critical metabolites to cancer cells and engages in tumor-promoting crosstalk with cancer cells [1]. The cytokines and chemokines elaborated by the stroma trigger signals that promote growth and metastasis of cancer cells, suppression of host immunity, and the recruitment of blood vessels [2–4]. The concept of

stromal-directed therapeutics for cancer is being tested in mouse models and in clinical trials and has begun to transition into clinical usage. Examples of drugs that target the cancer microenvironment include bevacizumab (directed against the vascular endothelial growth factor cytokine and blood vessel growth) and zoledronic acid (a modulator of immunity and the bone microenvironment). Critical mediators of cancer–stroma crosstalk are emerging, including γ -secretase, fibroblast activation protein, receptor activator of nuclear factor κ B ligand, interleukin-6, and chemokines (such as stromal cell–derived factor 1 and chemokine (C-C motif) ligand 5) or their receptors. Drugs that target such mediators are under active investigation [5].

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