**Introduction:** One novel target of cancer therapeutics is the stem cell niche.

The concept of the HSC niche was first proposed by Schofield in 1978 to describe a specific site in adult tissues where stem cells reside, undergo self-renewal and produce large numbers of progeny (differentiation). Structurally, the niche is formed by supporting cells that provide a microenvironment for stem cells as well as the signals emanating from the supporting cells. Understanding the biology and dynamics of stem cell behavior under normal conditions and examining how the dynamics change under conditions of stress is essential to our understanding of how these mechanisms might change during carcinogenesis.

**Discussion:** Using stochastic and deterministic models, significant progress has been made in understanding the dynamics of cancer initiation and progression, leukemic stem cell and progenitor population changes in response to therapy and the development of resistance. Chronic myelogenous leukemia (CML) represents a nice system to quantitatively study hematopoietic stem cell and progenitor dynamics. The translocation t, present in leukemic stem cells, multipotent progenitors, and their progeny of the myeloid lineage, leads to transcription of the BCR-ABL fusion oncogene which is thought to regulate cell survival. Therapy inhibiting BCR-ABL is one of the first examples where chronic administration of a molecularly targeted therapy has led to a dramatic clinical response.

Mathematical models have been used to demonstrate that leukemic stem cells are not targeted by imatinib therapy, and that successful therapy must target leukemic stem cells. Other models have highlighted the importance of leukemic stem cell quiescence as a mechanism leading to therapeutic resistance. Komarova and Wodarz used a stochastic model in which quiescence and reactivation of leukemic stem cells are considered. Their study offers hope that targeted therapy, used in combination with potential therapies that lead to activation of quiescent cells, could eradicate the stem cell-like compartment of a tumor.

Studies of the stem cell niche in model systems such as *Drosophila* have revealed adhesive interactions, cell cycle modifications and intercellular signals that operate to control stem cell behavior. For example the APC gene has been shown to regulate *Drosophila* intestinal stem cell proliferation. APC is well known to play a role in human colon carcinogenesis, and mathematical models have shown that stem cell proliferation leads to colon tumor formation in humans.

Unifying features of stem cell niche regulation are observed across tissues and across organisms. In tissue cellular populations comprising the bone and vascular niches include osteoblasts (OBs), endothelial cells, HSCs, multipotent progenitors (MPPs), common myeloid progenitors (CMPs), common lymphoid progenitors (CLPs), and differentiated cells. Signaling from Wnt, β-catenin, p21, p18, and bmi-1 regulate self-renewal, while Notch and GSK3 feedback from progenitors inhibit differentiation that usually accompanies self-renewal. Signaling from osteoblasts includes osteopontin (Opn) expression that inhibits HSC self-renewal, parathyroid hormone-related protein (PPR) which increases HSCs, N-cadherin which binds β-catenin, and Tie2/angiopoietin which regulates quiescence.

Populations of the intestinal stem cell niche in the *Drosophila* include ISCs, enteroblasts (EBs), enteroendocrine cells (EE), and enterocytes (ECs). Wnt signaling from underlying smooth muscle and Notch feedback from EB regulate ISC self-renewal, while Jak/Stat feedback from damaged ECs increases ISC self-renewal. Spindle orientation is well known to play a role in stem cell fate. Asymmetric division is regulated by maintaining the stem cell orientation, and this is regulated by its spatial relationship with the cells of the niche.

Induction of brain tumor growth has been demonstrated by altering stem-cell asymmetric division in *Drosophila* melanogaster.

**Conclusions:** Understanding the regulatory system of stem cell could lead to novel therapeutic approaches that directly target stem cells or niches.
The latest drugs targeting cancer stem cells or their microenvironments use this state-of-the-art strategy and are expected to minimize complications and improve patient quality of life at the same time. From both scientific and clinical viewpoints, the biology of the stem cell and its niche is expected to be one of the most promising fields of research over the next few decades.

References:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1451221/

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