Introduction

Obesity involves abnormal accumulation of body fat. As a result of a prolonged positive energy balance, adipocytes in white adipose tissue (WAT) accumulate lipid droplets, which have systemic repercussions. Accompanying dyslipidemia, insulin resistance, and other systemic metabolic changes are important long-term consequences of obesity (1, 2). Epidemiology revealed that obesity, being a component of the metabolic syndrome, is associated with accelerated progression of several types of cancer (3, 4). The state of chronic inflammation ensuing in both cancer (5) and obesity (1) may play a key role in linking obesity and cancer (2). It has also been proposed that WAT has a direct effect on tumor growth (6, 7); however, convincing evidence has been lacking (8, 9). WAT is a potent endocrine organ secreting adipokines, such as cytokines and growth factors (1, 10). Leptin, insulin-like growth factors (IGF), and steroid hormones have been studied as adipokines potentially implicated in cancer (8–11). For example, IGF-1, systemic levels of which are elevated in obesity, is sufficient to accelerate tumor growth in cancer models (12).

While adipokines are secreted by adipocytes, important angiogenic, immunomodulatory, and survival factors are products of infiltrating monocytic cells and of perivascular adipocyte progenitors, termed adipose stromal cells (ASC; refs. 13–15). ASCs are similar to mesenchymal stromal cells (MSC) originally isolated as bone marrow colony-forming unit (CFU-F) fibroblasts (16, 17). Accumulating evidence indicates that MSCs serve as progenitors of cells contributing to the trophic tumor microenvironment (18–21). Administered bone marrow MSC and ASC engraft tumors in animal models result in accelerated cancer progression (7, 22–24); however, the physiologic relevance of these results has been unclear. The capacity of mesenchymal progenitors to sense cancer as a site of hypoxia/inflammation has been proposed to explain their tumor homing (17, 25). ASC proliferation accompanies WAT expansion (26) and number of ASCs per gram of WAT increases in obese individuals (27, 28). Mesenchymal progenitors are normally undetectable in the peripheral circulation; however, mobilization of cells with the ASC immunophenotype in obesity, further elevated in patients with cancer (29, 30), suggests the possibility of their trafficking. On the basis of these observations, we have reasoned that ASC mobilization and their recruitment by tumors could be increased in obesity, leading to increased stimulation of tumor growth through the paracrine action of adipokines.
To this day, the role of WAT in cancer progression has not been proven. Studies showing that tumor growth is accelerated by diet-induced obesity (DIO) have not successfully uncoupled effects of diet from effects of WAT (11, 31). Here, we show that excess WAT promotes tumor growth irrespective of the diet in mice. To investigate migration of cells from WAT during cancer progression, we used a competitive repopulation model that does not rely on invasive cell injections. We show that recruitment of endogenous ASCs in obesity is associated with increased vascularization and adipogenesis accompanied by proliferation of malignant cells.

Materials and Methods

Animal experiments

Mouse studies were carried out under the Animal Welfare Committee of the University of Texas (Houston, TX). Mouse strains C57BL/6, C57BL/6-Tg(UBC-GFP)30Scha/J (termed GFP mice), B6.Cg-Tg(Actb-mRFP1)1F1Hadj/J (termed RFP mice), and B6.129S7-Rag1tm1Mom/J (termed RAG-1 mice) were from Jackson. For DIO induction (32), high-fat diet (HFD) D12492 (60 kcal% fat) and low-fat diet LFD (LFD) D12450B (10 kcal% fat) from Research Diets were used. Body composition was measured by EchoMRI-100T (Echo Medical Systems) as described (33). For tumor grafting, 10⁶ cells were injected with a 21-gauge needle onto upper back (LLC and ID8) or into mammary fat pad (E0771 and MDA-231). Tumor size was measured with a caliper; volume was calculated as length × width². Tissues were recovered from Avertin-anesthetized mice. Cells were isolated from tissues as described (7, 14).

Cell lines and primary cell culture

E0771 (from F.M. Sirotnak), ID8 (from F.C. Marini), and other cancer lines (from American Type Culture Collection) were cultured in Dulbecco’s Modified Eagle’s Media containing 10% FBS and authenticated by animal grafting and subsequent tumor histology. Blood was recovered by heart perfusion with 10 mL PBS/EDTA, and peripheral blood mononuclear cells (PBMC) were isolated as described (7, 30). Tissue suspensions were prepared as described (7, 14). Adipogenesis induction and Oil red O staining were conducted as described (14).

Flow cytometry

For fluorescence-activated cell sorting (FACS), cells were preagitated to exclude debris, cell clumps, contaminating polymorphonuclear cells, red blood cells, as well as dead cells based on 7-aminoactinomycin D (7-AAD) staining. Tissue cell suspensions, WAT stromal/vascular fraction (SVF) with adipocytes removed (14), or PBMCs were sorted into populations with FACSaria/FACSDiva software (BD Biosciences) based on red fluorescent protein (RFP) fluorescence (Texas Red channel), GFP fluorescence [fluorescein isothiocyanate (FITC) channel], and the following IgG clones: APC-anti-CD34 (RAM34), PE-Cy7-anti-CD31 or PE-anti-CD31 (MEC 13.3), APC-Cy7-CD45 (30-F11), and the corresponding isotype controls (BD Biosciences). Isotypes and the positions of previously characterized hematopoietic and endothelial populations on the plots (7, 14) were used to set gate cutoffs.

Tissue analysis

Formalin-fixed, paraffin-embedded tissues were sectioned and analyzed by immunofluorescence as described (14). Primary antibodies used were goat anti-GFP (GeneTex, 1:100); rabbit anti-RFP (Abcam, 1:100); rabbit anti-Ki-67 (Thermo Scientific, 1:100); goat or rabbit anti-CD31 (Santa Cruz Biotechnology, 1:100); rabbit anti-desmin (Abcam, 1:200); and rabbit anti-perilipin (Cell Signaling Technology, 1:100). Secondary donkey Alexa 488-conjugated (1:150) IgG was from Invitrogen and Cy3-conjugated (1:300) IgG was from Jackson ImmunoResearch. Nuclei were stained with Hoechst 33258 or TO-PRO-3 (Invitrogen). Images were acquired with a confocal Leica TCS SP5 microscope/LAS AF software or Olympus IX70 inverted fluorescence microscope/MagnaFire software. For quantifications, at least 10 random ×100 magnification fields were blindly scored and/or measured using microscope grid.

Statistical analysis was conducted by using the one-tailed homoscedastic Student t test.

Results

Diet-independent effect of obesity on tumor growth

First, we wished to uncouple the direct effect of obesity on cancer progression from indirect effect of the diet. We set up cohorts by rendering mice obese (body mass > 45 g) or lean (body mass < 30 g) by prefeeding with HFD or LFD. To exclude diet as a variable, lean and obese mice have been placed on regular chow for 1 month before cancer initiation. HFD prefed mice slightly lost weight upon diet normalization, however, still had higher body mass due to increased body fat (Supplementary Fig. S1A and S1B). After diet normalization, mice were isografted with tumor cells. Obese mice displayed accelerated kinetics of Lewis lung carcinoma (LLC) growth, as compared with lean mice (Fig. 1A). As tumors grew in size, obese mice gradually lost weight, whereas lean mice maintained it (Fig. 1A). Fat, but not lean, body mass decreased in response to cancer (Supplementary Fig. S1B), indicating that weight loss was specifically due to the reduction in WAT amount. Human breast MDA-231 adenocarcinoma orthotopically xenografted into the mammary fat pad of RAG-1 mice also grew faster in DIO mice, although the effect was subtle, coincidentally with obesity being less pronounced in this strain (Supplementary Fig. SIC). Using an ovarian ID8 adenocarcinoma model, we segregated animals into obese, lean, and DIO-resistant mice that had become only moderately overweight on HFD before tumor implantation. Despite HFD prefeeding, the kinetics of tumor growth in DIO-resistant mice was not significantly different from that in the lean LFD controls (Supplementary Fig. S1C), indicating that prolonged positive energy balance does not fully account for the effect of obesity. Combined, these findings show that tumor growth can be promoted by obesity irrespective of diet at the time of tumor implantation and growth. Our data indicate excess WAT as an important component in the obesity–cancer relationship. However, the contribution of systemic physiologic obesity consequences, remaining post-diet normalization (34), cannot be excluded.
Obesity results in ASC expansion

We next set out to test whether recruitment of cells from excess WAT by tumors is implicated in obesity effect on cancer. Obese mice displayed a 7-fold increase in body fat amount (Supplementary Fig. S1B). To investigate accompanying ASC expansion, we compared ASC quantities in lean and obese...
animals. Unlike bone marrow MSCs, ASCs express CD34 (15), which enables their enumeration by flow cytometry as CD34+/CD31-CD45- cells (7, 14). For intraperitoneal (i.p.) WAT, the major ASC reservoir (26), the ASC frequency was found to be 30.4% in lean and 32.6% in obese mice, respectively (Fig. 1B; Supplementary Fig. S2). On the basis of the total amounts of i.p. WAT recovered (1.0 ± 0.23 g from lean and 6.19 ± 0.25 g from obese mice), we calculated that the net number of i.p. ASCs is 6 times higher in obese mice (Fig. 1C). Frequencies of CD31-CD45+CD34+ cells were very low in the bone marrow, lungs, and liver of both lean and obese animals (Supplementary Fig. S2). Upon plating WAT stromal/vascular cells fraction, adherent ASCs appear as large fibroblasts with well-defined nuclei and nucleoli and can be clearly distinguished from smaller myelomonocytic cells internalizing India ink (Fig. 1D). Quantification of adherent ASCs from i.p. WAT upon enzymatic tissue digestion showed increased efficiency in their recovery from obese mice (Fig. 1E). Combined, these data indicate that WAT expanded in obesity serves as a reserve of extra ASCs.

**Obesity-associated cell mobilization and tumor infiltration**

To test whether ASCs traffic from WAT through the systemic circulation, we conducted a comparative analysis of PBMCs from lean and obese mice bearing tumors. Analysis of PBMCs (Supplementary Fig. S3A and S3B) showed that while circulating CD34+CD45- cells were rare in lean animals (0.06%), their frequency increased 6-fold (to 0.37%) in obesity (Fig. 1F). The majority of these cells had the CD34+CD31-CD45- ASC phenotype: the endothelial marker CD31 was expressed only by 5.9% of CD34+CD45- cells in obese mice (Supplementary Fig. S3A). Analysis of individual CD45+CD31-CD45- cells isolated by FACS showed morphology indistinguishable from that of ASCs sorted from WAT in parallel (Fig. 1G). Blood-derived CD34+CD31-CD45- cells formed colonies and accumulated lipid droplets upon adipogenic induction (Fig. 1H). The obesity-associated egress of CD34+CD31-CD45- adipocyte progenitors strongly suggests their ASC identity. To obtain evidence that ASCs may be recruited by tumors, we subjected tumor cell suspension to flow cytometric analysis. Indeed, tumors contained CD34+CD31-CD45- cells (Supplementary Fig. S2), and the increase in their frequency associated with obesity was consistent with their possible WAT origin.

**A bone marrow transplantation model for tracking WAT-derived cells**

To enable tracking of hematopoietic tumor stroma (17, 18, 35, 36) in parallel with ASCs, we designed an in vivo competitive repopulation assay. This obesity/cancer model is based on 2 syngeneic mouse strains: host ubiquitously expressing GFP from WAT recovered (1.0 ± 0.23 g from lean and 6.19 ± 0.25 g from obese mice), we calculated that the net number of i.p. ASCs is 6 times higher in obese mice (Fig. 1C). Frequencies of CD31-CD45+CD34+ cells were very low in the bone marrow, lungs, and liver of both lean and obese animals (Supplementary Fig. S2). Upon plating WAT stromal/vascular cells fraction, adherent ASCs appear as large fibroblasts with well-defined nuclei and nucleoli and can be clearly distinguished from smaller myelomonocytic cells internalizing India ink (Fig. 1D). Quantification of adherent ASCs from i.p. WAT upon enzymatic tissue digestion showed increased efficiency in their recovery from obese mice (Fig. 1E). Combined, these data indicate that WAT expanded in obesity serves as a reserve of extra ASCs.

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Figure 2. In-parallel tracking of WAT and medullary cells. A, transplant scheme. Bone marrow from RFP (red) mice is transplanted into lethally irradiated lean or obese (DIO) GFP mice, which are grafted with tumors after diet normalization. In obese mice, trafficking of GFP⁺ ASCs (green) from WAT (yellow) is increased. B, GFP (green) and RFP (red) fluorescence of tissues and cells (1 day post-plating) isolated from an obese GFP/RFP chimera. Leukocytes (arrows) of host (green) and donor (red) origin and host ASCs (arrowheads) are indicated. C, flow cytometric enumeration of circulating GFP⁺ cells among viable PBMCs from representative lean and obese E0771 tumor-grafted mice (left) and gating of the GFP⁺ cells from PBMCs of the obese mouse to enumerate CD34⁺ ASCs as a percentage of GFP⁺ cells (right). SSC-A, side scatter. D, total GFP⁺ cells from PBMCs of a lean and an obese mouse (C) were plated in culture for 1 day. GFP-fluorescent (green) adherent monocytes (arrows) and cells with the ASC morphology (arrowheads) are indicated. E, high magnification of obese mouse PBMC-derived GFP⁺ cells 4 days post-plating. F, lipid droplet formation (•) in a colony formed by an obese mouse PBMC-derived GFP⁺ cell ASCs 7 days after adipogenesis induction. Scale bar, 50 μm.
groups. Flow cytometry indicated that tumor GFP+ cell frequency was still higher in obese mice (9.8%) than in lean mice (3.0%), despite similar tumor size (Fig. 3F). Importantly, 20.0% of tumor GFP+ cells in lean mice and 30.1% in obese mice had the CD34+CD31−CD45− phenotype (Fig. 3F) indicating them as ASCs.

We tested whether a pericyte marker desmin could be used to further validate GFP+ cells as ASCs. Our data show that 91.3% of ASCs are indeed desmin-positive in WAT (Supplementary Fig. S6A). All PBMC CD34+CD31−CD45− cells and the majority (52.9%) of CD34+CD31−CD45− cells recovered from tumors also were desmin-positive (Supplementary Fig. S6A), suggesting that mobilized ASCs retain their pericyte identity. Four-color confocal immunofluorescence on tissue sections from GFP/RFP chimeras showed co-expression of CD34 and desmin on perivascular GFP+ cells in both WAT and in tumors (Supplementary Fig. S6B). Finally, immunoblotting revealed the presence of delta-decorin (ADCN), a recently identified marker of ASC (14), in tumor protein extracts (Supplementary Fig. S6C), confirming ASC recruitment by tumors.

**Tumor vascularization and cell proliferation associated with ASC recruitment**

Masson's trichrome staining revealed comparable deposition of collagen in tumors from lean and obese animals (Supplementary Fig. S7A). This analysis also revealed less extensive areas of hemorrhage and necrosis in obese mice. Immunofluorescence analysis revealed comparable fibronectin deposits typically devoid of GFP+ cells in tumors for each group (Supplementary Fig. S7B). These data show that the desmoplastic reorganization of the internal tumor matrix is not significantly influenced by obesity in the models used.

Blood vessels are essential for oxygen and nutrient delivery, and vascular patentcy predetermines tumor growth (35, 37). We therefore investigated whether ASC recruitment is associated with vascular remodeling. In obese mice, a higher proportion of endothelial cells were from the host, as revealed by luminal co-localization of CD31 with GFP (Fig. 4A and B). In lean mice, blood vessels were sparse in certain tumor areas, whereas in obese mice, they were abundant throughout the tumor mass (Fig. 4A). Quantification revealed a 2-fold higher vascular density in tumors from obese mice (Fig. 4C). Tumor vessels in lean mice were compressed and slim, whereas in obese mice, they were more hyderilated (Fig. 4C) and filled with circulating blood cells (Fig. 4A and B). Enumeration of vessels positive for desmin+GFP+ cells (Fig. 4D) indicated a trend for increased vessels maturation in tumors from obese mice (Fig. 4C). In addition, expression of α-SMA, a perivascular marker expressed on ASCs (7, 14, 23), was more abundant on perivascular GFP+ cells in obese mice (Fig. 4E). Combined, these results reinforce the notion that ASCs contribute to the pool of perivascular cells in tumors in an obesity-dependent manner.

An observation consistently made for tumors grown in obese animals was that tumor capsules were notably thicker than in lean mice (Figs. 3B and 5A and B). Tumor capsule composition also appeared different in obese animals (Supplementary Fig. S8A). Visually obvious increased adiposity was confirmed by immunofluorescence identifying perilipin, a marker of mature lipid droplets (Fig. 5A). Numerous large GFP+ cells were also observed dispersed throughout the tumor and contained unilocular perilipin-positive lipid droplets indicating them as adipocytes. While the presence of adipocytes at the tumor periphery could potentially be explainable by ingrowth of the surrounding connective tissue, the presence of separate adipocytes abundant within the tumor core indicates their differentiation from engrafted progenitors. Interestingly, the average size of adipocytes was notably larger in tumors grown in obese animals (Figs. 3 and 5), despite diet excluded as a variable.

To test whether recruitment of ASCs is associated with changes in malignant cell proliferation, we conducted immunofluorescence analysis to detect Ki-67 (Supplementary Fig. S8B). Tumors in obese mice were found to contain comparatively more widespread areas populated with proliferating cells (Fig. 5B and C). Importantly, up to 10% of tumor cells were positive for Ki-67 in the vicinity of intratumoral adipocytes, as opposed to only 2% in areas devoid of adipocytes for obese mice (Fig. 5D). Cell proliferation was even more strikingly associated with the vasculature containing GFP+ cells (Fig. 5C). In obese mice, up to 30% of tumor cells were Ki-67+ next to large GFP+ blood vessels and less than 5% in poorly vascularized areas devoid of GFP+ cells (Fig. 5D). This trend was also observed for tumors in lean mice, although the frequency of tumor Ki-67+ cells was overall 4-fold lower (Fig. 5D). Because adipocytes themselves are found in association with blood vessels in tumors, at this point, it is unclear whether adipocytes support malignant cell proliferation and survival independently of the vasculature. Combined, our data from independent mouse models suggest that WAT excess leads to functional ASC engraftment in tumor stroma.

**Discussion**

Our results indicate that obesity can accelerate tumor growth irrespective of concurrent diet. While there are multiple systemic effects through which obesity may promote cancer (34), in this study, we focused on the potential role of excess WAT. We hypothesized that in addition to systemically secreting adipokines, WAT serves as a source of cells recruited by tumors and stimulating cancer through locally secreted paracrine factors. While bone marrow is the bona fide source of hematopoietic cells contributing to tumor microenvironment (18, 35, 36), our results indicate that mesenchymal progenitors are recruited to tumors, at least partly, from WAT. Evidence for this phenomenon has surfaced in other recent reports (7, 22–24, 38). However, preceding studies have been based on data from invasive nonphysiologic models. Here, we provide evidence for ASC trafficking from endogenous WAT in vivo.

Our data suggest that a combination of elevated ASC availability and their trafficking signaling results in the net increase of ASC recruitment to tumors in obesity. Our findings are consistent with the previously observed cellular tumor microenvironment composition changes in obesity (9, 39). The observed obesity-associated mobilization of ASCs, concomitant with their accumulation in tumor stroma/vasculature, indicates that WAT contributes to the pool of mesenchymal
Figure 3. Recruitment of ASCs by tumors increased in obesity. A, tumor growth in lean and obese GFP/RFP chimeras grafted with E0771 cells at week 0 upon diet normalization (left) and concomitant changes in fat body mass measured by EchoMRI (right). B, confocal immunofluorescence on sections from E0771 tumors with anti-GFP (green) and anti-RFP (red) antibodies identifies host and donor cells, respectively. Shown for lean and obese mice are peripheral and internal tumor areas as indicated. RFP<sup>+</sup> cells within the stroma (red arrows), GFP<sup>+</sup> cells within the stroma (green arrows), GFP<sup>+</sup> vasculature-associated cells (green arrowheads), and tumor capsule (brackets) are indicated. Nuclei are stained with TO-PRO-3 (blue). C, adherent GFP<sup>+</sup> cells with ASC morphology (arrowheads) and RFP<sup>+</sup> monocytes (arrows) observed in culture 1 day post-plating of E0771 tumor cell suspension from an obese GFP/RFP chimera. D, adherent GFP<sup>+</sup> cells FACS-sorted from E0771 tumors grown in lean and obese mice 1 day post-plating. Cells with ASC morphology (arrowheads) and other cell types (arrows) are indicated. E, percentages of cells with ASC morphology among GFP<sup>+</sup> cells from D. F, flow cytometric analysis of cell suspensions from size-matched E0771 tumors grown in lean and obese mice. Viable cells were gated to separate RFP<sup>+</sup> (Texas Red channel) and GFP<sup>+</sup> (FITC channel) cells from malignant cells (blue). The combined GFP<sup>+</sup> and RFP<sup>+</sup> cells were then gated to visualize CD31<sup>+</sup> and CD45<sup>+</sup> cells. Finally, GFP<sup>+</sup>CD31<sup>+</sup>CD45<sup>+</sup> cells were gated to enumerate GFP<sup>+</sup> cells with the ASC CD31<sup>+</sup>CD45<sup>+</sup>CD34<sup>+</sup> phenotype (as a percentage of total GFP<sup>+</sup> cells). *, P < 0.001. Error bar, SEM. Scale bar, 50 μm.
Figure 4. Pericyte recruitment in obesity and tumor vascularization. A and B, confocal immunofluorescence analysis of sections from E0771 tumors with anti-GFP (green) and anti-CD31 (red) antibodies. Shown for lean and obese GFP/RFP chimeras are internal tumor areas at low (A) and high (B) magnification. Blood vessels (red) contain luminal GFP⁺CD31⁺ endothelial cells (yellow arrows) and perivascular/stromal GFP⁺CD31⁻ cells (green arrows). Note increased pericyte coverage and dilation of tumor vessels in obese mice. C, quantitative vasculature analysis in E0771 tumors from lean and obese mice. Vascular density was assessed as mean number of vessels per x 100 view field. Blood vessel size was assessed as mean lumen width for all vessels scored. Blood vessel maturity was assessed as mean percentage of vessels associated with desmin-positive pericytes among all vessels scored. Error bar, SEM. D, confocal immunofluorescence tumor analysis with anti-GFP (green) and anti-desmin (red) antibodies. Yellow signal upon digital channel merging indicates GFP⁺ pericytes, which is confirmed by 2-stack projections of median series for individual cells in the indicated magnified area (bottom). E, confocal immunofluorescence analysis of internal areas from E0771 tumors grown in lean and obese GFP/RFP chimeras with anti-GFP (green) and anti-α-SMA (red) antibodies. Nuclei are stained blue (TO-PRO-3). Scale bar, 100 μm.
tumor cells. Our data argue against the possibility that proliferation of infiltrating ASCs significantly adds to their increased abundance in tumors. While it is likely that ASCs may infiltrate the tumor from adjacent surrounding WAT by migrating through solid tissues, recent reports on mobilization of mesenchymal progenitors in patients with cancer (29, 40) independently indicate the bloodstream as a contributing route. Our recent data suggest that CXCL1 and interleukin (IL)8 secreted by tumor cells and signaling via receptors CXCR1 or CXCR2 is implicated in migration of human omental ASCs (24), and future studies will establish the underlying mechanisms further.

The specific molecular pathways through which ASCs may contribute to cancer progression are yet to be established.
Our data indicate that ASCs recruited by tumors become perivascular or differentiate into intratumoral adipocytes. Mesenchymal progenitors, including ASCs, had been previously shown to modulate cell survival, angiogenesis, and immune response (25), which could account for their tumor-promoting effects. While recent reports on tumor adipocytes in independent mouse models and in clinical specimens (41, 42) are in agreement with our findings, we have not observed accumulation of lipids in malignant cells reported in a recent study (43), which suggests that mechanisms of tumor lipid accumulation and metabolism may be cancer type-specific. Our data on obesity-associated increase in pericyte coverage of tumor vessels suggest increased vascular patency, resulting in increased malignant cell survival and proliferation, as a candidate mechanism of ASC effect. This possibility is consistent with reports on the pro-angiogenic effects of factors molecules secreted by ASCs (15, 44). On the basis of our combined data, we propose that increased adiposity and vascularization associated with obesity-associated ASC recruitment may be functional predeterminants of tumor cell survival and proliferation, both contributing to tumor growth (Fig. 6).

In summary, this study establishes recruitment of WAT-derived cells by tumors as a potential contributor to the stimulatory effects of obesity on cancer progression. We propose that several distinct ASC functions contribute to tumor growth induction observed in obesity. The apparent activity of WAT-derived cells in tumors raises a question about the safety of lipotransfer procedures in patients with cancer (45). Recent studies suggest the role of WAT-derived stroma in cancer metastasis (22), and development of approaches to targeted inactivation of ASCs will enable identification of their specific roles at distinct stages of cancer progression. We propose ASCs as a potential therapy target in cancer.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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Stromal Progenitor Cells from Endogenous Adipose Tissue Contribute to Pericytes and Adipocytes That Populate the Tumor Microenvironment


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