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Introduction
In 2014, approximately 1.5 million women worldwide will be given the diagnosis of breast cancer. Women in the USA, Australia, Scandinavia and the UK will receive the majority of these diagnoses. Nevertheless, the rate of new breast cancer cases is increasing in South America and Russia, as well as in developing countries. Approximately 400,000 lives will be lost to breast cancer in 2013. Worldwide mortality is close to 30%, a rate double that found in the USA. Mortality statistics are often released with concomitant statements that fewer lives would be lost if breast cancer was diagnosed at earlier, preinvasive and premetastatic stages. However, the reality is that identifying the majority of breast cancers before the disease becomes invasive or metastatic is at present unrealistic.

In addition to a lack of effectiveness of present-day chemotherapy against late-stage breast cancer, the side effects associated with these drugs can be life-threatening. For example, treatment of breast cancer patients with capecitabine can cause cardiovascular toxicity [1], and treatment with platinum-based compounds can cause nephrotoxicity [for a review, see 2].

We sought to determine a new approach towards treating patients with all stages and types of breast can-

Abstract
Background: Methyl sulfone is a small molecule that reverses cancerous phenotypes of a melanoma cell line. Here, we sought to determine whether methyl sulfone was effective against human breast cancer tissue. Methods: We studied normal and cancerous breast tissue obtained from 17 patients. Results: Methyl sulfone introduced structural order, with cancer tissue taking on the morphology of normal in vivo breast tissue; this structural order was sustainable over long-term culture. Methyl sulfone promoted proper wound healing, including migration of cells into wounded areas and establishment of stable contact inhibition once wounds were covered. Methyl sulfone decreased expression of two breast stem cell marker proteins, HCAM and OCT3/4, which are associated with aberrantly rapid migration of metastatic cells. Finally, normal and cancerous primary breast cells remained viable and healthy in methyl sulfone culture for at least 90 days. Conclusion: Methyl sulfone reintroduced a normal structural phenotype to human breast cancer tissues.
We chose to study the small molecule, methyl sulfone. Methyl sulfone is a molecule that displays no apparent toxicity to mammals, including humans [3–5]. Furthermore, methyl sulfone is a critical part of the oceanic-atmospheric-terrestrial life cycle of sulfur. Methyl sulfone and its metabolites that form methyl sulfone are natural molecules which are necessary for survival for many organisms including several species of plants, phytoplankton, algae, diatoms and fishes of coral reefs [6–8].

Certain plant species, such as broccoli, cauliflower, brussels sprouts, Swiss chard, onion and garlic, several of which have been consumed by humans for centuries, contain methyl sulfone. Several ancient plants also contain significant quantities of methyl sulfone. For example, the horsetail plant (order Equisetales) has populated earth for over 100 million years. The extraordinary long-term existence of ancient plants like the horsetail indicates the possibility that methyl sulfone has been in our environment for millions of years, which further suggests an important role for methyl sulfone in the maintenance of many forms of life on our planet. Regrettably, over the last 50 years the level of methyl sulfone in the foods we eat has fallen significantly due to mass industrialization of food processing [9, 10].

Methyl sulfone interested us initially because its chemical structure suggested anticancer activity [11]. In support of this hypothesis, we found that methyl sulfone generates antimetastatic cancer activity against a cell line of malignant melanoma [11]. In addition, Lim et al. [12] showed recently that methyl sulfone induced cell growth arrest in several breast cancer cell lines. Here, we chose to study the effect of methyl sulfone on the structural integrity of normal and cancerous human breast tissue. By analyzing both normal and cancerous tissue from the same women, we were able to compare the effect of methyl sulfone between an ‘internal control’ (normal cells) and malignant cells. Such a comparison is not possible with in vitro studies using normal and cancerous human breast cell lines [13]. Moreover, analysis of human breast tissue had other advantages. Firstly, because we chose to study tissue and not clonal cell lines, we were able to examine the effect of methyl sulfone on a mixture of cell types commonly found in breast tumors. Secondly, we were able to compare the effect of methyl sulfone on cancer tissue obtained from women with diverse pathology reports. Diagnoses varied from ductal carcinoma in situ to invasive ductal carcinoma with malignant heterologous chondroid/matrix and osteoclastic components, intraductal carcinoma with lobular extension, invasive ductal carcinoma with mucinous differentiation and invasive lobular carcinoma.

The Nottingham grading system is a compilation score that is used by pathologists and oncologists to determine prognosis and treatment and is based on the mitotic index (the higher the number of mitotic cells in the tumor tissue, the worse the prognosis), pleomorphism of nuclei (the more misshapen the nuclei, the worse the prognosis) and tubule formation. Tubule formation is the percentage of the breast tumor tissue that forms normal duct structures; the less structurally ordered the tumor, the worse the prognosis. Nottingham grades range from I to III. In the studies presented here, 50% of the patients had a Nottingham grade of III, the worst grade for prognosis.

We show here that regardless of diagnosis, methyl sulfone had the same effect on all tissue samples; that is, methyl sulfone imparted sustainable structural order at a tissue level and at a cellular level. In normal and cancerous human breast tissue, the structural order induced by methyl sulfone resembled biopsied samples of normal breast tissue. Wound healing proceeded normally only in the presence of methyl sulfone. In the absence of methyl sulfone, wounds did not heal properly; cells migrated and covered the wounded area at a much faster rate than in methyl sulfone-treated cells, but once covered, no contact inhibition was established. Because control cells migrated into the wound area much faster than methyl sulfone-treated cells, we examined two breast stem cell proteins, HCAM and OCT3/4, which are known to increase migration rates of metastatic cells. We show here that methyl sulfone decreased the expression of both HCAM and OCT3/4.

Materials and Methods

Materials
Methyl sulfone was purchased from Fluka/Sigma Co. (St. Louis, Mo., USA).

Cell Culture
Breast tissue was obtained from patients during surgery. In 11 of 17 patients, both normal and cancerous tissue was obtained from the same patient. In 5 of 17 patients, normal tissue alone was obtained. In 1 of 17 patients, cancerous tissue alone was obtained. Informed consent was obtained from the University of Connecticut Health Center Tumor Bank. Fresh tissue was deidentified by Tumor Bank personnel before it was given to researchers. Once the researchers obtained the tissue, samples were given reference code numbers. Code numbers were changed a second time during preparation of this article. The University of Connecticut Health Center Institutional Review Board deemed the research study exempt from IRB review. Tissue samples ranging in size from 2 to 4 mm³
were plated in three to five 35-mm culture dishes per sample obtained from the operating room. Tissue samples were collected from August 8, 2008, to August 25, 2011. The pathology reports for patients are shown in online supplementary table S1 (see www.karger.com/doi/10.1159/000351099, for all online suppl. material). Samples of data shown here were chosen randomly before the second set of code numbers was introduced.

Tissue was prepared for culture as described by Ince et al. [14]. Briefly, tissue was minced under sterile conditions, followed by treatment with collagenase A (Roche Diagnostics, Mannheim, Germany) at 1 mg/ml in Hank’s buffered saline solution at 37°C, 5% CO₂, for 6 h. Cells were plated in Primaria tissue culture dishes (Becton Dickinson and Co., Franklin Lakes, N.J., USA) in either DMEM with 7% fetal bovine serum (Invitrogen Inc., Eugene, Oreg., USA) or chemically defined WIT-P medium (Stemgent, Cambridge, Mass., USA). After at least 24 h in culture, the medium was replaced with DMEM or WIT-P medium without (control) and with methyl sulfone (100–1,000 mM). Medium was replaced every 48 h. Control cultures were maintained for up to 2 months. Methyl sulfone cultures were maintained for up to 3 months. For each patient, 500–700 photographs of tissue in culture were taken over time.

**Light Microscopy**

Light microscopy and photography were performed with a Zeiss Axio Observer A1 microscope using an N-ACROPLAN 10×/0.25 objective and an LD A-Plan 20×/0.30 objective.

**Hematoxylin Staining**

Hematoxylin staining was performed at the Histology Research Facility, University of Connecticut Health Center (Farmington, Conn., USA), under the direction of Kevin Claffey. Briefly, cells in Primaria plastic tissue culture dishes were immersed in a solution of hematoxylin for 2 min. This was followed by a 15-second wash in ammonia then several washes in distilled water. Images were photographed with a Zeiss Axio Observer A1 microscope using an N-ACROPLAN 10×/0.25 objective and an LD A-Plan 20×/0.30 objective.

**Wound Healing**

Cells were plated in WIT-P medium in 35-mm Primaria tissue culture dishes. When cultures were confluent, medium was replaced with WIT-P with or without 200 mM methyl sulfone. After 48 h, the cell monolayer was scraped with a sterile plastic 1,000-μl pipette tip. This left a cell-free strip (wound area) on the culture dish plastic that was surrounded by the remaining cell monolayer. Cells were washed twice with medium to remove cell debris and dish plastic that was surrounded by the remaining cell monolayer.

**Immunofluorescence Microscopy**

To maximize immunofluorescence data, cells were plated on 12-mm glass coverslips in DMEM medium in 35-mm Primaria tissue culture dishes at a low density and incubated at 37°C, 5% CO₂. These plating conditions allowed us to examine relatively flat cells with some separation between cells. After 24 h, medium was replaced with control medium (no methyl sulfone) or medium with 200 mM methyl sulfone. After 96 h, cells were fixed in 4% paraformaldehyde and processed for immunofluorescence staining of two breast stem cells markers, HCAM and OCT3/4. Rabbit polyclonal antihuman HCAM antibody and goat polyclonal antihuman OCT3/4 antibody were purchased from Santa Cruz Biotechnology (Santa Cruz, Calif., USA). Secondary antibodies, i.e. goat antirabbit Alexa Fluor 568 and rabbit antigoat Alexa Fluor 568, were purchased from Molecular Probes (Eugene, Oreg., USA). Nuclei were visualized with 4,6-diamidino-2-phenylindole. Images were obtained at the Richard D. Berlin Center for Cell Analysis and Modeling, University of Connecticut Health Center (Farmington, Conn., USA), with an Axiopted CCD Microscope equipped with a 63×1.4 NA Plan Apo immersion objective via Metamorph image acquisition and analysis software (Universal Imaging Corp., Downingtown, Pa., USA).

**Results**

**Minimum Effective Dose of Methyl Sulfone**

We examined a range of concentrations of methyl sulfone to identify the minimum effective dose that induced contact inhibition but did not kill the cells. Normal and cancerous tissue from 5 patients was incubated with 0, 100, 200, 300, 400, 600 or 1,000 mM methyl sulfone in DMEM or WIT-P medium. Cells were examined by phase contrast microscopy every 24 h for up to 30 days. Similar results were found in normal and cancerous tissues from all 5 patients, whether cultured in DMEM or WIT-P medium. At 600 and 1,000 mM methyl sulfone, cells died within 24–48 h. At 400 mM methyl sulfone, approximately 20% of cells died within 24 h. At 100 mM methyl sulfone, plates of cells demonstrated some areas of contact inhibition that were not seen in control cells (no methyl sulfone). At 200 and 300 mM methyl sulfone, cell monolayers became completely and stably contact inhibited. Therefore, we chose 200 mM methyl sulfone as the minimum effective dose.

**Methyl Sulfone Induced Contact Inhibition in Both Normal and Cancerous Breast Tissue Cultured in DMEM**

To determine how methyl sulfone affected the structural organization of normal and cancerous cells, we first examined tissue from patient 001 (for the pathology report, see online suppl. table S1). After 1 day in culture, medium (DMEM) was replaced with control medium (no methyl sulfone) or 200 mM methyl sulfone. Cultures were examined every 24 h and photographed every 24–72 h. After 33 days in culture, phase contrast microscopy demonstrated that without methyl sulfone (control), cells from cancerous breast tissue became pale, flat, spread out and vesiculated, with none of the hallmarks of healthy cell phenotype. Normal breast tissue cultures maintained contact inhibition and showed characteristic epithelial cell morphology.
These cells displayed no apparent contact inhibition, instead showing nondistinct boundaries between cells (Fig. 1). Conversely, culturing these tissues in the presence of 200 mM methyl sulfone resulted in contact inhibition and an ordered appearance with no vesiculation of the darkened cytoplasm (Fig. 1).

**Fig. 1.** Effect of methyl sulfone on contact inhibition in normal and cancer breast tissue from patient 001. Normal and cancer cells from patient 001 (for the pathology report, see online suppl. table S1) were plated into Primaria tissue culture dishes in DMEM. After 24 h in culture, medium was replaced with DMEM containing 0 (control) or 200 mM methyl sulfone (MS). Every 48 h, medium was changed and cells were photographed. Shown here are phase contrast photographs of normal and cancer cells after 33 days in culture. Control cells received no methyl sulfone. Methyl sulfone-treated cells were incubated with 200 mM methyl sulfone for the last 32 days of a 33-day culture.

**Fig. 2.** Effect of methyl sulfone on normal and cancer breast cells from patient 008. Normal and cancer cells from patient 008 (for the pathology report, see online suppl. table S1) were plated into Primaria tissue culture dishes containing WIT-P medium. Every 48 h, medium was changed and cells were photographed. After 38 days in culture, medium was replaced with WIT-P medium without (control) and with 200 mM methyl sulfone (MS). The top phase contrast photographs are normal and cancer cells after 45 days in culture in control medium. The bottom photographs are normal and cancer cells in 200 mM methyl sulfone for the last 7 days of a 45-day culture. The arrows delineate ductal/lobular-like areas and the arrowheads delineate areas resembling bands of myoepithelial cells. Scale bar = 20 μm.

**Methyl Sulfone Induced Contact Inhibition and Order in Normal and Cancerous Tissue Cultured in WIT-P Medium**

We next examined the effect of methyl sulfone on normal and cancer tissues cultured under conditions described by Ince et al. [14]. Single cells and cells in small organoids were plated into Primaria tissue culture dishes containing the chemically defined medium WIT-P. The results from patient 008 are shown in figure 2 (for the pathology report,
see online suppl. table S1). After 38 days in culture, 200 mM methyl sulfone was added to half of the plates. After an additional 7 days in culture, control and methyl sulfone-treated cells were photographed. In the absence of methyl sulfone, both normal and cancer cells appeared disorganized and overgrown with no distinct boundaries between cells (fig. 2). In the presence of methyl sulfone, normal and cancer cells became contact inhibited, forming an organized monolayer (fig. 2). There was a high cytoplasm to nuclei ratio. In both normal and cancer tissue in the presence of methyl sulfone, circular arrangements of cells were present that resembled ductal/lobular structures of the normal breast (fig. 2, arrows). Possible bands of myoepithelial cells lined the methyl sulfone-induced islands of cells and traversed between ductal-like areas of cells (fig. 2, arrowheads).

Online supplementary table S2 is a summary of phase contrast microscopy data demonstrating the effect of methyl sulfone on the structural organization of normal and cancerous tissues obtained from 17 patients. Normal and cancer tissue from the 17 patients responded similarly to methyl sulfone whether treated for 3 or 60 days. When cultured in DMEM with methyl sulfone, cells formed a stable contact-inhibited monolayer. When cultured in WIT-P medium with methyl sulfone, cells became organized into stable structures reminiscent of normal breast tissue.

Further representative phase contrast microscopy data of 2 additional patients can be found in online supplementary figures S1 and S2. Because tissue from the 17 patients produced similar data, we randomly chose patients 001, 008 and 011 (fig. 1–4) and patients 009 and 010 (online suppl. figures S1 and S2) as representative data; final patient numbering shown in online supplementary tables S1 and S2 was done after randomly choosing the data.

**Effect of Methyl Sulfone on Structure of Normal and Cancerous Tissue as Seen with Hematoxylin Staining**

We wanted to stain tissue as performed by pathologists so that we could compare the structure of our cultured tissue samples with the structure that is found in clinical pathology labs. Therefore, normal and cancer tissue from patient 008 was cultured in Primaria dishes and stained with hematoxylin. We omitted eosin staining because the plastic dishes would dissolve with the organic solvents for eosin. As shown in the top photographs of figure 3, in normal and cancer tissue in the absence of methyl sulfone, cells appeared disorganized and overgrown as seen in the phase contrast photographs of figure 2. The bottom photographs of figure 3 show normal and control cells after incubation with 200 mM methyl sulfone. Here, cells are organized into 2 general regions, namely the dome-like areas of cells with round nuclei (fig. 3, arrows) and areas of bands of cells with...
elongated nuclei (fig. 3, arrowheads). This difference in morphological regions suggests the possibility that the dome areas are ductal/lobular-like structures of epithelial cells and the areas of cells with elongated nuclei are myoepithelial cells. The large cytoplasm to nucleus ratio is apparent in both morphological regions.

**Methyl Sulfone Induced Proper Wound Healing in Normal Human Breast Tissue**

We sought to determine whether methyl sulfone induced proper wound healing in normal human breast tissue in culture (patient 011; for the pathology report, see online suppl. table S1). Tissue was cultured for 90 days; in half of the plates, 200 mM methyl sulfone was added for the last 60 days of culture. Cells were wounded at day 55 in culture and then photographed every 24 h for 5 days. In the presence and absence of methyl sulfone 2 and 5 days after wounding. Cells in the presence and absence of 200 mM methyl sulfone were able to migrate into the wounds as expected for proper healing. However, once the wound was covered or healed, cells in 200 mM methyl sulfone stopped migrating and once again became contact inhibited. In contrast, cells in the absence of methyl sulfone did not properly heal the wound; instead, these cells continued to grow and move, even though the wound was covered, forming what appeared to be tumor masses. Scale bar = 20 μm.

By the second day in the absence of methyl sulfone, cells quickly covered the wound but continued to proliferate and migrate, displaying what appeared to be disorganized tumor masses of cells (fig. 4). By the second day in the presence of 200 mM methyl sulfone, migration of cells into the wounded area was slower than in control cells. However, once the wound was covered, cells in methyl sulfone stopped migrating, and cells became contact inhibited.

**Methyl Sulfone Decreased Expression of Two Breast Stem Cell Markers in Cancerous Tissue**

The wound healing experiment shown in figure 4 demonstrates that cell migration into the wounded area was approximately 5 times faster in control cells than in methyl sulfone-treated cells. Two proteins that are known
to increase the rate of migration of cancer cells into wounds are the breast stem cell markers HCAM and OCT3/4 [15–18]. We therefore examined cancerous tissue for the presence of these two stem cell proteins and the possible effect of methyl sulfone on their expression. Using immunofluorescence microscopy, we tested cancerous tissue from patient 004 (for the pathology report, see online suppl. table S1) for the presence of HCAM and OCT3/4. Cells were cultured on glass coverslips for a total of 20 days; 200 mM methyl sulfone was added for the last 7 days of culture. As shown in figure 5, both HCAM and OCT3/4 were expressed in control cancer cells. However, upon treatment of these cells with methyl sulfone, expression of both stem cell markers was markedly decreased.
Methyl sulfone induced structural organization in cancerous human breast tissues obtained from a number of patients, each of whom had a unique diagnosis. For this reason and reasons outlined below, these data suggest the possibility that methyl sulfone may be a useful broad-based chemotherapeutic compound regardless of breast cancer subtype [19] and receptor status.

In the presence of methyl sulfone, two distinct cell culture media, DMEM with fetal calf serum and serum-free WIT-P medium, induced stable structural organization in normal and cancer tissue. These data suggest that this effect of methyl sulfone is not dependent on the type of medium used for cell culture.

We performed concentration studies with methyl sulfone on tissues from 5 patients, and the lowest effective concentration of methyl sulfone in all cases was 200 mM. Interestingly, this is the same effective concentration of methyl sulfone that we found for the metastatic melanoma cell line Cloudman S-91 (subclone M3) [11]. Similarly, Layman [20] found that 200 mM methyl sulfone induced growth arrest in cultures of aortic smooth muscle cells and aortic endothelial cells without causing cell death. Recently, Lim et al. [12] found that 300–500 mM methyl sulfone induced cell growth arrest in several breast cancer cell lines via the STAT1 and STAT5 pathway.

Another small sulfur-containing molecule, N-acetylcysteine, is used as a nutritional supplement. N-acetylcysteine alone has no effect on cell viability or apoptosis in vitro. Interestingly, N-acetylcysteine decreases the percentage of apoptotic cells induced by paclitaxel, a commonly used chemotherapy compound. N-acetylcysteine is thought to act by providing sulfhydryl groups for direct scavenging of reactive oxygen species, which in turn regulates the redox status in cells [21]. Since studies have shown that methyl sulfone can act as an antioxidant by scavenging reactive oxygen species [22], it is possible that the sulfhydryl group in methyl sulfone acts through a similar mechanism as N-acetylcysteine.

**Methyl Sulfone and Tissue Structure**

We could not have performed these studies on tissue structure without the pioneering work of Ince et al. [14]. This group developed a cell culture system for normal primary breast cells that includes the use of Primaria tissue culture plates and a chemically defined medium (WIT-P). Interestingly, as shown in our studies, normal and cancerous cells cultured in WIT-P formed 3-dimensional structures (fig. 3), while cells cultured in DMEM, a common medium for breast cancer cell lines, formed contact-inhibited monolayers (fig. 1). Since breast tissues obtained from patients contained several cell types (ductal epithelial cells, lobular epithelial cells, myoepithelial cells, fibroblasts, macrophages), perhaps WIT-P medium but not DMEM promoted architectural building of structures among the various cell types. Interestingly, the combination of methyl sulfone with WIT-P medium resulted in markedly improved structural architecture over the Ince culturing system alone.

In vivo, function is directly related to structure. For example, the architecture of normal breast tissue is ordered and structured, whereas the architecture of invasive nonfamilial breast cancer tissue and familial breast cancer tissue is chaotic, lacking order and structure [23]. Furthermore, the higher the degree of disorder within malignant breast tissue, the worse the prognosis [24–26]. Conversely, a protein that plays a role in maintaining tissue architecture, DEAR1, is also a tumor suppressor protein [27].

In the absence of methyl sulfone, human cancerous tissue appeared chaotic and disorganized upon attachment of cells to culture dishes. On the other hand, early cultures of normal tissue appeared either organized or chaotic. However, regardless of how the normal cultures started out, within 1–5 days in the continued absence of methyl sulfone, all normal cell cultures took on the chaotic appearance of malignant tissue. In fact, normal tissue cultured without methyl sulfone for more than 1–5 days was indistinguishable from cancerous tissue cultured in the absence of methyl sulfone. Ince et al. [14] described the same phenomenon with normal breast tissue cultured in Primaria plates with WIT-P medium; normal tissue takes on the appearance of cancerous breast tissue over long-term culture. In our studies, this chaotic appearance of both normal and cancer tissue seen in the absence of methyl sulfone was reversed upon addition of methyl sulfone, the cellular organization of cancerous and normal tissue subsequently becoming structured. After 4 weeks in culture, medium containing methyl sulfone could be replaced with control medium and the structure that had been established in the presence of methyl sulfone became permanent.

The structural organization induced by methyl sulfone was particularly apparent in tissue samples stained with hematoxylin, one of the dyes used by pathologists to examine breast tissue. In fact, methyl sulfone-treated normal and cancerous structures (fig. 3) look similar to images in textbooks of hematoxylin-stained normal biopsy tissues [28, 29]. Firstly, as shown in figure 3, cells...
Methyl Sulfone, Wound Healing and Breast Cancer Stem Cell Markers

Wound healing is of critical importance for patients undergoing cancer treatments. Surgery is the first mode of defense for patients with many types of cancer, including breast cancer, and in some cases cancer can inhibit the wound healing process [32–34].

We used the wound healing assay described here to examine two events of proper wound healing, namely the ability of cells to migrate into the wound area, followed by cessation of migration and establishment of contact inhibition once the wound is covered. Contact inhibition plays an integral role in healing wounds [35]. We demonstrated that both events of proper wound healing are promoted by methyl sulfone, albeit at a migration rate approximately 5 times slower than that in control cells (no methyl sulfone).

A truncated version of this wound healing assay is commonly used to measure the rate of migration of metastatic cells. Using this assay, several investigators have shown that the breast stem cell proteins HCAM and OCT3/4 increase the rate of migration of metastatic cells [15–18]. HCAM, also known as CD44, is an adhesion molecule that modulates cell-matrix interactions via binding to hyaluronan as well as other ligands [36]. OCT3/4, also known as POU5F1, is an embryonic transcription factor of the POU homeobox gene family [37, 38]. OCT3/4 plays a role in the self-renewal of embryonic stem cells. Evidence demonstrates that expression of both HCAM and OCT3/4 in breast tissue is associated with the presence of cancer stem cells or tumor-initiating cells and with carcinogenesis [16, 39–43].

Since we found in the wound healing assay that the rate of cell migration was significantly slower in methyl sulfone-treated cells when compared to control cells, we asked whether methyl sulfone affected the levels and/or distribution of HCAM and OCT3/4. We showed here that methyl sulfone decreased expression of both HCAM and OCT3/4, reducing the levels of both proteins in the cytoplasm and nucleus. These data do not prove but do suggest the possibility that methyl sulfone slows down migration of metastatic cells via HCAM and OCT3/4. This possibility will be the focus of future experiments.

Make Peace, Not War

For many decades we have been trying to eradicate cancer by killing cancer cells. We talk of the ‘war against cancer’ and our ‘arsenal of weapons’. For treatment of metastatic cancer, this approach has not worked, and since 90% of cancer deaths are due to metastatic disease,
this is a significant failure. The role of a metastatic cancer cell is simple, namely to stay alive and proliferate and migrate through the patient’s body. The cancer cell can use multiple pathways to achieve these goals. If one part of a pathway, for example for proliferation, is blocked by a highly specific chemotherapy drug, the cancer cell can ‘evolve’ so that it no longer needs that one specific part of that particular proliferation pathway. In fact, we believe that highly specific chemotherapeutic agents put selective pressure on metastatic cells to change and circumvent the targets or die. This approach may give patients some time, but ultimately we do not believe this method will be successful against metastatic disease.

An alternative approach is described by our studies with methyl sulfone. Here we are not trying to kill cancer cells, but instead redirect metastatic cancer cells away from cell proliferation and migration and towards the functions of normal differentiated cells. Using the approach with methyl sulfone, metastatic cells are under no selective pressure to circumvent proliferation pathways. There should be no selective pressure against acquiring these normal processes that lead to structure and differentiated cell function. This is what cells do naturally in our bodies all the time.

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References


