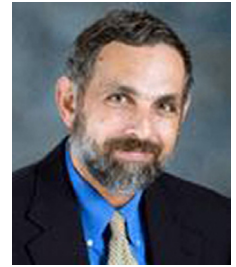


# Integrative Oncology Exceptional Patients - Thoughts and Reflections

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**How do we help our patients become exceptional patients? What are the lessons we learn from our exceptional patients that can positively impact how we practice?**

Sometimes without knowing, a personal experience leads to a change in your attitude and approach to significant issues in your practice. Seventeen years ago I was quite involved with the integration of complementary medicine with conventional medicine. At that time my approach to integrative medicine was very pragmatic. I suggested using complementary medicine whenever conventional options were not effective, with one exception, treatment of cancer. At that time I believed that complementary medicine did not have a role in cancer care.

I changed my approach after observing a complicated trajectory that one of my friends went through.

Suzanna, a good friend of mine, at that time in her late 40s, was divorced with three grown children and no extended family. She was a successful practitioner involved with complementary medicine. She was attractive and well respected in her field and we saw her occasionally at social events. She called us one day with a sense of panic in her voice -- she felt a lump in her breast. She quickly obtained a consultation with an expert, and a biopsy that was done with no delay confirmed the worse case scenario of having a diagnosis of breast cancer. The lumpectomy that followed confirmed extensive disease of invasive ductal carcinoma with involvement of lymph nodes. After the surgery the surgeon notified her that in addition to the surgery she would need to schedule an appointment with an oncologist to arrange adjuvant chemotherapy.

Suzanna was devastated. In an instant she went from being a well-known practitioner to a patient. Her first thought was, "I'm going to die." She was consumed with that thought. She felt alone, helpless and hopeless, a situation which is very common for people diagnosed with cancer.<sup>1</sup>

## The Most Significant Stressors in Cancer

Let's expand a little bit on those issues. Unwanted aloneness, or social isolation

is something that we tend to dismiss but when we look at the scientific literature, we find interesting facts. A meta-analysis of 148 studies on this issue revealed that there is a 50% increased likelihood of survival for people who have stronger social relationships.<sup>2</sup> It appears that social isolation is a leading risk factor for mortality. This risk factor is actually worse than most of the well known and established risk factors such as smoking. This is something that we have to think about.

The other issue is loss of control. This is very similar to helplessness. In the book *Anticancer* by David Schreiber, there is a description of a study that was published in 1982.<sup>3</sup> Three groups of mice were injected with tumor cells and studied for the ability to reject these tumor cells among those three groups. In the first group, which was simply observed, about 54% of the mice rejected the tumor cells, with the other 46% developing tumors. The second group of mice received electric shocks. The mice had no control over the electric shocks. Only 23% of those mice managed to reject the tumor cells. This means that 77% developed tumors. The third group was given control over the electric shocks. They quickly learned that they could stop the shocks when they pressed a lever. What the researchers found was that 63% of the mice that were able to stop the shocks were able to reject the tumor cells—only 37% developed tumors, which is even better than the mice that received no electrical shocks at all. When the researchers gave those mice a way to control what was happening to them, their immune systems

began to work much better, even better than those that didn't have to contend with shocks at all.

The third issue is hope. A well-known psychiatrist, concentration camp survivor and author, Victor Frankl, PhD said a long time ago, "There is direct connection between mood, courage and hope. The loss of hope and courage can be fatal."

According to Schreiber, many oncologists' greatest worry is not to give false hope. In every situation in cancer, even in the most advanced situation, there are a small percentage of people that manage to survive. There are documented recoveries of stage IV cancer patients, not many, but there are some patients that beat all odds. It raises the thought or question if we should be telling such patients that they have no chance at all of recovery. By doing that we actually create false hopelessness, which is much worse than giving false hope. Who is to say when hope is false?

Encouraging passivity and fostering a culture of hopelessness is actually encouraging false hopelessness. Scientific evidence shows that we can have a substantial impact on our body's capacity to diffuse the mechanisms of cancer, even in advanced situations.

On the other hand, being unrealistic about one's own situation, believing that thanks to using a variety of natural approaches they can refuse conventional treatments and obtain a cure is not a healthy approach either. Physicians need to walk a very delicate path, where they provide a realistic understanding of the situation but at the same time not cause patients to lose hope. However, most physicians find it very hard to deal with this delicate balance. As a result of the physician's fear of giving false hope, a large number of patients believe that they cannot do anything to protect themselves actively against cancer – before treatment, during treatment, and after the treatment is over.

## Defuse False Sense of Hopelessness

So how do we defuse this false hopelessness?



ness? One way is by moving the patient from passive to active. We need to provide knowledge and reliable information of simple non-toxic self-care measures as a standard of care. And we have to implement this knowledge into daily life, empowering patients and their families.

When I did my consultations with patients at MD Anderson, I discovered that patients wanted to hear about patients that had the same diagnosis as their own and actually survived the experience. Patients are looking for the exceptional patients that managed to survive. This is as a major source of hope for them.

## Hope

An interesting study about hope was published in JAMA in 1990.<sup>4</sup>

The authors wrote about hope as it might appear in the PDR, the Physician Desk Reference, covering indications, contraindications, side effects and so on. Are there any contraindications to hope? Hope is a belief that the present situation can be modified and that there is a way out of the difficult situation or a belief that better days or moments will come. Hope is an importance resource that influences an individual's ability to cope with a stressful life-threatening situation.

## Making Decisions

Getting back to my friend Suzanna, the following week after she digested the information given by her oncologist, she asked me, "Before I make a decision, I want to know what will happen if I don't take the chemotherapy. I understand that if I take the chemotherapy I have a 32% chance to live. But what happens if I don't take it?"

"Also," she said, "I would like to meet people that did not take chemotherapy. I want to meet those exceptional patients that managed to avoid chemotherapy and what happened to them." She came up with the idea of putting an ad in the newspaper looking for exceptional patients. The ad ran multiple times, but none of these exceptional patients showed up. She was very frustrated. At that time her request to be involved in the decision-making was unusual. This was 17 years ago, and the physician reaction was, "If you're not doing the chemotherapy you will die."

About twelve years ago the US Institute of Medicine produced a very interesting monograph called Crossing the Quality Chasm: Health Care System for the 21st Century. It concluded that patients should be involved in decision-making. "All patients should be given necessary information and the opportunity to exercise the



degree of control they choose over health care decisions that affect them."

Studies suggest that patients who more actively participate in their care are more satisfied with their care and may have better health outcomes.<sup>5</sup>

Suzanna sent me on a search of the medical literature to find out what happens without chemotherapy treatment. My initial thought was "That's easy. You are going to die."

At that time, 17 years ago, looking for information was complicated. We did not have PubMed. Obtaining that information was through something called Index Medicus. Index Medicus were big volumes updated monthly that were archived at each medical library. It took me a long time to obtain that information. To my surprise, it was not an 100% death sentence. The five-year survival at that time, for patients with Suzanna's breast cancer prognostic features that did not take chemotherapy was 26%.

Suzanna had to make a decision as to what to do. With treatment, overall survival was statistically 32%. Without treatment, overall survival was 26%. In order to balance the equation one also needs to know the cost of the treatment, not just the money costs, but also the side effects and knowledge about the toxicity of the treatment.

What about side effects? What was the percentage of life threatening side effects for patients taking the standard adjuvant chemotherapy? That also took a long time to find out. There's not a whole lot of information available about this issue. Researchers tend to report success and not failures or complications of treatment. I did manage to find a few that did. In those few studies that rate turned out to be 8%. That means that an average 8% of patients that take chemotherapy develop life threatening complications as a result of the chemotherapy.

So there was a 6% survival difference between doing chemotherapy and not. She was single, she did not have support, she lived by herself, and her family was not around if she did have complications from the chemotherapy.

On the other hand she was a beautiful lady, divorced and looking for a lifelong partner. Losing her beautiful hair, going through the complicated journey alone, and suffering from the side effects by herself made her wonder if this was something she wanted to do. She took all those figures of the benefit of treatment (6%), compared it to the side effects profile (8%) and she decided to hold off on the chemotherapy treatment.

Initially when I heard that, I said, "You're nuts. What are you doing? You're going to die. How could you do that?" Now when I look back, I see that we have to be unassuming in our convictions, and at times accept patients' decisions even if we do not agree with them.

## Uncertainty

So what are we doing in these days of uncertainty?

We try to base all our decisions on evidence. What do we really know in evidence-based medicine? The British Medical Journal Clinical Evidence in 2008 mentioned that benefits of treatments in general (not related to cancer care) carry a benefit supported by evidence only in 13% of cases, another 23% is likely to be beneficial, but 46% are uncertain, with unknown effectiveness. In 2011, the beneficial side shrank to 11% while uncertainty grew to 51%. So when we talk about evidence based medicine we might be humble as to our expectations from treatments. This relates to general practice. In oncology, it is much more complicated as most studies are not done in the evidence based medicine approach of randomized double blinded controlled trials. (Very few studies actually compare active treatment to placebo in a randomized way. Most studies compare new treatments to old treatments).

In the past we used to pay attention to disease oriented evidence; basically improvement in patient outcomes that are physiological, intermediate, or surrogate endpoints like blood pressure, blood chemistry, physiological function, and pathological function, that may or may not reflect improvements in patient outcomes (e.g. blood pressure, blood chemistry, physiologic function, pathologic findings). Today we are changing to patient-oriented evidence, what matters to patients, such as morbidity, mortality, symptom improvement, cost-reduction and quality of life. The advice that patients are seeking is a little bit different. They are looking for immediate relief, how to shorten suffering, speed healing, and what can eradicate this disease with limited suffering. Physicians

need to translate the evidence that they have into giving the advice that patients are seeking for.

### Overall Survival

When we are talking about patient-oriented outcomes in cancer, we are talking about recurrence and the gold standard in oncology, which is overall survival. The crucial question that runs through every patient's head is, "Am I going to live or die?" It is true that overall survival can give a statistical answer, but that might not be the right answer for the individual patient. And.... I think the individual patient should have these figures.

It can give a basic idea as to the seriousness of the disease, and if it can be treated by conventional measures. Recurrence rates give a general idea as to the statistics of the tumor coming back, but that does not mean that people die if the tumor comes back. More important is the overall survival, which encompasses the success of treatment but also includes figures that are hidden such as late side effects of treatment, which at times are not considered as directly related to the cancer treatment (congestive heart failure, pneumonia etc.) With these figures of overall survival, patients and their families can come on their own or with their physicians' help to informed decisions whether therapy is worthwhile or not. That is not the usual practice.

Oncologists are also living in a state of uncertainty worse than the patients because they have to make a decision with each patient. The patient has his own uncertainty but oncologists have to make decisions based on uncertainty every day, multiple times each day.

Physicians look for advice on how to deal with this uncertainty. Basically they gather all the evidence and present it to an expert committee and use clinical guidelines and standards in clinical practice as a way that makes the road of making decisions easier. But even that route can be at times very complicated, with a very ambivalent process of decision making, even to the most experienced ones.



### What can one do?

Decision making in times of uncertainty is problematic. But there are many things that patients can do on their own, supported by scientific data that can improve their survival rates in addition to the medical care.

In 2007 the World Cancer Research Fund published a very important document that summarizes reviews and viewpoints of thousands of research articles and studies. The document concludes that 30 to 40% of cancers can be prevented with food and nutrition, regular physical activity and avoidance of obesity. Another 30% of cancer may be prevented by the cessation of smoking (which causes not only lung cancer, but also breast, bladder, head and neck cancers, and leukemia). An additional major issue that is not emphasized in most oncology guidelines is addressing the issue of stress. In new recent studies there are hints that stress can affect tumor size and metastatic spread as well as survival and mortality.

### Exercise

I was surprised to learn about ten years ago that simple exercise such as walking every day for half an hour, seven times a week, basically reduces the mortality of breast cancer survivors by 50%. There is a reduction in breast cancer recurrence of 45% for women that actively walk.<sup>6</sup> This is better than taking Tamoxifen. Cancer institutions are beginning to include exercise programs because of many studies that are starting to accumulate. This important fact cannot be ignored.

In a prospective cohort study of lifetime physical activity and survival in women with breast cancer, 1231 women diagnosed with breast cancer between 1995 and 1997 were followed for a minimum of 8.3 years. Both moderate and vigorous intensity recreational physical activity decreased the risk of breast cancer death (26%-44% reduced risk of death). Moderate intensity recreation activity (intensity goal: 100 steps in 1 minute) decreased the risk of a recurrence, progression or new primary cancer by an average of 44% (0.66, 95% CI = 0.48-0.91).<sup>7</sup>

Another study done on patients with prostate cancer found something very similar. 2,705 men diagnosed with prostate cancer (non-metastatic) were observed from 1990 to 2008. Men who walked 90 minutes or more per week, basically 30 minutes three times a week, at a normal to very brisk pace, reduced the risk of mortality by 46% compared with shorter durations at an easy walking pace. And when



they increased this exercise to greater than 3 hours per week of vigorous activity, they had a 61% lower risk of death from prostate cancer compared with men with less than 1 hour per week of vigorous activity.<sup>8</sup> Simple things such as walking can have a very significant effect on survival. Exercise is clearly strong medicine against cancer and is not being adequately prescribed or taken.

### Green Tea

Multiple studies tell us about the importance of green tea. There is a very famous Japanese study where women that drank 3 cups of green tea, with a follow-up of ten years reduced breast cancer recurrence by 31%.<sup>9</sup>

### Soy

In the past there was fear of soy, due to its phytoestrogens content, but recent studies reveal that using soy in its natural forms and not as supplements has a beneficial effect. In one study, two servings per day of soy food intake, as measured by either soy protein or soy isoflavone intake was inversely associated with mortality and recurrence. There was a 30% reduction in the risk of recurrence.<sup>10</sup>

### Vitamin D

Vitamin D is attracting a great deal of interest in the past few years. There are many studies that hint that the use of Vitamin D in certain situations might be beneficial in certain types of cancer types. In one study with patients affected by breast cancer there was a 58% reduction in risk for breast cancer with higher Vitamin D levels.<sup>11</sup> There is still a great deal that is unknown about this vitamin in relationship to cancer treatment and probably, in the near future, more data are going to be accumulated related to this vitamin and its benefits.

### Stress and Cancer

Researchers from MD Anderson Cancer Center performed a very unique type of study that documented the effect of stress



on cancer development. The researchers divided mice into two groups, one with an intervention, and another group that just hung out, ate, drank and had a good time. Both groups were injected with ovarian cancer cells. The intervention was to put the mice under stress. They put them in an enclosed and trapped place so they couldn't move for two hours a day. Mice like to run around so this was very stressful for them and confirmed their stress by checking their levels of stress hormones. The levels of those stress hormones were high after two weeks of exposure to this type of stress.

The stress hormones of the group that just hung and out enjoyed life were at baseline. The tumors in the mice that were stressed grew almost 3 times in size compared to the group that was not stressed. Metastasis was 50% more in the group that was stressed. This was very significant. In the control group tumor growth was confined to the peritoneal cavity. On the other hand, the cancer spread to the liver and spleen in 50% of the stressed mice.<sup>12</sup>

Another study done with breast cancer was done in the same way with mice with breast cancer. In this study the tumor didn't change in size but in the group that was stressed, the metastatic spread of the tumor was 30 times greater than the group that was not stressed. The study concluded that chronic stress acts as a sort of fertilizer that feeds breast cancer progression, significantly accelerating the spread of disease in animal models.<sup>13</sup> When I read these studies I thought to myself, how can we not address this issue of stress in patients, from the moment of diagnosis through the complicated trajectory that each patient goes through. We need to integrate techniques of stress reduction as a routine to each patient's treatment plan, as an obligatory component

Another interesting study done at Ohio State University that was published in 2008 created an intense reaction in the cancer world.<sup>14</sup> The study was done with 227 patients with breast cancer. After they had surgery and standard of care breast

cancer treatments they divided the patients into two groups. One group received instructions about diet, stress reduction, smoking and exercise. The other group was followed with standard care only.

Patients were given instruction in a group meeting once a week for three months and then once a month for another eight months for a total of one year. Patients were followed for about 11 years. There was a marked difference between the intervention group and the group that did not get lifestyle instruction as far as breast cancer specific survival and overall survival. There was 56% reduced risk of death and 45% reduced risk of recurrence in the group that received stress management, diet, exercise, and lifestyle training. We cannot ignore these types of clinical outcomes data.

### Changes

In the case of Suzanna, she had to make tough decisions; she had to construct a plan taking the data that she collected. As mentioned previously, the survival benefit of taking chemotherapy in her situation was calculated at around 6%. Life-threatening side effects were calculated around 8%. But there was another factor that we cannot ignore. There are the other things to consider that actually make a difference, such as improved nutrition, exercise, stress reduction, and integrating complementary medicine. All those factors could change the 6% survival benefit to higher percentages of survival. She made an informed decision to wait with the chemotherapy and was determined to make major changes in her life.

So Suzanna went on a new journey. She went to multiple practitioners in complementary medicine. She was persistent. She changed her nutrition and changed her attitudes to life. Five years ago she wrote an interesting book documenting her experience, entitled, *6 Months to Live 10 Years Later*.

I changed, too. As I observed her journey I began to think that maybe I should change the restriction in my practice not to treat cancer patients and I became open to taking care of cancer patients. After my experience with Suzanna, I believed that patients affected by cancer need a different approach. This includes helping them with informed decision-making, which I have to admit even for physicians that are on the conventional side can be very hard to make.

I help them evaluate and explore out-of-the-box unique options of care. We need to provide hope and avoid hopelessness and expose patients to exceptional patients as



a source for hope. So what do we really know about exceptional patients?

### Exceptional Patients as Positive Deviants

Another term for exceptional patients is positive deviants. Ode Magazine is an excellent magazine for optimists. An article about bringing outliers inside discussed positive deviants as those innovative individuals who do things differently and succeed against all odds.<sup>15</sup>

In most cases a positive deviant does not know he or she is doing anything unusual. Positive deviants often succeed even though they share the same constraints and barriers as others.

So we have to awaken the mind. We are always thinking, that's just the way it is. We need to think about these things differently, we have to pay attention, to observe exceptions and look for the "who", the "what" and especially the "how". This is where the wisdom is.

When we look at a plane that crashed and we hear about miracle survivors we always want to know who managed to survive. What did they do, and especially how did they do it, with the thought that maybe one day I will be on a plane that crashes, and maybe I will remember those important facts that will help me survive.

Forbes Magazine in March 2009 dedicated an entire issue to miracle survivors -- patients whose tumors melted away and what science is learning from them. The issue did not talk much about science but it did talk a lot about the miracle survivors, cancer patients given just months to live staging a miraculous recovery, doctors dismissing it as a fluke-- yet the mystery may offer crucial clues to fighting cancer. Increasingly, there are books about this topic, blogs, common attributes to miracle survivors that are mentioned and what they did.

Patient centered research involves observing patients behaviors. We all know of one or two patients that exceeded all odds. We have to be sensitive to patient's concerns in trying to address this. If we listen, patients are always asking about the lessons from exceptional patients -- if we know of such individuals -- maybe they can



help us. We need to look for answers to patients' questions and keep evaluating whether we addressed those concerns and provided the needed answers.

### Learning from Exceptional Patients

Can we actually learn from exceptional patients? In order to answer that question I organized a study at MD Anderson in collaboration with the Tel Aviv Medical Center in Israel. We called it the *Exceptional Patient Project*.

An exceptional patient is someone who has a rare and spectacular occurrence of remarkable recovery, against all odds, that is totally inexplicable but real. Further understanding of this phenomenon and the possible mechanisms involved may have significant preventative and therapeutic implications. In order to learn more about these unique patients, an initial formal study was initiated employing qualitative techniques.

We did it as a multicenter study because we wanted to capture similarities in culture, experiences across cultures, and across continents. We followed the same protocol, which was approved in both institutions. Oncologists in both centers identified Exceptional Patients. We did qualitative research with these patients once we identified them. Analysis was separate in each country. We found 26 patients from both institutions and a hundred percent of them were willing to be interviewed. All had history of extensive metastatic disease, including metastatic breast cancer, pancreatic cancer, brain tumors (GBM) and others. Their average survival at the time was 12 years after diagnosis.

The first thing that we found out is that there was a common trait to all the exceptional patients. Those patients were active in their process of dealing with the disease -- all those 26 patients were active in participation in making decisions about their treatment. We published this in 2010.<sup>16</sup> All of the patients had positive and open communication with their physicians. Patients had major support from family and friends.



And in the United States, but not in Israel, there was a belief in a higher power. For some reason most Israeli patients did not believe in a higher power.

The AARP in 2009 published a survey that was done among people over 50 which revealed that patients that were more involved in their care were re-admitted less frequently to the hospital within 30 days of discharge from hospital, experienced fewer medical errors, and had better care coordination among healthcare providers. On the other hand, those who were less involved in their care were more disappointed and lost confidence in the healthcare system.

In the past hundred years we have managed to overcome tuberculosis, pneumonia, heart disease, we have our antibiotics and vaccines that are very effective in treating infectious diseases and we managed to conquer the causes of death that were prevalent a hundred years ago.

The life expectancy has been going up, we live longer, the infant mortality rate is dropping, and when we are talking about acute care we are doing pretty well. However acute care accounts only for a small percentage of the total medical care in both cost and volume,<sup>17</sup> and multiple chronic disorders now account for 78% of the expenditures on healthcare.<sup>18</sup> Over 45% of the US population is suffering from at least one chronic disorder.<sup>19</sup>

### New Trends in Oncology

The field of cancer continues to be the leading edge of personalized medicine. Cancer biomarkers are playing an ever-increasing role in the stratification of patient populations, the identification of new therapeutic targets, and the development of novel technologies. Nanotechnology, gene therapy, genomics, proteomics, glycomics, metabolomics personalized medicine, patient-centered care, functional genetics, therapeutic cancer vaccines, and cellular analysis, earlier detection and diagnosis, targeted therapies, minimally invasive surgery—a huge investment in research and new treatments—all these major efforts to eradicate cancer are worth mentioning, but still there is only a minute change in the overall cancer survival rate.

Survival rates for metastatic cancers of breast, lung, colon, prostate, bladder, etc, are essentially unchanged from 50 years ago. The major breakthroughs in treatment—chronic myelogenous leukemia, lymphomas, germ cell tumors and a few others make up a tiny percentage of the total population's cancer burden.



### Overtreated

We are also being overtreated. An excellent book, *Overtreated* by Shannon Brownlee says that somewhere between five hundred and seven hundred billion dollars is spent unnecessarily each year, which is hurting us economically.<sup>20</sup> Estimates place medical treatment at between the third and fifth leading cause of death in the U.S. with an estimate published in the Journal of the American Medical Association placing the number at 225,000 from iatrogenic (doctor induced) causes. We are not only given far more treatment than is necessary, we are likely to be harmed by the additional care. The estimate by the Institute of Medicine is that there is \$1 trillion in waste and overtreatment. The authors mentioned that overtreatment, on the whole is not only waste but also creates negative health outcomes.<sup>21</sup>

The United States stands as the first in spending in healthcare worldwide, compared to Cuba, which is the lowest in spending on healthcare and interestingly, they have the same life expectancy as in the US. Cuba and United States are both number 36 in life expectancy. We are desperately looking for cures. Medical research is not making progress rapidly enough. We are trying to solve this by taking another pill. We are looking for magic but we already have the magic—we're simply not recognizing and applying it.

### The Formula

Some of us feel that the secret of healthy life lies in an enclosed safe where the combination to open this safe is secret and unattainable, while many charlatans are trying to sell their ultimate solution.

I mention in many lectures that basically the combination to this safe is pretty simple. I mention the following numbers 0,5,10, 30,150. Most people look at me with a puzzled look and then I explain:

- 0 cigarettes,
- 5 servings of fruits and vegetables per day,
- 10 minutes of silence, relaxation or meditation per day,
- Keeping the body mass index less than 30 kg/m<sup>2</sup>

- And 150 minutes of exercise per week, that is the formula for good health.

How many cancer patients actually use this formula? A study that documented adherence to ACS Lifestyle Guidelines in Cancer Survivors revealed that the situation is quite upsetting. Close to 95% of cancer patients are not following this formula.<sup>22</sup> Only 4.5% of breast cancer patients, 5.1% of prostate cancer patients, and 4.6% of colorectal cancer patients actually follow the above formula -- we have a lot of work to do.

### Supporting the Terrain

We need to put emphasis on supporting the terrain, supporting nutrition, physical activity, stress reduction, hope, empathic communication, community, social connection and their combined effect. It's the combined effect that makes the difference. We need to shift our thoughts from war and fighting, as we tend to think about when we think of cancer. We have to move from a terrain filled with snakes and scorpions to actually supporting different types of terrain—gardens overflowing with flowers, fruits, vegetables, herbs, spices, a terrain filled with relaxation, peace, hope, trust, empathy, and compassion.

NCI is beginning to think in those terms of supporting the terrain. The tumor microenvironment is being increasingly recognized as a critical regulator of cancer progression. They call it the extracellular matrix. "The tumor microenvironment has been increasingly recognized as a critical regulator of cancer progression. The extracellular matrix (ECM), a key component of the microenvironment, is in immediate contact with tumor cells. The ECM significantly affects tumor biology and progression by providing factors for cell growth and survival and for stimulating the growth of new blood vessels to feed the tumor. Also, cell adhesion to the ECM triggers signaling pathways that can regulate various phases of cell growth."<sup>23</sup>

We need to nurture our body, mind, and soul. Let's take a fraction of that trillion of wasted dollars to reimburse individuals to support and nurture their own terrain. We need to:

- Support an informed decision-making process
- Reduce hopelessness and helplessness
- Enhance hope and find those exceptional patients and utilize their wisdom
- Reduce social isolation, provide support groups and other ways to reduce social isolation
- Offer instruction on Stress Reduction practices

- Massage, acupuncture treatments, nutritional treatments
- Integrative medicine consultations

A good friend of mine, Elad Schiff, a physician involved in integrative medicine in Israel, mentioned to me a few years ago:

"When we talk about integrative medicine, the challenge is not only to anticipate the future, but to actually create it."

I think we are moving in that direction.

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