“Molecular Integrative Oncology: In Addition to – Not instead of – Conventional Oncology treatment” (William LaValley, MD) [#134]

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“Seeing all the components in the tumor microenvironment through that lens of pro-cancer, anti-cancer directionality places a perspective for searching as well as understanding the information that's in the literature and that provides a structural framework for making choices and decisions about therapeutic agents.” – William LaValley, MD

“Because the cancer cells are producing molecules that induce or recruit, or could even be thought of as coerce and kidnap other cells that are good, desirable, necessary, normal, healthy cells in other circumstances and in other locations, now are forced into the service of supporting and maintaining and camouflaging the cancer cells. That means that we have to consider all of these cells concurrently and take an integrative, networked perspective of how to manage these multiple cell types concurrently to control the progression of the cancer, in addition to whatever is the conventional treatment, targeted treatment, immune-targeted treatment, conventional cytotoxic therapy, radiotherapy or other ablation therapies, all of those, in addition to this pre-clinical trial data access to make therapeutic choices about products that are already available, natural products and repurposed pharmaceuticals.” – William LaValley, MD

Meeting Summary

A cancer diagnosis can feel scary and overwhelming. Your doctor will typically focus on standard care—surgery, chemotherapy, radiation, immunotherapy—but may not know much about complementary treatments that can increase the effectiveness of standard care. Many cancer patients search for ways to boost their health and immune system. Reliable information is hard to find and even harder to turn into a safe plan. Working with a doctor or nurse trained in complementary treatments can help you make healthy choices like eating well, lowering stress, sleeping enough, and exercising. Most patients considering natural supplements or repurposed drugs want scientific evidence and medical guidance.

Dr. William LaValley is uniquely qualified to talk about a scientific approach to complementary cancer therapies. He has spent 36 years treating patients, and 25 years studying cancer biology. His “Molecular Integrative Oncology” protocols use research to create safe, targeted treatment plans that add to—not replace—standard care. These plans use natural compounds and repurposed medications backed by studies, designed to slow cancer growth and improve life quality. Patients or doctors contact Dr. LaValley to create personalized, evidence-based plans for local doctors to deliver.

Why do you need to understand the scientific approach to complementary molecular integrative oncology?

- Targets many parts of the tumor environment for stronger results.
- Uses data on molecular pathways to understand cancer’s complexity.
- Chooses natural products and repurposed drugs based on research, not guesswork.

What are the key elements of the molecular integrative oncology model?

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- Focuses on cancer as a network of pathways, not just single cells.
- Uses drugs already proven safe in other treatments for cancer effects.
- Identifies “pro-cancer” and “anti-cancer” processes to guide therapy.
- Builds on scientific evidence while adding to standard treatments.

What do you need to do to access this molecular integrative oncology approach (outside of standard care)?

- Work with an integrative doctor trained in natural and repurposed therapies.
- Get a personalized plan, reviewed and approved by your doctor.
- Start with low doses, increase slowly, and track results closely.
- Understand that risks exist due to limited clinical trials.

What are examples of treatment plans of evidence-supported and evidence-based recommendations using molecularly-targeted natural product supplements and re-purposed off-label drug protocols?

- Natural compounds like curcumin, green tea extract, or resveratrol with low-dose drugs like metformin.
- Anti-angiogenic supplements to block tumor blood supply.
- Immunity-boosting natural products plus repurposed immunotherapies.
- Agents that target cancer stem cells and key growth pathways.

How should you administer these natural and off-label products?

- Start with very low dosages
- Gradually escalate
- Closely track cause and effect
- Ensure treatment remains well-tolerated
- Reassess every three months

What are the potential risks of pursuing therapeutic interventions without comprehensive molecular insights into the tumor microenvironment?

- Unknown side effects or serious reactions.
- Reduced effectiveness if treatments aren’t well-matched to cancer biology.
- Resistance or poor tolerance if dosing isn’t carefully managed.

How can you learn more?

- Reach out to Dr. LaValley through his website at https://lavalleymdprotocols.com/
- Explore the use of liquid biopsies and cell-free DNA analysis to monitor the effectiveness of therapeutic interventions.
- See previous discussions we have had on complementary cancer treatments, such as:

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- “Evaluating Complementary Therapies in Cancer Care” (Martin Lužbeták, MD, MS) [#108]
- "A Patient’s View on Nutrition, Supplements, Integrative Oncology, and Complementary Therapies" (Robert Ellis and Glenn Sabin) [#33]
- "Terrain and the Whole Person in Cancer Care” (Nasha Winters, ND, FABNO) [#95]
- “Integrative Cancer Care” (Donald Abrams, MD) [#102]
- “Cancer Scams: Don’t Get Taken” (Bapcha Murty) [#94]

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Meeting Notes

KEYWORDS

Molecular integrative oncology, tumor microenvironment, pro-cancer, anti-cancer directionality, natural products, repurposed pharmaceuticals, pre-clinical trial data, cancer stem cells, vascular cells, immune cells, stromal cells, network pharmacology, personalized treatment plans, therapeutic interventions, molecular pathways.

SPEAKERS

Will LaValley (88%), Roger Royse (4%), Cindy Ness (4%), John P (4%), David Plunkett (1%)

CHAT CONTRIBUTORS

Roger Royse, Helen, Saed Sayad, Koryn DelPrince, Michael - Denver

SUMMARY

Will LaValley discussed the emerging field of molecular integrative oncology, emphasizing the use of a broad spectrum of therapeutic agents, including natural health products and repurposed pharmaceuticals. He highlighted the importance of understanding the tumor microenvironment, focusing on cancer cells, cancer stem cells, vascular cells, immune cells, and stromal cells. LaValley explained the concept of pro-cancer and anti-cancer directionality, guiding therapeutic interventions. He noted the lack of clinical trial data but stressed the potential of pre-clinical trial data to inform treatment plans. LaValley also addressed the challenges of managing treatment tolerance and the potential for resistance, advocating for a personalized, integrative approach.

OUTLINE

Molecular Integrative Oncology Overview

- Will LaValley introduced the concept of molecular integrative oncology, emphasizing its role in managing cancer.
- He referenced a landmark journal issue in Seminars in Cancer Biology, highlighting the use of a broad spectrum of therapeutic agents.
- The project involved 300 cancer researchers and oncology doctors, focusing on controlling cancer progression by intervening at each hallmark.
- He stressed the importance of pre-clinical trial data in guiding molecular integrative oncology.

Understanding the Tumor Microenvironment

- The tumor microenvironment, including cells and molecules within it, is important.

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- The concept of pro-cancer and anti-cancer directionality helps explain molecular pathways, how cells and molecules interact.
- The tumor microenvironment is divided into four main categories: cancer cells, cancer stem cells, vascular cells, and stromal cells.
- The role of vascular cells is supplying oxygen to cancer cells and there are interactions between cancer cells and immune cells.
- It is important to target pro-cancer molecular pathways with anti-cancer interventions.
- The imagery of cellular and molecular meetups describes how cells communicate and affect each other.
- Pre-clinical trial data can be used to make informed therapeutic decisions.

Challenges and Opportunities in Therapeutic Interventions

- Managing the tumor microenvironment is complicated.
- An integrative, networked perspective is needed to manage multiple cell types.
- Natural products and repurposed pharmaceuticals can be used for therapeutic interventions.
- It’s important to start with low doses and gradually increase to ensure comfort and tolerance.

Personalized treatment Plans

- John asked about the inputs used to identify cells in the tumor microenvironment and shared his experience with next-generation sequencing.
- Dr. LaValley explained the framework for pursuing information about cell types and molecular interactions and the limitations of current protocols and the potential for future advancements in understanding.
- John inquired about the use of liquid biopsies for monitoring treatment effectiveness.
- Dr. LaValley acknowledged the value of liquid biopsies and their potential for providing real-time information.
- Cindy Ness asked about the application of tumor microenvironment emphasis in standard of care institutions.
- Dr. LaValley described the collaborative process with local integrative medicine physicians to implement treatment plans.
- treatment plans need to fit the workflow of local physicians.
- Roger Royse asked about preventing resistance to therapeutic interventions, especially micro-dosing.
- Dr. LaValley explained the importance of targeting multiple molecular sites simultaneously to decrease compensatory signaling.
- Natural products and repurposed pharmaceuticals can enhance chemo sensitivity and decrease chemo resistance.
- Cindy Ness inquired about the influence of epigenetics and ethnicity on the tumor microenvironment.
- Dr. LaValley acknowledged the impact of epigenetics but noted the lack of specific information on ethnicity.

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Conclusion

- Dr. LaValley reiterated the importance of understanding the tumor microenvironment and the potential of molecular integrative oncology.

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TRANSCRIPT

Will LaValley
It's quite an honor to be here for this Cancer Patient Lab information exchange. I see this as a leading edge forum for bringing together ideas and this issue, it gets pretty challenging to understand the big picture and to piece everything together. There's a lot of different perspectives, and a lot of different points of view. I'm going to present the way that it looks to me to have a coherent, cohesive understanding of what we're looking at and what we're attempting to do in managing cancer. This is the field of molecular integrative oncology, in addition to conventional oncology treatment, not instead of, and based on what was found many years ago. It was published in a landmark journal, special issue, open access issue of seminars and cancer biology is a good place to start to look at the underlying, foundational concepts of using a broad spectrum of therapeutic agents, including natural health products as well as repurposed pharmaceuticals. Seminars in cancer biology, very high impact journal, generally not open access. And at the end of 2015, this series of articles, after Dr Leroy low had a project of 300 cancer researchers and oncology doctors who divided themselves up into 10 different groups, each looking at one of the hallmarks of the time. The three year project was to synthesize information about how to control the progression of cancer by intervening at each one of these hallmarks and came to the conclusion that it's a supported approach to provide a broad spectrum of natural products and repurposed pharmaceuticals. I'll point you to that open access journal, because it really is a good foundation for moving forward molecular integrative oncology. I think of it as one of the emerging edges of synthesizing the knowledge that we have and that this is primarily based on looking at the pre clinical trial data. So we don't have clinical trial data for this by definition, just start a pre clinical trial

The field is molecular integrative oncology. Integrative oncology has a very broad range of options, and we're narrowing the focus to the molecular biology of integrative oncology. And here is that article. Sorry, that special issue for reference is a three year project. The project is called Getting to know cancer, and they were evaluating the hallmarks and control of cancer using additional available therapeutic agents and.

What is it we're actually looking at, and what are the challenges? The core, from my perspective, is looking at the tumor microenvironment, and it's often neglected to emphasize all the characteristics of the tumor microenvironment, and that includes the cells and molecules in the tumor microenvironment, all of the cells and all of the molecules in the tumor microenvironment. We have the data that we know about those cells and the molecules in the tumor microenvironment is readily available, doesn't mean it's easily available. And the core seed that makes sense to me to plant is the concept of always looking at either pro-cancer or anticancer activity, pro-cancer or anti cancer directionality, that term pro-cancer or anti cancer directionality can be applied to all of the information we have about the cells in the molecules in the tumor microenvironment.

Seeing all the components in the tumor microenvironment through that lens of pro-cancer, anti-cancer directionality places a perspective for searching as well as understanding the information that's in the literature and that provides a structural framework for making choices and decisions

about therapeutic agents. Understanding this core concept is an important privilege in planting that seed here, because I think all of the additional information that we're pursuing comes back to that line. We're maintaining that line of understanding throughout the literature and using it and applying it regarding all the cells in the tumor microenvironment and all the molecules that we're discussing and reviewing.

When you look at the tumor microenvironment, oftentimes it's presented in ways that are quite confusing, very complex, and when we look at it from a high level overview, there's really four main categories that virtually every everything in the literature falls in these four main categories of cells, the cancer cells and cancer stem cells, the vascular cells, the immune cells, large category many different types and the stromal cells, which may be relatively neglected in the attention and are fundamentally relevant in the development of tumor, especially tumor once a tumor, population that community of cells proceeds and grows large enough that you can see it on imagery.

If we take a bigger expansion of that information, the vascular cells by the time a cancer cell is growing, dividing, accumulating, growing, dividing, accumulating, a group of cells that the center of that mass develops a lower oxygenation, hypoxia. And cancer cells, like healthy cells, are always attempting to survive. They produce molecules to induce nearby blood vessels to either turn and grow to supply more oxygen or to newly grow to supply more oxygen. That vascularization of the tumor is not normal healthy expression of vascular cells, and it is still vascular cells and endothelial cells and pericytes that are the tumor vasculature that are relevant, and the immune cells. There are many different types of cancer cells producing the. Immune messenger molecules to recruit, induce, even molecularly kidnap, certain components of the immune system that are generally associated with wound healing and anti inflammation, and there are the main cell types, the lymphoid cells with multiple subtypes, and the myeloid cells with multiple subtypes, and their interactions with each other. And then, importantly, as well, the stromal cells, which are structural support cells and maintenance cells, and that, by definition, tumor that exists with the cancer cells and cancer stem cells, let's Say at the center of our focus, that it's important to expand that focus, that awareness, to include all of these cells, because they are mutually reinforcing, the cancer cells and cancer stem cells, clearly at the center of our attention, the center of our focus, and because the cancer cells are producing molecules that induce or recruit, or could even be thought of as coerce and kidnap, other cells that are good, desirable, necessary, normal, healthy cells in other circumstances and in other locations now are forced into the service of supporting and maintaining and camouflaging the cancer cells, and that means that we have to consider all of these cells concurrently and take an integrative, networked perspective of how to manage these multiple cell types concurrently to control the progression of the cancer, in addition to whatever is the conventional treatment, targeted treatment, immune targeted treatment, conventional cytotoxic therapy, radiotherapy or other ablation therapies, all of those, in addition to this pre clinical trial data access to make therapeutic choices about products that are already available, natural products and repurposed pharmaceuticals.

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If you think about each cell type, the cancer cells and cancer stem cells, the tumor vascular cells, the various immune system cells and the stromal cells, principally focused on the cancer associated fibroblast, but also mesenchymal stem cells, that all of them have molecular pathway activities that we have some idea, or even a very large number of our large understanding of many pathways various cell types, we have greater or lesser understanding of the relevant pathways in the pro-cancer direction. By definition, the tumor microenvironment is the pro-cancer environment. We're looking at what are the expressions of the molecular pathways in each of those cell types, the pro-cancer molecular pathway activity in the pro-cancer molecular interactions among the multiple sites along those molecular pathways. We have a lot of that information we and we have it in many cancer cell types, and we have it with many therapeutic agents, the response to those, the use of therapeutic agents in counteracting the pro-cancer molecular interactions in an anti cancer molecular direction, and that understanding guides this methodology as we go forward, and that, if you think more deeply, that the pro-cancer molecular pathway activities at these molecular interactions are generally characterized as either pro-cancer upregulation activation or pro-cancer downregulation inhibition. Our approach then is to either use counteracting molecules as anti-cancer down regulation inhibition or anti-cancer upregulation activation.

We're looking first to identify the pro-cancer molecular orientation and identify where are there data supporting anti cancer molecular intervention, either at that particular molecular interaction, or perhaps cross stream or downstream, excuse me, or even upstream to that, And we have significant data about those options, about those possibilities, and so the progression of cells to pathways, to organelles, to molecular interactions. Importantly, whether those molecular interactions are the wild type or altered and the pro-cancer anti cancer directionality of them looking to drive and direct therapeutic interventions to counteract the pro-cancer molecular pathway activity among this group of cells In the tumor, micro environment. And when I'm talking with people who have come seeking these personalized treatment plans and their families that I use some terminology that's quite non scientific to illustrate some of the concepts and that when we talk about all of these cells in the tumor micro environment and the molecules inside them and between them, I use the imagery of cellular meetups and molecular meetups that the cells are talking to each other using molecules. Sometimes the cells are directly in contact with each other, direct contact. Other times, the cells are producing molecules that affect the other cells, other times nearby, other times they're producing molecules that affect cells far away, so para quin para Quinn signaling, autocrine signaling, where they're producing molecules that affect themselves, or a far away endocrine signaling. So we're talking about molecules that are released to affect other cells, and the affecting of those other cells often causes those molecules to be released that affect the cells in a feed forward cycle, a self reinforcing cycle, vicious cycle, if you will. And that this information gives us opportunities to look at where are their molecular pathway activities that can be intervened, in which we can apply molecules for anticancer molecular effects, using the pre clinical trial data to make educated or rational decisions about applying the therapeutic interventions targeting multiple molecular sites simultaneously, concurrently. And I have a large number of slides that I can move to in response to various questions. But the the general overview is we see that there are in virtually every tumor type, whether it's solid tumor, carcinomas, sarcomas or whether it's blood

hematological malignancies, that there are multiple molecular pathway activities and multiple molecular interactions along these pathway activities that show pro-cancer molecular effect, pro-cancer molecular expression, and that there are data showing the. Anti cancer counteracting anti cancer molecular effect of multiple natural products, repurposed non oncology pharmaceuticals, repurposed conventional oncology pharmaceuticals, including targeted agents

Will LaValley 20:22
and immunological targeted agents, and that these can be considered in a bigger picture as we move along and see that we're inherently targeting and managing molecular networks among these cells and within these cells that that there, this opens a bigger perspective of targeting with network pharmacology, broad spectrum of therapeutic concurrent natural products, repurposing pharmaceuticals to control the progression of the cancer by controlling signaling networks and cancer cells and cancer stem cells and tumor vasculature and immune system cells and the stromal cells. And so this is this opens a large arena for discussion on somebody's

Will LaValley 22:21
To recap, we're looking at the cells in the tumor micro environment, and there are numerous types of them, four main categories you can identify, easily identify at least 20 different cell types and the molecular pathways within those cell types, expressing, including through the organelles in those cell types, and the various molecular interactions that are either normal, wild type or altered, including mutated interactions in the through the lens of the pro-cancer anti cancer directionality, and that guiding the selection of therapeutic interventions, including the pre clinical trial data, the in vitro and in vivo, human and animal cancer cells in test tubes and in animals, of the therapeutic options, including those that are already on the market, the natural products and repurposed pharmaceuticals.

Any one of these aspects, we can go very deeply into discussion.

John P 24:16
My name is John, and I was just wondering about what you're using in terms of inputs to identify these sort of cells I had. I have pleomorphic liposarcoma. One of the things that I've had done is the BostonGene next generation sequencing, and they have a TME section on the report, and it was basically like, well, we don't really have a lot of data. And so they they have RNA sequencing files. I actually have those fast Q files, and I have a I spoke with a researcher who was. Was talking about how other NGS teams, you know, will focus more on the TME. And he was talking about the to say it's highly fibrotic. Might mean that's good or bad, so that sort of thing. But the takeaway that I kind of got was, at least from that particular report, it was kind of just saying, Well, we, you know, we identified some cells in the TME, but we don't really know what to tell you. And so I guess, in terms of this highly targeted makes, you know, makes sense to me, saying, Here's where you look at all of these different potential interactions and behaviors and how they might interact. How do you get the information about what cells you might have in a given TME,

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Will LaValley 25:47

What I'm presenting here is a framework for pursuing that information. Oftentimes, we have very little of that for a specific case, for a specific but either biopsy or pathology specimen that that there are now more there's more Interest looking at the cell types as spatial, spatial analysis looking at what cells are located in what positions in the tumor, but oftentimes we don't have the data that you'd like to see. What I do is look in the literature for what are the characteristics associated with that tumor type and the likelihood of greater in sarcomas, for instance, the greater activity for fibrotic activity or other extracellular Matrix development in the tumor micro environment, and what are the cytokines and chemo kinds, the immune messenger molecules or growth factors that are generally associated with those activities in that tumor type? And aim for that we're in very early days, and the protocols, even the leading edge protocols, the ones with the most sophistication currently, I think, are likely to be seen as quite crude first efforts, or early efforts, compared to where we'll be in a short period, I think in the next several years, we're going to have much more advanced understanding. And then that comes down to what tools are we actually willing and able to apply, what therapeutic molecules? And I think that the molecules, the natural products, which are already on the market. They're a reasonable set of choices, and it's still very crude. They're there. We're limited to the dosage forms that are available in retail, and that's not a good that's not optimal. And then the repurposed non oncology drugs, there are substantial data about using already available, repurposed pharmaceuticals, targeting fibrosis, targeting the inflammatory activities that are occurring in the tumor micro environment, and then those were very often still quite limited to dosage forms that are already available. We can dose them in off label dosing schedules. And I generally strongly support, start everything very low, at its lowest dosage increment or even lower, and proceed in a very gentle dosage escalation among all of the agents that are being therapeutically applied. And the underlying fundamental criteria for implementation is the treatment plan is designed and intended to always be comfortably, well tolerated. That means having a method for closely tracking cause and effect, cause and effect. So this is because the simple conclusion is, if the person isn't tolerating the treatment plan comfortably, then they will be struggling with it, and they won't be able to take it. And if they can't take it, it can't have any benefit, and so that fundamental requirement of developing a treatment plan scientifically really doesn't provide value unless it can be well tolerated and implemented in a manner that remains comfortably well tolerated in order to be able to administer or extended duration. And extended duration, I think, is well defined as, think three month increments and at the end of the because, commonly in the oncology evaluations, after three months, there's some follow up, imagery or some other evaluation the oncology team, and then a decision can be made about the next three months of therapy, whether it's A change in conventional oncology treatment or no conventional oncology treatment, or modification of the the Cancer Wellness Plan that the implementation based on the circumstances, so based on the indications at these intervals and many People can implement for three months and another three months and another three months, the use of the repurposed pharmaceuticals, I think, can have very significant impact on the tumor, micro environment, the stroma, the stromal cells and the immune cells in and and I hope that gave an outline for answering your question. We don't have the specific answer of, well, in this tumor with this characterization, use these drugs specifically, we're not there yet, I think, using the spatial analysis and identifying in your particular tumor type when a biopsy or a surgical

resection occurs, looking at the the spatial location, as well as the molecular profiling. The various omics options available can give some prioritization to the therapeutic protocols, aiming more in this direction versus that direction in the treatment plan. Okay, we have a question in that, did that get to where you wanted?

John P 32:52
Yeah, I appreciate that you actually kind of pre answered. The other question I had, which was this the signal or feedback loop in terms of if it's working, and it sounds like slotting into the usual surveillance scans and that sort of stuff. I'm wondering if we'll have in future opportunities along the like liquid biopsies line, where you're kind of able to see or the CF DNA, that kind of approaches to see if it's active without having to, you know, just do a CT that's spread out at that cadence.

Will LaValley 33:28
The liquid biopsies are, are quite valuable, quite important.

Roger Royse 33:42
We have a question in the chat. It says performing single cell RNA sequencing on both malignant and benign or normal tissue provides more opportunities to understand the underlying pathology and identify potential treatments. Any comments on that?

Will LaValley 34:07
The more omics, the better, from my point of view. So the when my patients have come to me or other doctors, patients that there, they will generally have a pathology document specifying their diagnosis, their specific cellular diagnosis, with some or another markers that validate that diagnosis. And then some people also have additional omics, genomics, transcriptomics, proteomics, sometimes metabolomics, and those can be helpful in directing the search for what therapeutic agents are relevant. And rational for counteracting those. Those are generally focused on the cancer cell, sometimes also the cancer stem cells. That that that guidance can provide better focus for therapeutic intervention, treatment plan development, but that we're still again in these early days. And what I'm proposing here is a framework for encompassing all of the therapeutic perspectives, all the therapeutic options by that directionality, that pro-cancer, anti cancer, directionality, looking at all of the cancer types, and then, I'm sorry, all of the cell types, and then using what data we have within each of those here, if You're talking about the the transcriptomic, the RNA data, or other omics data that at that can steer what we're aiming at and what We're aiming with.

Roger Royse 36:25
We have another new message: What are some of the harms in performing therapeutic interventions with minimal, non comprehensive molecular insights?

Will LaValley 36:41
Well, there's potential serious adverse effects, because we don't have the data about the range of adverse outcomes clinical trials, the gold standard that boundary between conventional

oncology and the pre clinical trial of the molecular integrative oncology, the clinical trials are the gold standard that I think of it as the top of the data mountain, The best data we have, and that that data, it gives us the likelihood of benefit and the likelihood of risk, and usually that risk is stratified. When you look at the data about the risk of one or another or therapeutic protocol, conventional oncology protocol, often along the lines of greater than or one to 30% chance of this, less than 1% chance of that, or some other form of stratification. And because we don't have that data, because of the lack of clinical trials, we have to acknowledge that there exists the possibility of serious adverse consequences that could could cause serious illness requiring hospitalization, or could even be fatal, and that that acknowledgement means we need to manage safety and tolerance very closely, and that's why start low and increase slowly, with very closely tracking. When you take this here's what we see, cause and effect, cause and effect, and there's a methodology for doing that. I think it's probably beyond the scope of our discussion today that managing that risk means acknowledging the unknown and managing it because it's unknown. Clinical trials are going to make this much better, but until now, you haven't had any clinical trials that are relevant this group that put this special issue together, getting to know cancer that that group went on to become to have a 2.0 version of itself, to develop potentially clinical trials, and I got invited into that organization, and it's called broad spec, dot, O, R, G, I think it has become somewhat dormant. At the moment. It looks like it may reactivate to do clinical trials in this methodology of using a broad. Spectrum of therapeutic agents targeting these multiple molecular vulnerabilities in network pharmacology and implemented in a manner that remains comfortably well tolerated.

Cindy Ness 40:32
Thank you for such a wonderful talk. It feels like it's really the cutting edge of what we should all be thinking about, and it's much more dynamic than, I think, what the conversation sounds like inside standard of care institutions. You talk about what we're doing, and I assume that a lot of what you're talking about is outside of, let's say, the big institutions. Guess my question is, what if any of this tumor microenvironment? Emphasis, you know, certainly there's research on it, but clinically, what if any of this is going on inside of, you know, in standard of care institutions, and if it's limited, could you give us a sense of why that is? I'm sorry my video isn't on. For some reason it's not turning on,

Will LaValley 41:37
I'm not involved with any big institutions, so I can't accurately speak to what the current approach in any particular institution is. I know that there is much more emphasis in discussion about tumor microenvironment. So maybe this is helpful, that there's an opportunity here to discuss the evolution of how the tumors are occurring so a healthy cell, because I think it can drive some of the discussion that I think you're pointing to, you know, healthy cells have some sort of adverse changes that then they become malignant, that called Transform to become malignant cells, and that there Are two characteristics, or Hallmark characteristics, that, I think, from which the other characteristics can be derived, that the growing signaling, so one, one cell, one one molecular interaction signaling, the next, the next, the next that growing signaling, those Growing signaling pathways are turned on. They're turned up, and they'll stop growing. Signaling pathways are turned off. They don't have the mechanism to turn off the growing

signaling and that causes the cell to grow. It reaches a specific critical size now divides and accumulates, grow, divide, accumulates, and that the adverse interaction from various stimulation of various environmental factors, triggering is quite different Among various cells, and that most of the time, the cell that now has become transformed is by itself, and it's not necessary. We're talking about at the beginning, at the initiation, and that that that it can put molecules on this on the margin of the cell, in the membrane that identified as malignant and the anti cancer immune system comes along and very quickly eliminates that cell, or the cell becomes so dysfunctional that it then triggers automatic program, cell death, apoptosis, automatic program recycling. I often call it to people when I'm talking to the to late lay persons, and that once in a while, the transform cell is nearby or next to a stromal cell, a fibroblast. And the fibroblasts, I think, are generally not well described or emphasized. And now, what are they doing? Those cells are producing molecules that are essentially attempting to help whatever cell they're next to be better and. So the structural and maintenance support that's coming from fibroblasts, which are ubiquitous in all our organs, that they're now receiving signals from the malignant cell, and they're saying, Okay, how can I help you? How do I make you better? How do I make you stronger? How do I protect you? How do I support and maintain, and that is a big issue with regard to focusing on tumor microenvironment, the chemokines and cytokine that the immune messenger molecules and growth factor molecules, the molecules that are exchanged between these and among the cells in the tumor micro environment, we have some excellent targeted agents already available, some for cancer, others for other diseases, including or other conditions, fibrotic conditions, immunological dysfunction, or people who have inflammatory conditions, and those molecules could be used in orders of magnitude lower, potentially much lower, dosing, in off label dosing, I Think of it as mini dosing, or even micro dosing, when you when you look at the tumor, micro sorry, the immune system cells, so using molecules that are already on the market and much lower doses that are in off label dosing to target the changes in the extracellular matrix, the tumor microenvironment, development of fibrotic tissue, in addition to targeting the molecular pathways in the cancer cells and cancer stem cells.

Cindy Ness 46:57
First of all, I'm not a physician, so that's really interesting to me, and I'm learning, and I'm always trying to absorb in my practice, which is a psychology practice, I have three patients that, and I see a lot of folks who have a cancer diagnosis who need something more than what they're finding in standard of care institutions. What I'm trying to get at here is, how does the patient outside of standard of care institutions access this kind of thinking, this kind of approach to their own treatment, if they, in a sense, want to go as an independent and I mean, what would that look at look like? I mean, I'm always interested in how all these good ideas work, sort of on the ground, so maybe you could tell me. So what does the application look like? If someone says, Wow, this is, I think this is really right. This is what I need. Now, what?

Will LaValley 48:02
So? The people with a diagnosis of cancer diagnosis or their families will reach out to us, and I collaborate with local integrative medicine physicians throughout the US and Canada, sometimes overseas in Europe or Australia or New Zealand, about the doctors receiving a treatment plan for their particular patient, And then a method for implementing that treatment

plan so that that it fits right into their local integrated medicine physicians workflow, because the integrative medicine physicians are generally accustomed To using natural products and off label pharmaceuticals in addition to conventional care, and that they're there so that they're familiar with that I will have a collaborative relationship with them, and they can receive a set of treatment plan recommendations, review it, revise it, in whichever manner they choose, and then administer it, and we follow up very quickly with a training about how that doctors selected treatment plan can be efficiently implemented. So we stay very focused on only that implementation of what that doctor has authorized and is being implemented. That's a practical way of allowing people access where they live, because this information takes some, quite some time to assist. Late and to to put into a comprehensive treatment plan for application, for an implementation.

Roger Royse 50:12
We have a question in the chat. It's actually the question I was going to ask you about, and it's about resistance. And the question is: is there anything to prevent cells from becoming resistant to therapeutic interventions, especially micro dosing? Do you have any comments on that?

Will LaValley 50:32
Yes, actually, I do. Let me go here

Will LaValley 50:39
just one second.

Will LaValley 50:50
So we're aiming at all of the hallmarks, and

Will LaValley 51:00
We have some natural products and some repurposed pharmaceuticals that can target the hallmarks and that the methodology, rationale is to target the molecular networks in all of these cells. And what is displayed here is the Kyoto Encyclopedia of genes and genomes, the big picture pathways in cancer map and the hallmarks or characteristics associated in the cancer cells. So this is not the whole tumor micro environment. This is the cancer cell. Got the boundaries of the cancer cell, including major pathways, and how we can emphasize targeting pathways for particular characteristics, and that when we looked at then the next major resource, the pain cancer Atlas, and the main signaling pathways that were published in the pan cancer Atlas, I think about about eight years ago, including what are called the top 10, what I call The top 10 that is defined as the flagship paper, oncogenic signaling pathways in cancer, that those 10 major pathways demonstrating actionable alterations. And so that's an important aspect of these pathways is the emphasis that each one of the molecular interactions identified in this particular perspective of these 10 pathways, each one is actionable, potentially therapeutically actionable, because of the alterations, in order for them, for in order for it to define focus on targeted and combination therapies. And here's the outline of that map. And then when you fill it, it's still quite overwhelming. So to simplify it, an animation made it easier. I animated it so I could understand better. Here's an example of an important pathway, cascading

molecular signaling. Each one of these molecular targets potentially actionable alteration that results in cell proliferation, grow, divide, accumulate, grow, divide, accumulate, cell survival and protein production and each one of these pathways associated with particular activities, if we fast Forward among all of them, through all of them. Importantly, they're all connected, and that's where the issue of managing resistance is, I think, presents a great opportunity that when we have a particular targeted agent that's targeting a specific molecular address, a specific molecular site.

Will LaValley 54:37
Because the natural products and repurposed drugs target multiple molecular sites simultaneously, as the cells are attempting to compensate. Through that compensatory signaling, we're meeting their attempts to compensate with a greater anti cancer. For intervention, and that the concept is to decrease the capacity of the cells to compensate, to use that compensatory signaling to adapt to the adverse intervention. And so there are data showing natural products and repurposed pharmaceuticals can have enhanced effects to increase the ability of the chemotherapy or targeted agents to target and eliminate the cancer cells, enhance chemo sensitivity and decrease chemo resistance. Okay, I'm sorry I forgot that I wasn't sharing.

Roger Royse 55:49
From the chat: To what extent do the epigenetics and ethnicity influence the micro environment of cellular and cancer dynamics.

Will LaValley 56:12
I don't know any information about ethnicity. I do know that epigenetics can have significant impact. The challenge is how to navigate that and manage that, and I think diet, stress management, other environmental exposures, as well as the molecular therapeutic interventions have capacity to have beneficial effect.

Roger Royse 56:46
How do people get a hold of you if they want to follow up?

Will LaValley 56:51
Through our website. It's https://lavalleymdprotocols.com/.

“Molecular Integrative Oncology: In Addition to – Not instead of – Conventional Oncology treatment” (William LaValley, MD) [#134]

CHAT DISCUSSION

00:30:33 Roger Royse: https://www.sciencedirect.com/journal/seminars-in-cancer-biology/vol/35/suppl/S?sdc=1
00:41:04 Helen: Reacted to "https://www.scienced..." with 👍
01:00:15 saed.sayad: Performing single-cell RNA sequencing on both malignant and benign (or normal) tissue provides more opportunities to understand the underlying pathology and identify potential treatments.
01:07:00 Helen: Have you resumed recording for Brad’s notes?
01:07:20 Koryn DelPrince: What are some of the harms in performing therapeutic interventions with minimal or non-comprehensive molecular insights?
01:18:35 Koryn DelPrince: [If we have time!] Are there any techniques to preventing cells from becoming resistant to therapeutic interventions? Is microdosing a part of this?
01:20:18 Michael - Denver: To what extent do epigenetics and ethnicity influence the microenvironment of cellular and cancer dynamics?
01:26:51 Koryn DelPrince: Thank you, this was very insightful!
01:27:30 Helen: Thank you so much for this presentation!!. Can we contact you with questions?