

Yale CANCER
CENTER

answers

WNPR Connecticut Public Radio



Hosts

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Chinese Herbal Medicine

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Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and an internationally known expert on colorectal cancer. Dr. Miller is a Medical Oncologist and Director of the Connecticut Challenge Survivorship Clinic. He also specializes in pain and palliative care. If you would like to e-mail questions to the doctors the address is canceranswers@yale.edu. You can also call 1-888-234-4YCC. This evening, Dr. Chu and Dr. Miller will be talking about Chinese Herbal Medicine. They are joined by Tommy Cheng, The Henry Bronson Professor of Pharmacology at Yale School of Medicine. He works closely with Dr. Chu

Chu We are so pleased to have you join us on today's program.

Cheng Thank you.

Chu Your approach to treating patients is very, very different from our experience here in the United States. Here we focus on the active ingredient, and typically for Chinese herbal medicine, it is a mixture of different herbs and spices if you will.

Cheng Chinese medicine goes after more than just a target in a given tissue. It goes after the whole body with the hopes of reaching homeostasis among the different organs and trying to improve the whole body function. It does not necessarily go after a specific target, but tries to improve the health of the individual and conquer the disease.

Miller It is a very interesting concept. Ed, I know you collaborate on this. You brought up how today medicine goes after one target, but that perhaps we should have another goal. Can you say a little bit more about that?

Chu What is interesting, especially with the whole Gleevec story for the treatment of chronic myelogenous leukemia, is that all the focus was on one drug and one target. With that, this whole era of target therapy was ushered in. We are now beginning to understand how the cancer cell works; those cancer cells are brilliant. They can very quickly come up with different pathways that get turned on if you inhibit a pathway, so, I think now the view, even in Western medicine, is that a so-called multi-targeted approach that hits different targets may be better. It is interesting that now the new Western approach in many ways follows the so-called Eastern approach, or Chinese oriental approach, as Tommy said has been around for 4000 to 5000 years.

Miller Along those lines, if a patient who lives in a village in China has a problem, who would they see? Can you tell us about the holistic approach to care?

Cheng First of all, the likelihood is that they are going to go to a Chinese doctor, but if there is

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a medicine program or medical care going on in the neighborhood, then they will use the holistic approach. In most of the cases they will actually use both.

- Chu I went to visit an herbalist when I was visiting Taiwan, and Tommy helped arrange this a number of years ago, but what fascinated me is that the herbalist was actually in the farmer's market area. The day-to-day life for individuals is that they would go to the meat market to get the meats, the fish market to get the fish, the veggies and fruits, and then they would stop off and see the herbalist who would, and Tommy can explain this, feel their pulse, look at their tongue, take their temperature and then go to the shelf and get various herbs, roots and extracts. They would either blend these or have a tea extraction. Tommy what has been your experience in that regard?
- Cheng Yes, and that is correct. You should recognize that Chinese medicine is not only focused on treatment, but also prevention and to improve quality of life. That is what mainstream medicine is trying to achieve, not only for the treatment of medical clinic needs but also for prevention and quality of life.
- Miller For example, when someone goes to an herbalist and is given herbs, how many compounds, how many different things, are in a mixture? How many roots and herbs are added, and how many different chemicals and compounds?
- Chu Tommy really is the pioneer in this whole field trying to understand the individual components.
- Cheng As I mentioned before, this has evolved over thousands of years. Before 1900 we didn't have a clear idea as to how to isolate compounds in the herbs that are involved as a mixture for the treatment of disease. Some herbs indeed are related to one compound, while some could be due to several compounds within it. The question is, what's the evidence to say one way or another? This is one area where we should try to figure it out. At this juncture, we consider them all active until it is proven inactive.
- Miller Tommy, your lab here at Yale has been studying this very fascinating Chinese herbal medicine called PHY906, which we will get into in a little bit, but about how many individual components are there, or that you think are specific to PHY906?
- Cheng Using that as an example, it is a formula first described 1700 years ago for the treatment of diarrhea, nausea, vomiting, and fever. Some people also claim it worked for fatigue. It consists of four herbs. Why four herbs and not one herb? That I have already told you; at least four ingredients are needed to be biologically active. If you analyze each herb, you find there are 100's of compounds. Many of those compounds relate to each other so metabolically they may all come right into the few species and have many interactions

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among themselves, which is the open question. With time it will be simplified and will not be as complicated as you think. But at this juncture, we have to prove if it is active or not active. If it is active, then it is worthwhile to explore it further and be assessed as a future medicine to come. If it is inactive, then forget it and we move on.

Miller Let's focus on this fascinating drug that you have been working with, PHY906. Is it of help to patients with cancer?

Cheng Yes. The developmental therapeutics program is basically taking a two-pronged approach in developing treatment strategy. One is continuing to look for new compounds, which have the most selectivity against cancer or cancer tissues. We have a very good program going in that direction. As far as I know, there is no particular Chinese formula; at this juncture there is that clear indication. As a second approach, we are trying to decrease the side effects associated with cancer chemotherapeutic drugs. The strategy is not to compromise chemotherapeutic drug actions against the tumor tissues and also, increase the dosage of chemotherapeutic drug targeting on tumor tissues without sacrificing quality of life. We hope to get better activity of the chemotherapeutic drugs. This can improve the quality of life of patient's undergoing therapy. I elected to explore the second strategy, the herbal medicine formula, with hope to decrease the side effects of chemo.

Chu Our group, that works closely with Tommy and his laboratory group, have found that this herb PHY906 can in fact reduce GI side effects such as nausea, vomiting and diarrhea that are associated with a very active drug used to treat colon cancer; that drug is called irinotecan. It was quite striking when we did a study where patients on one treatment cycle received irinotecan plus herb, and in the other cycle they received irinotecan plus placebo and the patients, nurses, fellows and even those of us who were involved in the study, could tell there was a clear difference in the treatment cycles. The beauty of the study was that it was a blinded study so the physicians themselves didn't know what the patients were receiving. When we broke the code we were surprised to see that those patients that were feeling better and had less side effects, were receiving the Chinese herb. We are about to embark on the next generation of study that looks at it in a different way, giving irinotecan plus PHY906 in patients with colorectal cancer. James Lee, myself, and Dr. Saif are involved with that.

Miller We are going to take a break for medical minute. We would like to remind you to e-mail your questions to us at canceranswers@yale.edu. Please stay tuned to learn more about Chinese herbal medicine and cancer treatment with Professor Tommy Cheng from the Yale School of Medicine.

Breast cancer is the second most common cancer in women. In Connecticut alone approximately 3,000 women will be diagnosed with breast cancer this year. But there is new hope for these women. Earlier detection, noninvasive treatments and novel therapies

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provide more options for patients to fight breast cancer. In 2007, more women are learning to live with breast cancer than ever before. Women should schedule an annual mammogram beginning at age 40 or earlier if they have risk factors associated with breast cancer. With screening or early detection and a healthy lifestyle, breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center to make innovative new treatments, which have not yet been approved by the Food and Drug Administration available to the patients. This has been a medical minute. More information is available at yalecancercenter.org.

Miller Welcome back to Yale Cancer Center Answers, this is Dr. Ken Miller and I am here with my co-host Dr. Ed Chu and Dr. Tommy Cheng who is discussing with us the research on Chinese herbal medicines. I would like to go back to reducing side effects. How do you make sure that at the same time you are not reducing the benefit?

Cheng That is a good question. We did an animal study to address that issue. If you give irinotecan to the animal colon cancer model, it clearly shows that irinotecan suppresses the colon cancer growth. In combination, we give this Chinese medicine orally. Based on this method, which has been used for many years by Chinese medical doctors, it turns out that not only does it not compromise the irinotecan action against the tumor, but it enhances the action of irinotecan against the tumor cells. When looking at irinotecan toxicity on animals, based on weight loss and the mortality of the animal caused by irinotecan treatment, we found that there is a decrease in the weight loss seen in the animals as well as decreased mortality of animals treated with the irinotecan. Based on these animals study, we feel very comfortable bringing it to clinic. That's why professor Chu and his colleagues, together with other institutions, set up this phase 2 trial.

Chu It is a very good question that you raised and this next study that we are going to do will be directly addressing whether or not the herb may somehow reduce activity, but our feeling from the experience is that it does not. There is another study that Dr. Saif and Dr. Lee have here at Yale looking at the drug capecitabine, which is an oral 5-FU approved drug to treat breast cancer and colorectal cancer. What is remarkable about this study is that Dr. Saif has been able to give very, very high doses of the Xeloda with very little toxicity; these are very heavily pretreated patients. They are able to survive for a lot longer than many of us would have expected. That gives us a signal that the herb is not compromising the clinical activity but really helping in terms of reducing toxicity and improving quality of life.

Miller The ability to give a full dose of chemotherapy or a higher dose may in fact be helpful to the patient.

Chu Yes, and that is our feeling, but we are going to have to do further tests to really address this issue.

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- Miller I will ask both of you, how do you manage quality control? We talked about how pharmaceutical drugs are well tested and characterized; how do you do this with Chinese herbal medicines?
- Cheng You raised a very critical issue that is the reason why Chinese medicine is not in mainstream medicine currently. At Yale, together with the sponsor company Phytoceutica, we established a technology called Phytomics technology. This encompasses three parts. One is the chemical finger printing where we consider every single chemical we can detect; we consider it as a biological active until it is proven inactive. This is a very intrusive, instead of extrusive, approach. With biological fingerprinting, in addition to conventional enzyme or receptor sensitivity testing, we are using cells as the sensor, DNA as a responder and RNA as a reader. In other words, we are assessing the changes of the RNA pattern of cells among treatment with an herbal mixture. We are saying that no matter how many active components there are in the mixtures, we would like to have some biological pattern using 20,000 genes as a tester. Then, together with biostatistics professors and their faculty, particularly Professor Zall, we set up informatics technology to compare the patterns and digitalize the differences. Using this sophisticated technology, we tested PHY906. I am glad to say, if it is prepared in the GMP facility, which we do, three different batches can give you almost the same pattern. We prepare them five years apart; that means a different batch of the same herb is involved. Those batches are chosen by experienced Chinese medicine herbalist and what is amazing to me is that they are very consistent. In other words, Chinese medicine can be prepared in a consistent manner, but it is case by case and cannot be individualized as people often think.
- Chu This issue of quality control is critically important. It is what, in many ways, has hindered the progress of Chinese herbal medicine and alternative medicine, because the experience has been that there are a lot of contaminants and impurities. Tommy has really been the pioneer in trying to develop high quality methodologies for quality control.
- Miller Chinese medicine has been treating patients effectively for many years, and you are working very much on quality control and testing these drugs. What is the potential, are there other treatments out there that may benefit all of us?
- Cheng Chinese medicine has often been used for ageing disease scenarios and symptoms. Some of those may actually shed light on the process of slowing down ageing or symptoms associated with ageing. This is an area that should be looked at more. And with cancer, as I already mentioned, it initially started with the idea of preventing side effects. Now we are seeing enhancement of anti-cancer drugs actions. Eventually, if we figure out the chemical components involved in those processes, perhaps in the future we can make the formula much simpler and easier to be controlled. We may also use different herbs which have similar chemical components as a substitute. In this study, the impact is not only on Chinese medicine, but actually on traditional medicine around the world. Each culture,

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based on human experience, has something very unique. We often forget history and I think it is time for us to revisit history and base at least one approach on future medicines.

Miller You are chair for this consortium for the globalization of Chinese herbal medicine. Can you tell the listeners out there very quickly what that is that all about?

Cheng The mission of that is to advance Chinese medicine, or herbal medicine, and to benefit human health. The basis of the consortium is to develop platform technology that is required in advancing herbal medicine. There are four areas that are highly emphasized. First is the quality control methodology; second is bringing it to the clinic; the third one is database sharing; the fourth is herbal resource. Once this becomes an important medicine, this resource can be an issue and the environmental impact has to be considered upfront. We have 16 institutions, with Yale as one of the founding members, and within less than four years we have 78 institutions around the world. 8 industry afflicted members are seriously interested in doing research in this area. This organization is growing, and therefore the number of people with this same view is growing.

Chu What is really impressive is the fact that Tommy and I were in Beijing, China two weeks ago for the sixth annual international meeting. When this started it was all Chinese, and I will call myself Americanized Chinese, but at this meeting two weeks ago it was quite remarkable how many Canadians we had, how many folks from Australia, Great Brittan, and Germany. It has become globalized and people understand that we need to branch off and merge between western and eastern style medicine if we are going to be able to move medicine forward.

Miller There have been other major advances from plants and trees. Ed, can you share couple of examples?

Chu For our listeners, in the field of cancer drug development it is fair to say that 30% to 40% of cancer drugs used in the clinic today come from natural products; barks, plants. In fact, there is one drug that we have studied together, Dr. Cheng and I, irinotecan, which originally comes from the bark of a tree found in China. There clearly is history showing that we can get a lot of very active compounds from these natural products.

Miller This discussion has been a big reminder to me to keep an open mind and to look at history and culture, which is broader than we typically do. I would like to thank Dr. Tommy Cheng for joining us on Yale Cancer Center Answers. It has been a wonderful discussion.

Chu Tommy thanks for joining us. We look forward to having you come back for a future show and tell us the results of the new clinical trials. Until next week, this is Dr. Ed Chu and Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.

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If you have questions, comments, or would like to subscribe to our podcast, go to www.yalecancercenter.org where you will also find transcripts of past broadcasts in written form. Next week we look at new developments in the study of melanoma.