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# Nanotechnology in Oncology

What is nanotechnology and how is this field of technology revolutionizing drug delivery and cancer treatment approach? The Director of National Cancer Institute and Nanotechnology Characterization Laboratory Dr. Anil Patri discuss some of the advantages of having nanotechnolgy as an option for new oncology drug research.

**Full Transcript:**

**Priya** : Hello everyone, and welcome to the Cure Panel Talk Show. I am Priya Menon, Scientific Media Editor, Cure Talk, and along with the Cure Talk team I welcome all of you this evening for the discussion on nanotechnology in oncology. As always, we will be moderating the call and bringing people live on the show.

The Cure Panel Talk Show is organized by Cure Talk, the blog of trialx.com, an online platform to connect patients to clinical trials of new treatment. For information on clinical trials for all conditions, please visit trialx.com/ask. This is the 15th episode of the Cure Panel Talk Show and we are excited to announce that we will be turning 1 in August. We have quite a few interesting shows lined up for you for the rest of the month. Later in the week, we will be discussing yoga for trauma with David Emerson from Justice Resource Institute. The monthly panel discussion on multiple myeloma will feature Major League Baseball coach, Don Baylor, and eminent myeloma expert, Dr. James Berenson from Institute of Myeloma & Bone Cancer Research. Our live on-air myeloma support group meeting will be conducted on June 27th at 6 p.m. eastern time. Today, we are discussing nanotechnology in oncology. Before we begin, I would like to mention that towards the end of the discussion, we will be taking questions from callers. They can let us know by pressing 1 on their keypads and we will bring them online live.

Now, it is with great pleasure and honor that I welcome Dr. Anil K Patri, Deputy Director at Nanotechnology Characterization Laboratory at the National Cancer Institute, Frederick. At NCL, Dr. Patri heads a team of scientists from multidisciplinary fields who are working together to facilitate the development of nanomaterials intended for clinical use. Dr. Patri is involved in physicochemical characterization and standardization of nanomaterials for the NCL and collaborate with scientists at the NIST and FDA. Welcome to the show, Dr. Patri.

Today's show is co-hosted by Gary Petersen who is editor of myelomasurvival.com. He works with myeloma specialists to provide life expectancy and survival rate data through his site. Welcome, Gary.

On the panel, we have noted myeloma author, blogger, and survivor, Pat Killingsworth. Pat was diagnosed with multiple myeloma in April 2007. Pat is author of four myeloma books and he maintains two blogs, Living With Multiple Myeloma and Help With Cancer. In addition, on the panel we have Kimberly Blozie. Ms. Blozie is a senior clinical research professor and entrepreneur. She was manager of Chemical Research at Columbia University's Herbert Irving Comprehensive Cancer Center. Welcome to the show, Kim.

We have a student expert with us today, Sarthak Sinha, who is a student at Henry Wise Wood High School in Calgary, Alberta. Sarthak has been working the past two years doing graduate level research in Jeff Biernaskie's experimental medicine and stem cell biology lab, University of Calgary. He is at present at Canada and contributed towards field of medicine in many an international competition.

I welcome all the panelists to the show.

Before I hand over to Gary, please remember we will be taking in calls at the end of the discussion. People

who have called in can press 1 on the keypad, and we will bring them online to ask their questions to the panel.

Gary, its all yours. You are on air live.

**Gary** : Go on and happy birthday. You are 1 year old.

**Priya** : Thank you. Thank you.

(Laughter) And, first and foremost, I want to acknowledge all the participants, patients, caregivers, and the panel members that have chosen to join us in this discussion of nanotechnology and oncology and of course, I would like to personally thank the folks from Cure Talk for providing us with this forum and it's been so crucial, I think, for a lot of people.

One of the things that I had found originally is that nanotechnology seems to have a great place in science fiction TV with shows like Revolution, but I feel that now after some eight years that the program that was started by the National Cancer Institute with a 150 million dollar grant was to develop nanotechnology for the use in cancer treatments.

Now, as we all know, as cancer patients or some of us who are cancer patients know that from the time it becomes an idea or a clinical test to the time it becomes a drug that's FDA approved takes some 10 years. Now, the National Comprehensive Cancer Center that the doctor is the Assistant Director of admits to have started in 2005 with this 150 million dollar budget from the government. This is something that I feel is important because with multiple myeloma and lot of blood cancers as well as any stage IV or metastasized cancer, its all over your body and as a result, you need something that's either like an immunotherapy or another targeted approach and what I see here is that this is a potentially targeted approach that the liver is more drugged to where it is intended and that is the cancer cell. This, I think, is critical than all these other cancers, especially in a cancer, a stage IV cancer, any stage IV cancer, because now the cancer has gone further away from its original site and we need to have a targeted therapy.

Now, given that process, I would like to say that we are honored to have Dr. Anil Patri here, who is not only the Deputy Director at the Nanotechnology Characteristics Lab, which is, I think, the largest lab from this 150 million dollars that was originally acquired but also has done a heck of a lot of work in this area at the University of Michigan and also at the University of South Florida. So, I am honored to have the doctor, Dr. Patri, discuss nanotechnology oncology and, doctor, welcome and thank you very much for your time and your efforts.

**Dr. Patri** : Thanks, Gary.

Thanks for the kind invitation and introduction. It is my pleasure to participate in the Cure Panel Talk Show along with the other panelists to share and discuss about the latest developments in nanotechnology for cancer. Gary, I should… You mentioned that this 150 million dollar program is for NCL, it is actually NCI wide Alliance For Nanotechnology and so most of the funding is to the centers of cancer nanotechnology excellence that went out, but nevertheless, our lab is interested in the clinical translation of promising cancer nanotechnology drugs and imaging agents and I am going to talk briefly about all that towards the end.

So, let me first start by defining what we mean by nanotechnology. Probably people heard of nano before, but the NNI has a very good definition, the National Nanotechnology Initiative. So, nanotechnology is understanding and control of matter at the nanoscale. This is roughly in the range of 1 to 100 nanometers, where unique phenomena enable nano application. So, in other words, just a material being in that size range may or may not have any propberties. So, some material because of the size range have some unique properties. Again, for the benefit of listeners, nanometer is a measurement unit which is a billionth of the meter. For example, in a biological world or DNAs that are around 2.5 nanometers in diameter, we hear about antibodies and antibodies around 13 to 15 nanometers in size. So, most of our proteins, enzymes, and other natural biological components are at the size range and function is at this nanoscale.

So, again, there are many different kinds of nanomaterial, some are from the colloidal world that are there for a long time. Polymers are also now can be self-assembled and called nanomaterial. Liposomes are also nano because of their size range and some unique properties because of their size and surface characteristics and there are many others that are relatively new based on new technologies, new proteins, new core shell nanoparticle. So, most of the nanotechnology development in medicine is in oncology. So, if you look at all the nanotechnology medicines, I would say around 80% of those medical applications are in oncology area. Early detection of cancer is a challenge as we all know, but once a patient is diagnosed, there are only limited options available to patients. So, surgery, radiation therapy, and chemotherapy are the most common treatment options depending on the type and the staging of cancer. With nanomaterials, the options are much better. For example, for early disease detection, imaging of the disease, new materials are being developed to aid in the surgery and better chemotherapy using nanomaterial platforms for targeted drug delivery, as Gary mentioned before.

So, I will briefly touch upon each of these topics. So, we have made significant advances in the preclinical development with nanomaterial-based vaccines for prevention of cancer. Many different kinds of nanoscale material-based devices are in development that can detect cancer biomarkers at very low concentrations in biological fluids, this means we can detect the cancer early. Again, early detection is the key for better outcome. Detection of different biomarkers simultaneously again, this can aid in the future in the personalized medicine area and those kinds of concepts are in the research and development phase of development. Another very active area of research for over two decades now is the development of in vivo imaging modalities using nanomaterial. Due to the extended blood circulation based on size and surface characteristics of nanomaterial, if an imaging agent is tagged to these nanomaterials, one can image areas in the body that are otherwise not visible using conventional imaging techniques. Many blood pool agents and lymphatic imaging agents are in development and will aid in the detection and confirmation of cancer.

Then, there are these new concepts to assist in surgery for surgeons. So, these are colored dyes or fluorescent markers that are tagged with a nanomaterial and they can be frayed during surgery and this will aid the surgeon in defining the tumor border. Sometimes, you know, they can see the residual nodules that are otherwise left in the patient and again cancer can come back if such a thing happens. So, these are in preclinical development and then hopefully we will see them, some of these, in the surgical realm pretty soon.

So, predominantly when I say nano for cancer, these are mostly the concepts involve the drug delivery and this is where our lab has done lot of work, working with more than 100 different kinds of concepts in the preclinical assessment. So, there are many different kinds of nanomaterial as I mentioned, including liposomes, emulsion, dendrimers, polymers, metals, metal oxides, nanoparticle. They have unique features that one can use for cancer. So, in general, they reduce the toxicity associated with chemotherapy while increasing the efficacy of the chemotherapeutic. There are many other concepts that use the gene delivery and they are also into preclinical development, advanced stages of preclinical development.

There are some that are very unique, that are in clinical trials. These are core shell nanoparticles such as the gold nanoshell containing silica core gold shell and they have unique absorption range that can be tuned based on the size and the shell thickness. So, one of these concepts actually is in clinical trial, phase I clinical trials for thermal ablation of tumors. Cancer is a very complex disease and we know that the tumors at the primary site are different from the metastatic site. So, medicines that work on a certain tumor type do not necessarily take care of the other disease type. So, again, this is where nanotechnology is useful. One can have multiple drugs in the same nanomaterial platform to address and then deliver chemotherapy to the tumor site and finally, a small, I guess few sentences about our lab.

The nanotechnology lab is a part of the National Cancer Institute. It is a centralized core facility and we conduct a preclinical assessment of nanomaterial concepts that are beyond proof-of-principle efficacy. In other words, we start with the concepts where people show efficacy in a mouse model to cure cancer in mice, if you will. So, we collaborate with many industrial partners, academic, and government agencies to enable clinical translation of promising and safer cancer therapeutics and imaging agents. So, in other words, our works, you know, really is in the translational side. We don't conduct basic research for most part, but really our focus is clinical translation to aid companies. So, we have close collaborations with Food

And Drug Administration and we also have a collaboration with the National Institute Of Standards And Technology in this clinical translation effort. So, in this effort, we conduct thorough material characterization, biological assessment in cell cultures and human blood by compatibility experiment and we also conduct in vivo studies in rodent models in both the rats and mice. So, with that, I will stop here with the introduction of nanotechnology in cancer and I will be happy to discuss these further with the rest of the panel.

**Gary** : Okay. I have… I know that Priya has a few questions. Do you want to ask one of those to begin with, Priya, and I will rotate you in.

**Priya** : Gary, I think you can start with your questions.

**Gary** : Okay.

**Priya** :I will keep mine to the end. Yeah.

**Gary** : Yeah. All right. Doctor, one thing that I noticed and as I was reading through some of the information on nanotechnology is that there is a technology called Stealth and that technology was used with doxorubicin which is an old line chemotherapy for, I believe, it was used in VAD way back when but wasn't very effective and that once the Stealth technology which is a nanotechnology was used with doxorubicin that it became a new drug called Doxil and Doxil has shown far improved efficacy without the problems that they used to have with heart issues actually and what it shows is that far more of this drug seems to get to, you know, far more of this drug which really didn't use to be very effective is now getting into the cancer cells and as a result is far more effective and has shown in a number of clinical trials of being actually quite good in refractory and resistant multiple myeloma, for high-risk multiple myeloma, which is something that nothing really has in the past been able to be very effective other than our standard therapy hype, you know, our big gun and our big gun in myeloma has to be Revlimid, Velcade, and dexamethasone. So, my question is that this Stealth technology works so well with Doxil, you know, why on earth isn't it, you know, combined with Revlimid, Doxil, Velcade, and dex in a little, you know, myeloma atomic bomb and just wipe that stuff out? Why isn't that technology there today?

**Dr. Patri** : So, again, Gary, this is a very good example of how nanotechnology works. So, you mentioned that doxorubicin, which is a small molecule drug, has cardiac toxicity problems and usually most of the small molecule therapeutics when they are injected, they have a very quick blood circulation. They clear very quickly. These are hydrophobic drugs and less than 1%, in most cases less than 0.1% of the injected dose goes to the tumor. So, you are essentially wasting more than 99% of the drug. It goes elsewhere and then causes toxicity. So, what these people have done actually was developed originally by Frank Szoka and his colleague at UCSF and so they prepared a liposome which is around 100 nanometers in size and they coated with polyethylene glycol, which gives its self property, meaning that once it is injected into the blood stream, our immune system recognizes anything that is foreign, so once if you coat the particular, in this case, liposomes with polyethylene glycol, then they escape the immune system recognition. Now, its called reticuloendothelial system recognition.

So, then, if the immune system is not recognizing the particle, then the particles will have prolonged blood circulation. They stay in the blood for extended period of time and for extended half life or extended blood half life, it is called or PK changes, the pharmacokinetics of the drug changes. So, along with that, because of the size and surface characteristics, because of the biodistribution being different, it gets away or the cardiac toxicity associated with the doxorubicin is minimized. So, once it is encapsulated or once it is packed inside this liposome, now doxorubicin behaves as a liposome and not as a doxorubicin initially until it is released. So, this combination, this is a common feature of most of the nanomedicines or nanotechnology for cancer. So, you are masking the drug from immune system recognition and through there are certain concepts such as enhanced permeability and retention. Now, this is also called EPR, where you can localize the drug at the tumor site better than if you have a small molecule drug with this EPR phenomenon, then so you have limited side effects. So, that is how it is developed, but your main question about the combination with other chemotherapeutics, it is entirely possible, I am not aware, but that doesn't mean that these are not happening in the clinic.

**Gary** : So, would it work the same way for like Revlimid which is like thalidomide-dexamethasone, which I am sure you are familiar with and…

**Dr. Patri** : Right and so they can be encapsulated in the liposome or they can be encapsulated in a different liposome and then can be given as a combination of Doxil and the liposome encapsulated by, you know, other drugs. So, it is possible.

**Gary** : What prevents this from being done? Is it… Is it… Yes, I know Doxil, you know, long ago has run out of patent protection, but Revlimid and Velcade are probably well protected, still is. Does that have anything to do with it?

**Dr. Patri** : No, so if there is patent protection, those are patent issues, but there are a lot of liposomes in development. For example, paclitaxel is packed into a liposome, this is something in, I think, in phase 1 clinical trials. There are many dozens of different liposomal formulation packing different kinds of drugs are in the clinical phase of development.

**Gary** : Okay. It would just be nice to see it speeding along. Okay, Pat Killingsworth, your question.

**Pat** : Hi, Gary! Hello, doctor!

**Dr. Patri** : Hello, Pat!

**Pat** : So, maybe I was… My initial question was correct that I was going to ask you how does nanotechnology translate from research to actual therapy? You know, I think about little many submarines swimming around, zapping cancer cells and we definitely thought about originally when we hear that term and listening to you and I did little research, it sounds like it is more or less delivery system, so maybe that's not so far of. Are we talking about a new type of drug or compound or is this basically how you are going to deliver existing chemotherapy or the type of drugs that researchers are working at?

**Dr. Patri** : Yeah. That's a very good question. So, it is both. So, many of them are these packing kind of platforms, where whether it is polymer-based platform or a liposome or an emulsion, you know, any of these are traditionally they were not called nano before, but because of the size and function, they became nanomaterial these days. So, many of them do use that kind of packing and escape the immune system recognition. Sometimes in some cases, you want the immune system to recognize this is the case of Robaxin, so you can quote possible in such a way that certain components of the body recognize these material. In some cases, the composition itself is recognized by the body. For example, if you have phosphorus-containing material, depending on the composition the body recognizes them in certain ways and localizes them to certain organs or certain parts of the body. So, in those cases, we are using the strength of the composition of the material and send the drug to the site of action. In other cases, if you know, for example, in case of targeted therapy, these nanomaterial can be functionalized with the targeting ligand on the surface such as antibodies or portions of the antibodies, peptides, and small molecules to bind the tumor overexpress receptors on the tumor and that way they localize to the tumor size and so thereby delivering more drugs to the tumor site then if you just have a small molecule-based therapy. So, to answer your question, it is both as a carrier of plasma as well as based on composition and targeting modality, you know, you can enhance the delivery of the drug.

**Pat** : So, at last year's ASCO, the blockbuster, you know how there is a blockbuster or two that the media picture upon every year, that was a cancer, a combination cancer therapy using a delivery system that allows chemotherapy to not be released until the actual cell was located and it sounds like that, that's a perfect…, and I am sorry I don't remember the name of the drug, maybe you know what the drug sounds like, but the therapy does sound like the perfect example of what you are talking about the nanotechnology. Are you familiar with that one?

**Dr. Patri** : No, I don't know exactly which one that you are talking about, but generally that is true. The advantage with nanomaterial is that you can have these, these are called multifunctional nanomaterials. On

the same particle, you can have a targeting ligand, you can have a therapeutic halo, one or more combination, concoctions of drugs and as well as for example, an imaging agent to see where these therapies are going. So, these are all multifunctional platforms and in fact, NCI funded these programs in the late 90s, 1990s, its called Unconventional Innovations Program. So, the next phase of the program is Alliance For Nanotechnology In Cancer in 2004. So, yes, these are all, you know, the targeted delivery, so instead of 1% of the injected dose, if we can increase it to 10%, that is in order of magnitude more that is being delivered to the cancer and then we will have much better outcome.

**Pat** : Sure and theoretically, you could use a lower dose if its more efficient. Correct?

**Dr. Patri** : Exactly. So far, what we have seen in the preclinical area is that you could actually deliver more drugs and you are right. Ideally, you know, if you could get away with using less drugs, you will have less side effects.

**Pat** : Wonderful. Thank you.

**Gary** : Very good. Thank you, Pat. Kimberly!

**Kimberly** : Hi, yes! Can you hear me?

Yes.

Yeah.

Great. Great. Oh, hi everyone. Thanks for having me on the Cure Panel and hello, Dr. Patri. It's a pleasure to speak with you. My question for you is so I worked in cancer research for many years and at the tail end of my stay at Columbia University we did begin to get into some drug delivery kind of nanotechnology-based system, but I was always questioning why the kind of drug delivery systems were only targeting kind of either the cancer cells or maybe some kind of signal cascade with proteins or, you know, some essential nutrients of the cancer, but we have never or it seems like, at least I didn't know about, any research that was targeting the genes of the cancer, the actual genetics inside of our genomes that maybe self-cancerous or not and I would love to hear from you, you know, what the limitations have been? Is there being research done on that? Just any comments you can make on that would be great to hear about.

**Dr. Patri** : Yeah. In clinical gene delivery, so beyond drug delivery, there are many concepts that are in preclinical development, I should say, for gene delivery. So, for example, saRNA is something that lot of people are interested in delivering the cancer and so if you were to just inject saRNA, then you know, its immediately clear and then so using nanomaterials, most of them use some kind of cationic nanoparticle and attach or bind these saRNA to the nanoparticles and then inject, so most of that work, it is done in an in vitro system, in other words in a cell culture system that works great, but once you get into the in vivo systems or into the animal model, then the complexities are lot more difficult to overcome, but certainly there are many saRNA delivery systems. Different kinds of platforms use saRNA and we have seen some promise in the preclinical area and then I am sure some of these end up in the clinical phase pretty soon. There are some others that take these genes ex vivo, in other words re-train our immune system and then let's our immune system take care of cancer. So, yeah, this is going to be the best outcome for cancer patients from my perspective because most of us are, I should say all of us have cancers it's just that our system takes care of the cancer. Its only when the immune system fails and one cell becomes cancerous and eventually years down the road that becomes a tumor from my cancer biology. So, if we can re-train our immune system using nano which some hospitals are trying to do and then re-inject those therapies, I think that will be the best outcome for patients down the road.

**Kimberly** : Great and just a quick follow up on that. Whatever you just said in the beginning is that it seems we have gotten pretty good at targeting the sections of the army you need to deliver to the genome to shut on or off different cancer genes, it's just once it gets introduced into the body, a living creature, that's when all the complexities and difficulties set in. Did I get that right?

**Dr. Patri** : Yes.

Okay.

**Kimberly** : So, in an in vitro system, it is a more controlled system. It is easy to have a proof of principle, but once you inject into an animal for example, then you have more complexities because of all the different kinds of cells and proteins…

Sure.

…that try to tear these particles apart.

Okay. Got it. Great! Thank you.

**Gary** : All right. Sarthak!

Ah, yeah.

Your question?

**Sarthak** : All right. Umm… So, Dr. Patri, my name is Sarthak. I am a grade 11 student here in Calgary. One of my questions was the use of nanotechnology in relation to heat shock therapy. I would really appreciate if you could go a little bit in detail, so how we are trying to attempt that and where we are, Sir, in developing heat therapy?

**Dr. Patri** : So, if you are asking about the thermal ablation therapy, is that your question?

Yeah.

Okay. Because there are heat shock proteins and I hope its not the one that you are talking about. So, in the case of thermal ablation, again, this is the uniqueness of nanotechnology. If you take a gold salt, it behaves certain way and if you make it into a gold nanoparticle, it has absorption around 500 nanometers or so and has absorption in that range, but if the same gold nanoparticle, if you make it into a rod shape instead of a spherical particle, if you just make it into a rod, then the absorption shifts, so depending on how long the rod is, the wave length of absorption shifts, so you can actually modulate that synthesizing different shapes of this particle. In terms of thermal ablation, so you can go with an external energy source, away from the rest of the body absorption range, this is called the water window.

Oh, okay.

These particles have around 800 nanometers absorption, so they absorb this energy and give out heat and that's when if they are near the cancer cells or inside the cancer cells, then you can kill the cancer cells specifically without harming the rest of the normal cells. So, there is one concept, but then the concept that is actually in clinical trials, which is in phase I clinical trials, work out of Christ University is a core shell particle. This is a silica core gold shell nanoparticle and then they coat these with polyethylene glycol to escape the immune system we talked about before and localized these therapies around 150 nanometers in size in cancer and then go with an external energy and then ablate the tumor and one limitation there is the depth of penetration of these lasers that they use and they cannot penetrate, so they can use this kind of therapy only in limited cases where they can actually have an access.

**Sarthak** : Okay. So, another one of my questions was are these facilities dendrimer-based nanoparticles, are they degradable once they go in vivo or do they leave some potential after effects?

**Dr. Patri** : Yeah. So, dendrimers are, in a general layman term, these are like polymers. These are organic polymer systems, so you can make literally a branched molecule out of any bifunctional molecule and so

there are literally thousands and thousands of different kinds of dendrimers. There are only few that are commercially available, that are, for example, PAMAM dendrimers or polyamidomine dendrimers or polypropylenimine dendrimers, but they can be made biodegradabale. They are called biodendrimers that are actually biodegradable. So, you can make them biodegradable. You can synthesize them in a very uniform fashion because it is just like any other organic synthesis and for most part, they are eliminated from the system, some based on the size. If they are less than 10 nanometers in size, for example, they are quickly eliminated through the kidney and eliminated from the system. If they are larger than 10 nanometers, then they may go through a liver excretion process, but they are eventually excreted and some are actually biodegradable. So, they are an excellent platform for drug delivery.

Okay and you know in terms of drug delivery, sorry.

Yeah, we need to go on to the next question.

**Sarthak** : Oh, yeah. Of course, of course. By all means.

**Gary** : All right. Doctor, on the, you know, talking of drug deliveries, well, you also have a breast cancer drug that just was recently approved called Abraxane, I believe.

Uh hmm…

And I was wondering if this same technology, just talking about chemotherapy drugs like Revlimid, Velcade, and Kyprolis, I believe there is another one, can that particular delivery technology also be used for these other drugs?

**Dr. Patri** : Yeah. It is certainly possible.

…with that Stealth technology?

Yeah. So, unlike the doxorubicin encapsulated liposome, the Doxil which is a self nanoparticle, it has a prolonged half life in the blood. Abraxane is a formulation of human serum albumin with the paclitaxel, which is the drug. So, paclitaxel is also delivered with a Cremophor, its called Taxol and that's also used and so…

So, Abraxane is paclitaxel. The active drug is paclitaxel and it is packed in with human serum albumin. So, the main difference between Taxol and Abraxane is that you don't have Cremophor-related toxicity with Abraxane. So, Cremophor is essentially, these are formulations to make these small molecules soluble. They use oils and things like that and they can be toxic and that's what happens. You have more toxicity from the formulation, not necessarily from the drug with the Cremophor formulation. It's called Taxol. Compared to Abraxane, which just gives us human albumin, which we have anyway and then delivers the drug, but there is no real drug delivery. You are just getting away from the toxicity associated with Cremophor and in case of Abraxane, once it is injected, it really falls apart quickly. It is meant to fall apart quickly and deliver or release the drug into the blood stream. So, your question of whether you can use the same technology to formulate other drugs, it is certainly possible.

**Gary** : One of the things that I noticed when I read about it is that apparently this coding, this nanotechnology coding is the cancer cells which apparently love to eat things, I mean, that insatiable appetite that considers it food and as a result it kind of targets the cancer cells. Did I read that incorrectly?

**Dr. Patri** : Yes, there are some, you know, these are still in clinical… I guess they are looking at this in the clinic or from the clinical data that such a thing is possible, but for most part, Abraxane has human serum albumin and we have in our blood stream we have this albumin, tons of albumin in our blood stream. So, once it is injected, it quickly falls apart and releases the drug. So, whether it gets accumulated, we don't see at least in the preclinical stages. We don't see any significant difference in the pharmacokinetics of the drug because the drug falls apart very quickly…

Okay.

…and so unless it is intact with the protein-bound drug and somehow circulates, maybe there is certain portion of the drug that gets circulated that way and then have better efficacy, but for most part it is free in the blood stream.

**Gary** : Okay. In followup also to my last question and has to do with that Stealth technology, in 2006 researchers at UC San Francisco and UC Berkeley had found a way to combine, I think is doxorubicin…

Yeah.

…a dendrimer together treatment that cures colon cancer in mice on treatment and this was given as a possible cure for colon cancer. Has this progressed to human trial or how long till to have the approval?

No. Yeah. So…

That translates from mice to people.

**Dr. Patri** : Yeah. So, we are… At least I am intimately familiar with this work because this is an excellent beautiful work done by my friend, Frank Szoka from UCSF and John who is another dendrimer professor in California, but this has never gone into clinic. So, in this case, they use a degradable poly-dendrimer, that's an earlier question about dendrimer degradability and the conjugated doxorubicin and they had a remarkable anti-tumor efficacy upon single dose IV administration, but this is similar to liposomal doxorubicin which is Doxil. So, they had remarkable efficacy, but that efficacy is similar to existing approved drug, Doxil, and so Doxil is incidentally developed by Frank Szoka, the Doxil formulation and which eventually came to the market through Johnson & Johnson. So, as far as I know, this concept has never been pursued to get into clinic. There may be multiple reasons for that, complications with the complexity of the multi– dendrimer with the chemistry, but it has a similar efficacy compared to an approved drug. So, when commercially you have to show advantage over existing therapies and that's where we usually start, is beyond a proof-of-principle and most of them may not get into the clinic because of that.

**Priya** : Okay. Well, thank you so much, Doctor.

Okay. I have got a question from one of the participants and it says what treatments are in the works for stage IV colon cancer? What clinical trials are now in development for solid tumors like colon cancer?

**Dr. Patri** : Umm… I am not really qualified because I am not an oncologist to talk about this, but certainly if they can go to the website, there is a website called clinicaltrials.gov, www.clinicaltrials.gov and type in colon cancer. So, there are literally many dozens of clinical trials for different stages of colon cancer and they can easily find that information on the website.

**Priya** : Dr. Patri, I have a question for you.

Yeah.

What are the negative implications of nanotechnology with reference to cancer?

**Dr. Patri**: So, that's a good question. So, whenever we talk about nanotechnology, there is this question that comes up about the health implications of nanomaterial, environmental implications of nano. So, particularly for cancer, the ones that we went through in the preclinical assessment, I would say there is no significant limitation because most of the toxicity is coming from the chemotherapy that is encapsulated and all the material that we have seen at the dose that we administered were less toxic than chemotherapy. So, for example, there is concern over potential toxicity of carbon nanotubes, but these are all… One has to look at in terms of benefit to cancer patients, so it is a risk versus benefit. So, when one goes to FDA, as we all know, no material is safe. It just depends on the dose and then so the risk versus benefit, actually you have much

better benefit with the nanomaterial than the risk, especially for cancer. That's the reason most of the concepts, I would say, 80% of the medicine involved with nanomaterial is for cancer.

**Priya** : Doctor, when I was just reading up about nanotechnology while planning this, I came across about a lot of issues regarding people being concerned about accumulating nanoparticles in a healthy body tissue. How true is this?

**Dr. Patri** : Yeah, that's a very good question. It is true that some of the metals containing nanoparticles such as gold or others do stay in the body for longer period of time. In other words, your body's immune system eventually recognizes and then takes this nanoparticle either to the liver or spleen and these particles may stay there for an extended period of time, but many others, the platforms that we talked about today, including dendrimers, liposomes, and emulsions, these are all organic material and they are either biodegradable or eliminatable from the body. So, I would say, yes, depending on the composition, they may stay in the body for extended period of time.

**Priya** : Thank you, doctor. Kim, would you like to ask a question to Dr. Patri?

**Kimberly** : Yeah, sure. I have a bit of a comical question but also slightly real in my mind anyway as well so I read a lot of science fiction. I also write science fiction and of course, there are the pictures of little robots being injected into the blood stream with little scrubbing brushes and arms that clean different things away from blood vessels or, you know, little cancer cells, things like that, but I currently work in an imaging group called Nanotronics Imaging and we make our automated fibroscope and it looks at mainly semi-conductors, but we are getting into the life sciences, but I bring that a lot because semi-conductors and also related men's devices are getting into the nano level of being able to store information and data, but also, for example, on men's devices, there's little microfluidic channels where different proteins can be analyzed and different molecules can be tested on, you know, enzymes and things like that and that's at the micro level. I am wondering if on the nanoscale little robots being injected into the body is a reality down the road, is that in development? I know along the physical side things like that are becoming more and more possible, but I am wondering on the bio side where we might be at with all that.

**Dr. Patri** : That's a good question because of some of the novels that came by and actually even movie…

Right.

…on robots, you know, being injected and then somehow tiny people come out of those and talk to you. (Laughter)

Its tough finding little people, right?

Those are the… Those are the nano people coming out of the microns as robots and cancer cells and then, that is not true in terms of real people, you know, people are really alarmed about these new technologies and then really robots somehow manipulating things, that is not true, but certainly there are really truly new technology. For example, the micron science technology, this is what recently I have seen from MIT. So, if you inject a micron size particle, this is a specialized micron size particle, not nano, but then when it hits in the blood stream and when it has certain pressure, for example, when you have plaque in the blood vessel, the pressure change differential makes these particles to fall apart and release the enzymes, that dissolve the plaque. This is a very beautiful technology, very good example of use in the technology, but then this is very sensitive to those slight differences. We talked about microfluidic and nanofluidic.

So, you know, one of the problems whenever you make these, you know, microfluidic devices is the pressure and then so the slight change in the pressure at that site of action if it delivers or if it disintegrates to release enzymes and things that get rid of plaque, you know, that is an amazing technology. So, these are real in terms of robot but not in a way that we think of bugs coming out of some kind of… (laughter).

**Kimberly** : Right. That was great. Thanks so much.

**Priya** : I think we have a caller. I think we have a caller on line. Person calling from 212, please ask your question.

**Caller** : Yeah. Hi! I was wondering what is the most exciting or groundbreaking development in nanotechnology that you expect over the next five years?

**Dr. Patri** : Ah! So, that's a good question. The next, I would say, five years, we would definitely see, there are some very exciting targeted nanomedicines currently undergoing clinical trials. So, I am pretty sure some of those will be out in the market to benefit cancer patients worldwide. We will definitely have few more tools for early detection of cancer and these kits will become more affordable, I would say between 5 to 10 years to benefit patients, especially in the developing countries. So, what I mean by this is that these are almost like kits that we use for sugar strips for diabetes and then so they are in development and especially for personalized medicines, I certainly foresee the personalized kit for example, therapy monitoring for cancer and these will be coming out in the next, I would say, 5- to 10-year time frame.

**Priya** : We have a last couple of minutes left. Pat, would you like to add anything? (Pause) Pat, are you… Would you like to add anything?

**Pat** : I appreciate being included and I learned a lot, but I am not sure I was able to contribute much.

Thanks.

**Priya** : Sarthak, would you like to add something? We just have couple of minutes left.

**Sarthak** : Oh, no. I mean, thanks once again for having me and thank you, doctor, for your insights on that technology. I think, you know, at the very least it will definitely be a field with enormous potential and it really relies on leaders like yourself and your enthusiasm around, you know, for the society to be able to make some of the translations and I think it will be a very exciting field to watch.

**Priya** : Thank you, Sarthak.

Dr. Patri, it was great having you here. Pat, Kim, and Sarthak, it was a great discussion and, Gary, as always, you were wonderful. Thank you so very much.

Thank you.

Cure Talk thanks all its listeners and participants. Thank you, all, for your support and we look forward to having all of you join us for the next Cure Panel Talk Show on Thursday to discuss yoga. For more details of upcoming shows, please visit trialx.com/curetalk. The link for today's broadcast will be sent to all panelists and participants and also made available on Cure Talk within 24 hours. Thank you. Thank you very much. It was great having you here.