Science Forward-Cancer

A production of Macaulay Honors College http://cuny.is/scienceforward

TEDx Narrator: A tiny, double strand of DNA. Not but what would be two single codons had it been located on messenger RNA.

Jill Bargonetti, Hunter College and The Graduate Center: I always tried to get students to move so that they could see that molecular biology was nothing like the textbook. It wasn't static. It wasn't round red and blue balls.

Language fails in a lot of places to describe chemistry and biology, but when you're seeing it or you're thinking about, "How does a cell know to communicate this? There's no language inside of the cell."

TEDx Narrator: The great helicase, roaring across the nuclear plane.

Jill Bargonetti: There's only movement and charge and energy in the cell.

Emily Rice, Science Forward Host: To explore complex systems like the human body and complex diseases like cancer, we need to use many different methods of understanding. Dr. Bargonetti and her students at Hunter College have been using the creative and physical experience of dance to help feel and know how the body's chemical and biological processes work and what happens when, as in the case of cancer, they break down.

[Science Forward theme music]

Research in cancer presents a particular challenge. Our understanding of exactly what cancer is has changed over time and it is clear now that a single cure for cancer is not a realistic goal. Different types of cancer are going to require different types of tactics.

In this video we will discuss what cancer is and how it can be investigated at many different scales, from molecules, to tissues, to people, to populations. Let's start with the basics. What is cancer?

Sarah Schlesinger, The Rockefeller University: Cancer's not a single disease.

Jill Bargonetti: There are many different forms of cancers, even in a particular cancer of a body part. There are organ-specific cancers, but even those organ-specific cancers are all very different cancers based on the genetics of the cancer.

Niroshana Anandasabapathy, Weill Cornell Medicine: If you think about how a cancer arises, it starts off with your normal cell that then becomes increasingly more abnormal.

Jill Bargonetti: I would say all cancers are cellular in origin. We can say that as a definition of cancer. They come from a cell replicating out of control. Certainly, our understanding of cancer

has become more molecular biology oriented. It's clear now that cancers can share things across different organ systems.

Breast cancer can be very, very similar to ovarian cancer based on the genetics. I think that our genetic understanding has moved cancer understanding along.

Sarah Schlesinger: If you read the history of medicine, the paradigm for understanding things has changed, or not changed, over centuries. Cancer means a tumor that has the ability to invade and metastasize.

Invade means push the boundary, typically of the basement membrane of the organ or tissue in which the cancer is arising. Metastasize means spread and form distant colonies that are autonomous and growing on their own.

When people talk about a cure for cancer, it's like saying a cure for infectious disease. I don't believe we're ever going to find a single silver bullet that's going to cure all cancer.

Emily Rice: Cancer research requires different types of experimental work, from molecular assays at the lab bench to clinical trials. At any scale, cancer researchers need to think about how to properly design their experiments. They often work with model organisms.

Dr. Bargonetti investigates molecular pathways that are involved in the development of cancers.

Jill Bargonetti: There are two basic pathways that we study in the lab. They concern two particular molecules or proteins, p53 and Mdm2. Both are made from genes.

The experiments that we do in this lab are biochemical and molecular biology based. We use a number of different model systems. We use cell culture where we are able to genetically engineer human cancer cells to get rid of the proteins in question. When we put those cells into animal models, we can see that those cells that once were metastatic are no longer metastatic, that they change their aggressive qualities.

It helps us to, then, figure out what are the pathways that are pushing those aggressive qualities. We also use patient-derived cancers and put those into animal models to try to figure out ways to better detect the cancer cells based on our targeted therapies.

Lastly, we use a microscopic worm model and try chemotherapeutics in the microscopic worm model.

All three of our models are looking at dysfunctional p53 regulation. They all have that in common. We try to utilize similar drug approaches in all three. That means that we are treating the mice. We are treating the tissue culture. We are treating the worms all with the same chemotherapeutic drugs at similar concentrations and dosages and looking to see how they affect those downstream pathways that we're interested in.

Emily Rice: Even though these experiments take place using different models, they can complement each other.

Lissette Delgado-Cruzata, John Jay College: The questions that can be answered depend on the system that you're using. When we are working in a cell culture environment or we are looking at cells, the cells can be manipulated easily. We can manipulate their genome. We can manipulate what do we want to do inside the cells. Express genes, proteins, and modify things.

We can do a lot of studies that tell us about the regulation of, let's say, a particular pathway that is relevant on disease, or the modification of the protein. However, when we're looking at individuals, we can measure things but we cannot really manipulate anything. So we use these two different systems to confirm information and to guide us.

Cell culture experiments are usually carried out on individual cells that are growing not in the form of a tumor. We try to imitate the best possible of that environment by growing cells in culture, but the conditions will be very different.

However, the molecular mechanisms underlying this process should be very similar.

Emily Rice: At the lab bench, scientists work with cells in Petri dishes and with model organisms like mice and microscopic worms. How do we get from that to figuring out what is happening in a human body?

The answer is translational research.

Niroshana Anandasabapathy: Initially, we thought that we would be at the bench, that we would be able to translate bench findings into patients. That was what the old definition of translational was, that you're doing some science. You're doing that on a mouse. You find an interesting gene. You develop antibodies against that. Now, you put those into patients. That is an example of very direct translational research by the old version of it.

Now, translational has come to mean almost anything that also involves human tissues. We're doing so much. We're learning from our patients now, directly. We use that to actually go the other way, to inform. We say, "Bedside back to bench."

Some people go bedside to bench and back, or bench to bedside and back. I define translation as anything that involves human populations, human genomes, and human tissues. Anything where there is direct clinical relevance I think of as translational.

Sarah Schlesinger: Training in clinical investigation is not a typical part of medical school or hasn't been, though I think many schools are now including it in their curriculum. Historically, there's basic science, which is really understanding how the world works, which frankly is immensely fun and very cool.

And then there's clinical care, which is taking care of patients, which is also very interesting, very important, and I don't think anybody who does it ever goes home at the end of the day and wonders why they went to work that day.

But the bridge between the two, how to bring basic science into the clinic, is called translational science. That's what I do. That's what our training program trains people to do.

Typically, in one's PhD, if one does a PhD, one learns basic science. In medical school you learn clinical care. You learn how to take care of people. You learn how to operate on people. You learn what to do in an emergency room. All of that's wonderful and important.

But to combine the two, this new discipline of translational science has developed.

Emily Rice: How are experimental approaches different when you are working with humans or human population data?

Sarah Schlesinger: Clinical investigation is like any other experiment. One of the things that I think is most important is to understand that the rigor that you would bring to any basic science experiment absolutely has to be brought to clinical investigation because, at the end, you need an answer you can believe. The only way you can get an answer that you can believe is by bringing as much rigor to the process as possible.

Lissette Delgado-Cruzata: Population studies are studies that involve individuals. Therefore, it's quite important to consider that we cannot have any names, or we can't have any private information. It is important for the students to understand that clinical samples are quite precious because individuals have donated their time and their actual sample to participate in this study.

I stress to almost no end the importance of being extremely careful with this material but also how important it is that we actually have access to some samples that came from a person that has a particular disease and they're willing to give us some of that sample for us to understand what's happening.

Sarah Schlesinger: At the end of the day, it is still an experiment. Therefore, it needs controls. A control is a group of individuals who don't receive the treatment or they receive what's called a placebo. A placebo is a blank treatment. It could be sugar water. It could be salt water. It's something that you think is going to be inactive.

With human beings, placebos are particularly important because a lot of how people respond to things has to do with what's in their head. There's what's called the placebo effect.

One of the really key parts of most clinical trials is that people are what's called blinded. It means we don't know who's getting the intervention and who's not.

Not only do the participants have to be blinded, but the investigators do, as well; it’s best to get the most, the clearest, most correct, truest result. I think if I had to give you a single takeaway, the most important thing that we teach our clinical scholars is the same dictum of first, do no harm applies to clinical investigation because it's human beings.

When you sit with a research participant, you wear two hats. You wear the physician hat and you wear the scientist hat. The physician hat always has to come first. The day it doesn't is the day you need to leave, in my view.

Emily Rice: The topic of cancer biology is enormous, encompassing multiple scales and fields of scientific inquiry but ultimately, we are trying to figure out a problem that so many of us face, personally or through people we know. It is a topic that unites us.

TEDx Narrator: The polymerase wants to help.

Jill Bargonetti: In our performance at the end of the semester, the performance is their final exam. They've all written a paper about a cancer gene and then they choreograph a piece for it. They use choreopoem in their pieces and they use contact improvisation in their pieces.

In addition to them doing their pieces, I also perform one piece, which is a choreopoem piece which has to do with how cancer unites the human family. One of the things that I'm trying to teach them is that these genes are in common between all of us.

There is no discrimination between the races for people getting cancer. All races get cancer. All people get cancer. Those genes are in common.

[Science Forward theme music]

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