Discovery of the "HeLa Bomb" with Dr. Stanley Gartler

[GENTLE CHIMING]

PHIL MIXTER: Let me start by saying the Common Reading Program began at WSU in 2007. And in this program, each year a book is selected that students use in a wide variety-- literally dozens-- of first-year classes. This spans a lot of disciplines across our campus. This includes the WSU Global Campus and programming that occurs primarily in the residence halls on campus.

This year's book is The Immortal Life of Henrietta Lacks. A large component of the Common Reading Program is the weekly-- or almost every week-- guest expert lecture series. It offers freshmen and other students of our community a chance to hear from the expertise we have on campus, as well as bring in some experts from outside our campus to talk about the book and its related topics.

We're very honored to welcome to WSU Dr. Stanley Gartler. Dr. Gartler is a professor emeritus from the University of Washington. I understand, Dr. Gartler, this isn't your first visit to our university. You've been with your friend, agronomy professor, [? Demark ?] [INAUDIBLE]. And you've managed to put on some hiking boot miles in our wonderful Palouse countryside earlier. So welcome back to what I would normally call the dry side of the state. But today would not qualify as a dry day, I guess.

Dr. Gartler is a molecular biologist and a human geneticist. He's a professor emeritus from the Department of Medicine and Genome Sciences at UW. He has worked there since 1957. Most days, he will walk his dog and head to the laboratory. He enjoys working with faculty and students there.

Dr. Gartler accomplishes-- has accomplished many things. But one of the first things that's relevant to our topic today is he offered conclusive evidence for the clonality of human cancers in his work in the 1960s with Walter Nelson-Rees. It ties him directly to the Common Reading book. He identified that HeLa cells had actually contaminated the many cell lines that researchers were using throughout the country and had previously thought were unique.

So Dr. Gartler made a presentation at a conference, informing the scientific community of this result, that he had identified genetic markers that distinguished HeLa cells. And at that time that sort of work with genetic markers was virtually nonexistent. So, as he says, the idea that lab errors had created contamination were clearly unaccepted at the time and proven by Dr. Gartler.

When Rebecca Skloot was working on this book, she consulted with Dr. Gartler, sent him a draft, and asked that he review the published work for scientific merit. So please join me in welcoming Dr. Stanley Gartler, and if you would, share a good cougar welcome with him.

STANLEY GARTLER: Well, thank you very much for the kind introduction and the cougar welcome. And I'm very happy to be here and to talk about this book, which I think is one of the more interesting books and brings up a lot of interesting questions that we can discuss. You'll find that I don't agree with everything that's written, or for the tone of it, but it does bring up important questions.

Now the-- from the title of the book, The Immortal Life of Henrietta Lacks, it essentially is, for the title, it's the story of a cell culture which was derived from this woman in the early 1950s and turned out to be the first human permanent cell line ever derived. And as I'll indicate, there was a tremendous amount of interest in obtaining such a cell line. And because of that, it became extremely widely used.

Now, some of you-- maybe most of you-- don't even know what a cell line is, or a cell culture is. And I'll just take a second to talk about, since that's essentially what the book is about at the beginning. And that is if you take a piece of tissue from your arm, just a teeny bit of tissue in your arm, piece of skin, you put it into a flask that's sterile and has just a mixture of nutrients. In a short time, that piece of tissue will attach and cells will grow out. And for quite a period of time, cells will continue to grow out and to divide and multiply. And this is a normal cell culture.

And-- but with time, that piece of tissue, and the cells that come out from it, will stop dividing. And that's invariably what happens with a normal piece of culture tissue today, if you don't do anything special with it, and that was always the pattern that happened in the days when the HeLa cell line was derived. And so for a long time people could produce cell cultures, but they would die out. But they always-- and especially a man named George Gey, who developed the HeLa cell line-- he wanted to be able to get a permanent cell line and isolate it directly from the tumor, because he had in mind that with such a cell line isolated directly from the tumor, he might be able to find out causes of what leads this tumor and maybe even arrive at such therapy.

So at any rate, what this is about, The Immortal Life of Henrietta Lacks is a cell line that was taken well it was part of the biopsy that was taken from her when she was in the hospital in 1950. And George Gey put it in culture and a cell line arose, the first permanent, human permanent cell line. And it was quite in demand, and that's led to a great deal of the story. Now the major emphasis in this book, for those of you who have read it, is about the fact that this cell line is immortal, or it's permanent, as some people would call it.

And what they're concerned about, really, or thinking about, is what sort of uses has this cell line been put to? Did Henrietta Lacks, the origin person, originated this cell line, or she given complete counseling and did she give informed consent for taking it? And so the major emphasis of the book is on what I call the bioethics of the cell line. It-- were all things carried out properly? And then the other major reason is since the HeLa cell line became so popular and important, and used so widely, was there a significant amount of money that was made to companies or to individuals to the cell line, and should the family have received some income from this? So those are her major interests.

And I just want to call your attention to an earlier book on the cell line written by an author named Michael Gold called The Conspiracy of Cells. It was written in 1986, and again about the HeLa cell line. And the major aim, interest of the author at that time was the fact that the HeLa cell had tended to contaminate a great many other cells. So you had a horrible problem of contamination, which, by the way, is still going on in this day. And the book focuses on the career of one young scientist who decided to devote his entire life to cleaning up the question of contamination. And it's very well done, very interesting, and it brings in a lot of interesting psychology.

Just as a quick sideline, this man was very-- was not very gentle in his remarks. When he found somebody out had a contaminated cell line, he told them very, very frankly, also published it if he could. And so in a short time he wasn't very well-liked. But what he was trying to do was a very important job of trying to control the question of cell contamination.

So what I'm going to do then, in the time here, is talk about two aspects of the HeLa cell line and The Immortal Life of Henrietta Lacks is talk about the bio ethical aspects, which I think is a major interest of Rebecca Skloot in this book. But then I'm going to talk again, at the end, about the question of cross-cell contamination and what it means at the scientific level.

So this is what I just pointed out that the two main issues are, the bioethics of tissues removed at surgery, given in this specific form, and then the question of cross-culture contamination, where we go on. So since 1981, there has been at every kind of institution, whether it's a medical school or what have you, or any kind of investigative research is done, there is what's called an IRB, institutional review board. And what-- the main function of these boards are twofold. One is to make sure that somebody who is taking part in some kind of a study or an experiment is doing something that's safe, nothing is dangerous, and that their mental health is protected also. That's important.

And that has been-- I'd say most people would agree-- that these aims are achieved quite well by institutional review boards all over the country. And as I said, they were established formally in 1981. But even before 1981, and at the time when the HeLa cell was established, that was the practice at universities and medical schools, that the subject was protected physically, mentally. And probably the major thing was that the privacy, or the anonymity, of the subject was protected as well. That was a very important feature.

And so one of the main things, then, in protecting privacy is that the name of the individual who was taking part in the project, or let's say, of who was self-culture was started from, or any other sort of thing-- so the main thing is to protect that person's privacy. Now, it turned out that when George Gey, the originator of the HeLa cell-- when he realized he had found the first permanent human cell line and he knew that Henrietta Lacks, the donor of the cell line, was dying of this adenocarcinoma of the cervix-- a very serious and fatal type of a tumor-- he realized quite ahead that this was going to be an important finding, this first permanent human cell line.

And so he wanted to name the culture, actually, Henrietta Lacks. Which, even though there were no institutional review boards at that time, it was already realized that you would want to keep something like this private. You would not want to reveal the name. And so he had a number of conversations with colleagues about this, and they all cautioned against doing this, naming it Henrietta Lacks. And they felt they should give it just an anonymous type of a name. But he wouldn't listen completely, and so he ended up calling it HeLa, which are the initials of the first and second name. So that in itself, today, probably if you had a culture like that and were going to name it, and you had to go through the institutional review board, that would not be approved today.

Now, George Gey died in 1970, as you can see from here, and an obituary was written about him in Obstetrics and Gynecology by close friends of his. And in his obituary, where they talk about him, then without any-- giving any good reason, they actually reveal the name of the donor of the HeLa cell line as Henrietta Lacks. And that again-- there again was no formal institutional review board, but that would not have been listed.

So in 1971, when his obituary was published, we then real-- people realized who HeLa came from, what her full name was. And, as I said, it was going-- would be completely against custom today. And I think-- as far as I know, no one-- I shouldn't say no one knows-- but I don't know if anyone really knows why that information was revealed in this paper. But my own suspicion is that it was probably Gey's last wishes, that he felt so strongly that the-- Henrietta Lacks should get credit for this culture that he asked them to do. But I don't really know.

As a result of this obituary, the name was released. So that was the first time that the name had been released, of the donor of the HeLa cell. And that was-- and it was only with that name that Rebecca Skloot could carry out-- could write this book she did, track down family, and do this amazing job of going into this family background and interviewing these people. So without this obituary, I guess she couldn't have written her book. And I wouldn't be here talking to you, either, which may be something you might think about one way or the other. And so-- so then soon after this paper was published, there was an interest, then, in trying to find out something more about the family.

And one of the most interesting things they want to find out is what was her genotype for a particular gene? And this was for the G6PD gene, glucose 6 phosphate dehydrogenase. It's just one of the many millions of genes you have. And it had already been shown-- I showed this some years ago-- that the HeLa cell came from an individual who had the genotype of G6PD-A. So this would be [INAUDIBLE] X. And that was determined just simply from her-- from looking at that the HeLa cell culture. And so some-- a group of people wanted to know whether she was AA at both-- you know, or I should remind you, of course, that this gene is on the X chromosome.

Females have two X chromosomes. Males have one X. So all we knew from the original study that I did a long time ago was that she had the G6PD-A gene on one X chromosome. She could be-- have both A's, on each-- one A on each X, or an A on one X and a B on the other. That is B,

a heterozygote. And the question this group was particularly interested in was, if she was a heterozygote, G6PD-AB, and her tumor, we knew, was just A, then that would be compatible with the idea of the tumor arising from a single cell, which was an interesting and important idea at that time.

And so they wanted to-- in order to find this out, was she a heterozygote or was she-- just have the AA-- they had to then look at the family. So this was the first time that the family could be located because the name was revealed in that paper. And in that case, the family was looked at. And you can see that her husband was B and the two sons, who just have a single X, one was A and one was B. So that meant, then, that she was AB, or heterozygous, had an A allele on one X chromosome, a B allele on the other, and therefore she was heterozygous. And that, then, was compatible with the fact that, since the tumor is only A, that it may have started from the single cell. And there's one more thing.

So one other thing you have to know is that, in the female who has two X chromosomes, only one of these X chromosomes is expressed in each female cell. It's something called X chromosome inactivation. And each cell and its descendants express the same X. So if a tumor originated from a single cell, and it had it had two X's, but in that cell only the XA was active, then all the cells that grew out from that tumor would still be A. And then-- so if a cell has two different X-linked traits for a gene, G6PD-A on one X, G6PD-B on the other X.

A tumor originating from a single cell would be either A or B, whereas the tumor only-- the tumor only expresses both A and B if it begins from more than one cell. So that if the individuals a heterozygote, the tumor has both A and B cells in it and it starts from multiple cells. OK, that's just to show you one important point. And this work was done by this group of people. Cusick is a famous professor at Johns Hopkins, and they were the ones that were-- so that this was the first major paper after the obituary, where the family was contacted and mentioned.

Well, let me mention a couple other things at this time. So the-- so when Henrietta Lacks was in the hospital, and she was examined and they realized there was some kind of a tumor in her cervix, then a tissue sample was excised for pathology. And, as was the practice in those days at Johns Hopkins, that every time a tissue was taken at surgery, that a piece was sent to George Gey so that he could try and grow it in cell culture.

And he was particularly interested in tumors. So the tumor went to him. Now, a question that Henrietta-- or, Rebecca Skloot-- has raised in this book is, was that Henrietta Lacks properly informed about the taking of the tissue and the giving it, giving a piece to George Gey so he could form a cell culture. Well, the practice-- now at that day there was no institutional review board. Today there are. But today, I think the practice will be exactly the same. Once a person goes into the hospital and is having surgery, which he or she has agreed to, then that means that the material that's removed at surgery no longer belongs to the patient in any way.

It then is the property of the hospital for the pathologist and whoever else may be involved to carry out studies on those-- on that piece of tissue. And probably without any exception, most if

not all of the studies will have to do with the diagnosis of the patient and with some possible treatment that may be involved. So I think, in terms of Henrietta Lacks being informed about the taking of the tissue, I think that that is something that would be done today, just as well, and it was the practice in those days.

Now, as far as the cell culture goes, George Gey had-- his major aim was to try and understand how tumors came to be. The basic idea at that time was that viruses cause lots of tumors. And he thought if he could put a tumor directly in culture, he might be able to get some handle on how to deal with or treat it in some way. So I think our question that the [AUDIO OUT] even anybody is illegal. So that's something where I disagree with Ms. Skloot on this point.

Now one of the-- a point that I think important also is something about the HeLa cell and whether-- and its abnormality. It's not really a normal cell. And you might even expect or anticipate that since it's a tumor, it's not going to be normal. And there's one thing that I would criticize Skloot for is that she doesn't really emphasize the abnormal aspects of the HeLa cell. And here-- just got to show you first-- is looking at chromosomes of cells.

And here we have just the normal chromosomes, or chromosomes of a normal male and female. And these are called, are karyotypes. So here we have karyotypes of normal male, and here's a normal female. And so these are the autosomes and there's the sex chromosomes of the male, X and the Y, and two of every kind. And here is the [INAUDIBLE] [? for a ?]. So this is the normal one up here. And here's-- and so the difference, then, between the male and the female, there would be two Xs and no Y. Otherwise everything else will be the same chromosome.

And here's the karyotype of a HeLa cell. And by the way, if you look at 100 HeLa cells, it would probably be very difficult to get them all to be exactly the same and match like this, because there's so much variation going on in the formation of the HeLa chromosome. But anyway, if you would count these, you would see get close to 70. Here the correct number of [INAUDIBLE] is 46, 23 pair. Now some of them you can arrange in pairs, but many of them, you can't arrange at all. So at the karyotypic level, in terms of the number of chromosomes, the cell is quite abnormal.

And one might argue, well, the HeLa cell has been in culture for years and years, ever since the 1950s. And so is it possible that some or even maybe all of these chromosomal abnormalities occurred in culture? Well, that's a possibility. But then we don't have any way of knowing now, of course. But I should point out that at the time that Henrietta Lacks died, her tumor had already metastasized. It had spread to a lot of different parts of the body. And so from what we know at that stage, there probably were lots of chromosomal abnormalities that have already occurred. So I would say that it's very likely that most of these chromosomal abnormalities, the deviation from normal, were already there in the tumor.

Oh, the-- one point I should make with respect to the question of whether abnormalities can occur in culture. They can, of course. But if you take the-- when I started off early on, told you

about starting a cell culture from a small piece of normal tissue, you can put that in culture, and after a short while you can harvest cells and actually look at chromosomes. And if it's from a normal individual, normal piece of tissue, that culture-- karyotypically, in terms of chromosomes-- will remain normal throughout the life of the culture. So for many cell divisions, not nearly as many as the HeLa's gone through. Culture doesn't necessarily lead to chromosomal abnormalities.

One of the things which goes back a little bit is really the-- is the question of-- goes back to George Gey and the question of naming cell cultures. It shows here the HeLa cell. And this was the status of chromosomes back in 1966. And you'll see lots of names of different cell lines, Detroit Six, Minnesota E, Embryonic Lung. The great majority of them are sort of anonymous names.

They purposely put that way in order so that somebody working with it would not be able, with any ease, to trace it back to the origin of it. Now there's, like one here, there are some names here, but it turns out they aren't really related to any personal name. There's one famous one here called-- [? Chung ?] liver is not related to an individual's name. But that was the standard, and the only real difference, as I mentioned earlier, was HeLa, and that was due to the fact that George Gey wanted to give some credit to Henrietta Lacks. And I think they did, finally, in his obituary.

So I want to take you back now to-- well, let me bring up one more point before I go into a discussion of contamination, which is a question I am particularly interested in. But the-- one of the main questions that should be discussed with respect to the-- one of the main interests of the book is when the family was revealed, when we know the name, we know everyone, a question comes up now, which really is a general question about keeping privacy. Was this good or bad or indifferent for the people in the family, or for anyone else?

And of course, we'll never know what Henrietta Lacks would have wanted, whether she would have wanted to be revealed or not. I personally would not like to be remembered for a cancer cell, but who knows? On the other hand, the question then of whether there was a large amount of money or funds made, that's a very difficult one to go over completely.

I can just say that in terms of the many, many thousands, probably 100,000s of HeLa cultures that were sent to people, maybe even sold, that the great majority were sent free. George Gey sent them out always without even charging postage, I think. The American Type Culture Collection is sort of a semi-governmental agency, was set up to distribute important cell lines, and they were a nonprofit institution. So in terms of the selling of the-- maybe millions of cell lines that were sent out, I doubt if much money was made that way.

Now, in terms of things like, for example, the question of polio. In the book there is mention made that the cell line was very important in the years of polio. Well, if it was really critical to it, then probably there was a fair amount of money made somewhere, because there were huge numbers of dosages given. But the question of whether it was really critical to polio is

questionable, because the original work on the polio virus was done by a man named John Enders and his colleagues.

He did the work before HeLa cells were available, so he learned how to grow them in different ways. The Salk vaccine was produced in monkey cells. So the HeLa had some role in it. Whether it was a really critical role, I don't know. So anyway, determining whether there really is a lot of money made from something is very difficult. I personally would feel that a family is justified in getting some funds from a-- biomedical research that lead to large amounts of money. Now, not everyone is, but I think that's justified. Fine But in this case I think it'd be very, very, very difficult to find-- to determine that.

Let me go-- let me switch now, for the last 10, 15 minutes, to the question of cell contamination. Now, I got into the story a number of years ago. I was-- this was in the 1960s-- I was interested in trying to set up a genetics of human cell cultures. And any time you want to do anything in genetics, you need markers. You need hereditary differences between individuals, AB, all blood groups, the [? MN ?] blood groups, any number of things. And it turns out, unfortunately, that many of the hereditary markers that we knew of at that time were not expressed in human cell cultures. So they weren't of any value to use.

And so I finally picked up a couple that I knew I could detect in human cell culture. One was the G6PD marker that I talked about earlier, an enzyme that is present in all our tissues and which we know there's a lot of hereditary variation. And this is-- just this is G6PD-B, a slow-moving band. This is a heterozygote, which has two bands, and this is G6PD-A. So it's very easy to mark. And I think the-- this, in fact, is a marker for phosphoglucomutase, which is another hereditary variant you can tell in cell culture.

So anyway-- so I had these two markers to begin my studies with, of looking for useful hereditary variance in cell culture. And so I collected the avail-- this was 1965-- I collected the available cultures that were at the time. HeLa was one of them. And the list I just showed you before, [? Aradi ?] and [? Ristar ?] and Wish, they were also available. When I collected them, there were some 20 cell lines, all including HeLa, and it turned out that they all had exactly the same genotypes with respect to G6PD and PGM. And that wouldn't have been so terribly unusual, except that I knew they all had G6PD, G6PD-A. This is-- so they all had-- they were all the same in both the PGM and the G6PD type. But they all had G6PD-A. Every one of them had A. And I knew that G6PD-A was found only in individuals of African descent. And George Gey had told me that Henrietta Lacks was of African descent. And that was the first cell line, permanent cell line, established. And these were all permanent cell lines.

So it was clear then, to me at least, that what had happened was that George Gey had sent the HeLa cell line out to anybody who wanted it. And people had it, were growing in their labs. And then there was an interesting thing happened, that although no one had been able to get an established human cell line growing until George Gey had done it in the early 1950s, suddenly within a few years, there were a lot of different established human cell lines growing.

And these were the ones I analyzed. So it's clear to me that what had happened was there had been a contamination. People had let the HeLa cells, by sloppy techniques, grow into another thing, which, they thought they were starting a new cell line and it turned out to be HeLa. And since at that time, the people doing cell culture didn't really have much feeling for the field of genetics, they didn't think of using markers such as this to check whether their cell lines were true or not. And so they missed this.

And I wanted to tell you a little story to indicate how different scientists were at that time about such things. I had been invited to this tissue culture meeting in which I was going to present this data. And I happened to be chatting with the chairman of our department, Herschel Roman, who was a father of yeast genetics, a very experienced man in microbial genetics. And he knew I was going to a meeting. And he asked me what I was going to talk about.

And so I told him I had found that these cell lines were contaminated with the HeLa using G6PD-A to detect it and that's what I was going to talk about. And he looked at me as though I was some sort of idiot. He said, "You're going to talk about cell contamination at a scientific meeting?" He was just completely flabbergasted. And that was the difference in concept. I was a little surprised and worried. But when I got there, I realized that the people were not quite aware of this. And what it represented was a totally different attitude of how you look at your material.

Somebody in genetics microbial genetics, like Herschel Roman or anybody working in genetics, first thing you have are hereditary markers to characterize your material. And so if a contamination occurs-- which, it can always occur in it doing bacterial genetics or microbial genetics-- you can pick it up right away. But the concept of the cell cultures of the day was that they just were working with something so simple that you had to have all sorts of other markers to detect it or characterize it. It seemed to be that when they looked at it under the scope, even though to me it was a simple cell, they really could tell the difference between that cell and an amnion and this one and the other. So it was a totally different thing.

So when I presented this data, that there was not complete acceptance of it by the people. But essentially, it-- what went on. And I think what it represents, in a way, is a difference in how you look at what you're working on. And I think the major criteria that I think a lesson can come out of this is that you have to be very skeptical of whatever you're working on. Cell culture is a minor field, really, in the whole field of science, a very minor field. But no matter whether it's physics or cell culture, what have you, you tend to be-- which is natural-- be overall optimistic, overly optimistic with what you're working on, and not question is this right or wrong?

Now, surprisingly, we now come a long time since 1966. And technology is really advancing, if we can sequence the whole genome. So detecting, really detecting a particular biological organism is not very difficult, exactly, so. And yet, to this day, there are still large numbers of contaminations that are going on. Let me see if I can get this next one up. Yeah. Just this year,

this is the article in April of this year in the Wall Street Journal, of all places. They had a major article on cell culture contamination.

And of course, the main reason they would have it in the Wall Street Journal is they could point out that lots of government funds were being wasted here. But it's amazing how many mistakes were still being made when the number of markers are thousands and thousands. There's no way picking it up-- no way missing it. If you really wanted to take your culture and make sure that you knew what you were working with, it's a small fraction of your budget to have it tested by several places that test cultures to see what they are. But they aren't being done here.

And this is interesting. You know, like for example the-- in this case, they'll point out well, if your work is looking at something that's so-called basic biology, then maybe it doesn't make any difference whether you're working with a HeLa cell or with a cell from someone's liver or with a cell from the white cell. It's basic biology. But of course if you're-- think you're working with breast cancer cell lines and you're working with a cancer of a cervix, that is-- it must be horrible. And it is horrible.

But I didn't come to think that the basic idea, which I shared at one time, that if you're dealing with basic biology doesn't matter whether it's a HeLa cell or a white cell or another cell. But I think that's not true. Most of our cells in the body are different in many ways. Their DNA is the same, but what's being expressed, quite different. And so you if you're looking at basic biology, I think you have to know what cell you're looking at. A very important feature.

So I think want to save a few minutes for questions and stuff. I think to close, again, now with the main point I get out of the scientific implications of this work, and that is, you want to remain skeptical of what you're doing. You've got to ask questions about it. And we always get overconfident, I think, and I've done it all the time. Everyone has done it. But in the case of something, a rather minor field, it's just a huge amount of mistakes going on. We now have-- at the time of HeLa there was a small number of cell cultures.

Now there are thousands of cell cultures. Anybody can start one and anybody can make them permanent. At one time HeLa was fantastic because it was the first permanent cell line. Now we have techniques-- any cell line can be made permanent. So there's probably going to be a lot more cell culture contaminations occurring, unless a major effort is made to controlling that.

And I'll just close with a little quote, which I will read from Francis Bacon of the 16th century, who probably was one of the earliest to talk about skepticism. And-- that's great, well, didn't last very long. Just up-- there we go, OK. So this is, in a way, talking about skepticism, I think. If you begin with certainties, you're going to end up in doubt. And you begin with doubt, you're a little better off. Thank you very much.