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FINAL TRANSCRIPT

Narrator:	Clarence "Bud" Ryan
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Interviewed By:	Julie Kerssen
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Julie Kerssen: This is Julie Kerssen. I'm here with Dr. Bud Ryan at Washington State University on March 18, 2004. And Dr. Ryan, can you tell me what your job title is here currently?

Bud Ryan: I'm the Charlotte Martin Distinguished Professor of Biochemistry and Plant Physiology.

JK: That's quite a title. What are your main responsibilities here in that position?

BR: Well, I'm primarily research right now. Actually, I retired two years ago and then they hired me back at 40%, which is about 90% in reality. But it's to do research, and it's what I love to do. So I just keep the same research program going that I had going before and I do less teaching.

JK: You still do some teaching?

BR: A little bit. Not too much.

JK: Could you describe – we'll get into more detail later – but describe in a nutshell what your area of research is?

BR: My area is plant defense. It derives out of a discovery we made back in 1972, when we found that plants were able to sense when they were under insect attack and send messages throughout the plant to turn on defense genes to protect the plant. We've been studying that ever since.

JK: That was a big discovery…

BR: Yeah, it was important.

JK: Let me go back and talk a little bit about your background. Where are you from originally?

BR: Well, I was born in Butte, Montana, and my parents moved to Helena when I was ten years old. That was shortly before the war. And so I grew up in Helena, and I went to Carroll College in Helena. It's a small Catholic, private liberal arts college. It was a case where I had to pay my way through college. It was fairly cheap then, but when I got through at the end of four years – and I graduated in chemistry – I took a job with the Montana Highway Department for a year, just to pay off my debts, and I drove cab at night. I got married in May of that year to [Patricia Meunier], a little gal from Wolf Creek, Montana.

JK: Did you meet her in college?

BR: Well, I met her at a barn dance in Helena. So then I didn't really plan to go to graduate school. There was a woman who had graduated two years before me, [who] was at Montana State getting her Masters in Chemistry, and she kept calling my house and saying, "You've got to go to graduate school." She must have called me three or four times, and then she called one day and said, "I made an appointment for you with the chemistry department chairman, so you'd better go down and talk to him." So I did, and he offered me a job. They didn't have assistantships then, so I worked in the ag experiment station, and I worked in teaching laboratories for analytical chemistry and for a lot of freshman chemistry. And that way I got through school. [Pat and I] got married [in May and I started school in September. We] had three kids when I was in graduate school.

And then when I graduated, I had the opportunity to [join industry]. I graduated in cereal chemistry, which is the part of the part of chemistry that deals with the starch and protein in cereals. I had some job offers in the Midwest, with corn products in Chicago, and Miller Brewery in Milwaukee, and a small company in Manitowoc, Wisconsin. And at the same time, we had a new young assistant professor up at Montana State, Don Reed. He'd just [received] his degree from Oregon State. And he came [to me] one day and said [that the Oregon State Biochemistry Department was] looking for a post-doc. I really felt like I hadn't gotten as much of an education at Montana State as I really wanted – there wasn't a lot of research there. There was two of us [who] graduated that year [with] PhDs in chemistry with a biochemistry emphasis; we were the first two [from Montana State University], so we really were missing a lot and I felt I needed to learn more.

So this post-doc at Oregon State was in marine biology, marine biochemistry. They had a grant from the Office of Naval Research, and they wanted somebody to study with Dr. Tsoo King on the respiratory metabolism of the mollusk. The mollusk has this catch muscle that holds the shell together. It's one of the strongest, if not the strongest muscle [known], called the paramyosin smooth muscle. [The Oregon State University scientists] were interested in why it's so powerful and how its respiration and respiratory system worked. And so I [researched] that for two years.

JK: It sounds like quite a jump from cereals.

BR: It was. It was great, though, because I learned new [approaches] and new techniques. I was in a department that wasn't studying plants at all; it was studying animals. But I wanted to get back into plants. It was just something that I liked when I was in graduate school. So I wrote a grant, and then I wrote a professor at Berkeley and asked if I could go there to work. And he said he didn't have any room in his lab, but he called a fellow at [the U.S.] Western Regional Lab, which was down in Albany, [California], not too far away. So I called [Dr. Sig Schwimmer] and he seemed pretty excited about it. So I [and my family moved] to San Francisco, and [the U.S. Department of Agriculture] gave me a job there for three months while [I waited to] see if my grant would go through. I wasn't sure at all if it would or not.

But [another] scientist, Dr. H.K. Balls, who [had been] a former head scientist at the Enzyme Laboratory in Washington, DC; had retired from Purdue [and joined the Albany Pioneering Lab] just down the hall. He had just been awarded the first NIH grant in a USDA laboratory, and he was looking for a post-doc. So [Dr.] Schwimmer says, "Well, why don't you go talk to [Dr. Balls], because you don't know if your grant's going through or not, and this is a wonderful opportunity," because [Dr. Balls] was a pretty famous [scientist]. So I went down and talked to him, and it was pretty interesting, as we sat and talked for maybe fifteen or twenty minutes. He asked me about my background, and I told him, then he started telling me about his background. He was 71 I think at the time. And he had a wonderful background. We kept talking and it was just a pleasant time. And [finally] he said, "Well, I'll let you know tomorrow."

Then he said, "Before you go, have you got just a minute?" I said [sure]; and he says, "Well, sit down a minute." I thought, uh oh, what is this? And he said to me, "Are you lucky?" Very strange question, I thought. I sat there

thinking, wow, how do I answer this? Finally I said, "Well, what do you mean by lucky?" And he said, "[If] there are ten bottles on the shelf up there, and you're doing an experiment, and you know one of those bottles is going to work. Are you the kind of a guy that would pick up the right bottle the first time? Or would [you] go through nine of those bottles before you get to the [right] one?" And I thought, oh boy, I'm on the spot. [Laughs] I looked up and I said, "Dr. Balls, if you hire me, I'm lucky, and if you don't, I'm unlucky." And he went, "Oh!" [and slapped his knees as he said], "I'll talk to you tomorrow." And the next day, he hired me. [Laughs] That led to the discovery of the proteinase inhibitors in potatoes.

JK: That happened at that lab?

BR: That happened at that lab and changed my life. So that's kind of the history of things up to when I really started my science.

JK: We'll jump back to that point, but were you interested in science as a kid as well? Was that always something that you wanted to do?

BR: Yeah, and I don't know why that is. My dad didn't even get through grade school. His father was killed in the Butte mines when he was about twelve, so he and his brother had to go out and get jobs to take care of his mother and sister. And my mom just went through high school. But they always encouraged us to learn and go to college, and it was just a natural thing. I just was interested in science.

JK: In plants specifically, or more in chemistry?

BR: There was a program on the radio when I was a kid. We had this radio – everybody liked listening to [it], and there was a program by [DuPont] Chemical, it was called "Better Things for Better Living Through Chemistry." It told about how scientists went in the jungle and found these plants that had these chemicals in them and they brought them back and they turned out to be this or that. That was on every week or so, and that really kindled my interest in chemistry. So when I got to high school, I took chemistry. From the time I started high school, I said I'm going to be a chemist; that's what I'm going to do. And I had a great teacher in high school – Sister Evangelista. I went to a Catholic School – St. Helena. And she always liked to talk about mental gymnastics. Which, you know, used your mind to figure out things. And she had a great science class, and that kind of really got me interested.

JK: How did you get specifically interested in how chemistry applies to plants? Did that happen in graduate school?

BR: That came when I went to graduate school. I was working on the starch and protein in barley. And then we had made a finding in potatoes. Soluble material in potatoes was doing some kind of strange things, and we were trying to figure out why it was affecting the starch. It just was kind of fun to work with plants. I really didn't like killing animals or working on mice. There were some mice in a lab and I got allergic to them, so I couldn't even be in the room with them. And again, I have no explanation of why I was so interested in science or plants. It just was a natural thing for me. I'm really lucky because that doesn't happen to a lot of kids, but I just followed what was interesting to me.

JK: So you said the discovery in [19]72 changed your life?

BR: Yeah. That had a background too. When I went to work for Dr. Balls [in 1961], it wasn't on plants. It was on the digestive enzymes of animals. And that goes back into the history of science, where, in the early days, the scientists were trying to find enzymes, trying to find out what enzymes were. Kunitz and Northrop, a couple of scientists, I'm not sure where they were – Rockefeller, probably. They had found that if they [removed a fresh] pancreas out [from an animal], it didn't have very much proteolytic activity, but if [they] let it sit around for a while, it developed this huge amount of activity [and digested itself]. This is the organ that makes and secretes the enzymes that digest your proteins in your gut. So it was clear that they were making a precursor, and then the enzyme was being activated and that's what caused the increase in activity in the pancreas. So they fished out two enzymes – chymotrypsin and trypsin – and their precursors, and they won the Nobel Prize. And [they were] the only enzymes that were available [to scientists], except for an enzyme called urease that was very difficult to make and so very difficult to study. So Kunitz and Northrop were able to make gram quantities – huge quantities – of these enzymes. And actually there was a man named Worthington that worked in that lab [who] went into business and started to sell the first trypsin and chymotrypsin.

And so Dr. Balls was interested in his early days in why can trypsin and chymotrypsin chew up proteins. Is there an active site there? Or is it something about the protein? And nobody really knew this in the [19]40s. He

was trying to find an enzyme to study. And it turned out that in the Fort Dietrich laboratory, [scientists] were studying nerves and nerve gases. They found that a compound called diisopropylfluorophosphate, when [supplied to mice], it immediately killed it. And they found that it was killing [the mice] by destroying the cholinesterase enzyme, [an enzyme at nerve synapses], so it had to be happening very specifically in very tiny amounts. Cholinesterase being an esterase – that means it splits esters, which is a type of chemical. He thought, and rightly so, that if he could just find another enzyme that was an esterase, then he could purify it and then see if [the nerve gas] inhibited [the enzyme] too. Then he could label the nerve gas and find out where it's acting on the enzyme. So they tried to isolate pectinesterase from orange peels [as a model enzyme].

So Dr. Balls was looking for this esterase in orange peels and it turned out to be a horrendous job; they just couldn't purify it. He was working with a fellow [scientist] named Gene Jansen, and one day Jansen was reading [an article in The Biochemical Journal written by] a young scientist named Hans Neurath, who later became head of the biochemistry department at the University of Washington and built it into a great department. He was just a post-doc in the lab [of a scientist] named Schwert, who was his mentor. [They] had synthesized some esters [and looked] to see if they were substrates for chymotrypsin and trypsin. [The enzymes] split the esters and they published [their results]. When Jansen saw that, he said, "My gosh, trypsin and chymotrypsin are esterases, so let's do the experiment." They bought some diisopropylfluorophosphate [DFP] – and those must have been nervous days, because this stuff is a nerve gas and it's tremendously potent. They reacted chymotrypsin with DFP, and it totally knocked the enzyme out. This was the first demonstration of an active site in an enzyme. Dr. Balls [became] quite famous at that time.

Just after I went to work with him, a fellow named Floyd DeEds, who was the head of the Pharmaceutical Division of the Western Regional Lab, came in one day with a journal in [his hand] – it was the *Iowa Journal of Science*, I think – and he said, "Look, Dr. Balls, there is something in potato peels that inhibits cholinesterase." And Balls went over and said, "Potato peels and esterase, hmm." I got into the conversation; [mainly] I listened. [Dr. DeEds said], "I wonder if there's something in potato peels that would inhibit chymotrypsin," so I said, "I'll go get a potato." There was a potato section at the Western Regional Labs, [but] they didn't have a single potato. They had [processed] every one of them.

So I ran across the street and bought three Russet Burbank potatoes at a little grocery store and brought them back to the lab. We had this instrument that could measure the activity of chymotrypsin. So I scraped the peel [from a potato tuber] and ground it up in some buffer and we put it into the spinning cup, an instrument that would measure the change in pH when the esterase [substrate for the enzyme] was split. Nothing happened. Dr. Balls said, "Hmm, try it again." I scraped into the tuber and got some of the meat [under the skin] and ground it up [in buffer], and then we saw an inhibition [of the enzyme]. So I [took] just the meat itself and ground it up and it knocked the chymotrypsin flat. I diluted it and diluted it and diluted it, and it was still inhibiting the enzyme. We made some calculations; we said, "My God, a potato is jammed full of a chymotrypsin inhibitor."

Well, nobody [that we knew of] had ever seen a chymotrypsin inhibitor in any [plant tissue] before that. So I went into the literature and started looking, and I couldn't find any evidence that anyone had ever seen anything like that. So I asked [Dr. Balls] if I could try to purify it. And he said, "Have at it – it's not what I hired you for, but go ahead." I used to come in early, as we only lived about a block and a half from the Western Regional Lab on the Albany hill. I went back to Kunitz and Northrop's methods, because they had actually isolated a proteinase inhibitor from soybeans that would inhibit trypsin. So I used that method as a guide to get this inhibitor out of the potato.

[After about three months of trying to isolate the inhibitor, I came in one morning about 6:30, and I had the material precipitated. I [slowly] dissolved the material in a buffer. I was standing there looking at the early sun that was coming through the window, and [the mixture] cleared, and then all of a sudden this sheen appeared in this tube. It just got thicker and thicker and [settled] to the bottom. I looked at it [under a microscope] and there were beautiful hexagonal crystals. I thought, "My God, I crystallized this thing." I centrifuged [the crystals] and took [them] back up again, [and they] did the same thing – the crystals got bigger and more beautiful. Gene Jansen came in and I said, "Gene, look at this – I think I've crystallized the inhibitor." And he said, "Well, did you check it for protein?" And I said, "Oops, no, I didn't." And he said, "Ah, it's probably just magnesium sulfate crystals you've got there." So then I [felt] defeated. I went back and centrifuged [the crystals] again and dissolved [them in buffer, and showed that] it was protein, and it wasn't the magnesium sulfate crystals. It was the inhibitor. And then [Gene] got excited. Dr. Balls came in about 8:30 and I told him what I'd done, and he

says, "Let's go someplace and have a drink!" He was so excited. [The crystals] turned out to be [what we still call inhibitor Roman I] from potatoes.

JK: So in layman's terms, why was that such a big discovery?

BR: Well, because nobody had ever seen anything like that before. It offered the opportunity of having a protein – rather than being a substrate for chymotrypsin – was now an inhibitor. Then we could learn, just from a scientific standpoint, [something about] protein-protein interactions. By having a pure inhibitor and a pure enzyme, we'd be able to learn how those two came together, and learn something about the mechanism of enzyme action. Dr. Balls said he didn't want to study [the inhibitor after I left], he wanted to [continue to] study chymotrypsinagen [activation]. So I wrote an NIH grant [to study the inhibitor]. By then two years had gone by, and I started looking for a university where I could [begin studying] the inhibitor. I knew there was another inhibitor in [the tubers] because once the first crystals came down, a second group came down, and we [didn't study them].

So I [submitted] the grant and it was awarded, [but] I had to find a [university to accept me. The grant] was called a Career Development Award. [NIH] gave the winners of these awards five years of their own salary to go where they wanted to study. I had never been [to Washington State University, but] there was a fellow here who was head of the Ag[ricultural] Chem[istry] department. His name was Romey Legault, and he used to be a section chief at the Western Regional Lab. A local ACS meeting [was to be held at WSU] and my former boss at Oregon State was in charge of selecting speakers. So he called me and asked me, "How are things going?" and I told him about our discovery. He said, "Why don't you come and give a talk at Washington State, where we're having this meeting?" And I said, "Well, you better talk to Dr. Balls because I don't have the money, and he makes the decisions." [Dr. Balls was very positive and said], "Go on up there and give a talk." And he told me about Romey being here.

And so I gave the talk and looked around. [WSU] had hired several young biochemists at the time. The Ag Chem department was [associated with] the Biochemistry and Chemistry departments; they were [physically] all together. I told Romey about my NIH grant and he said, "Well, why don't you come here? I'll [arrange to] give you a lab in Ag Chemistry to do [the research]." I wanted to [return to] the Northwest, and Oregon State also offered me a place to do the work. I didn't want to go back to [the same] place I'd been, and it

was just kind of fun to come [to WSU to] build a program where nobody knew me and where there were young people trying to develop [their careers]. It just looked like a tremendous opportunity to come here.

JK: So what year was that when you came here?

BR: 1964. [When] I came here I started working on the mechanism of the [inhibition of chymotrypsin by the] inhibitor. While doing that I was in an ag college getting closer to plants. I was the only plant biochemist in the whole university at that time. So I started wondering, if this inhibitor is in the tuber, I wonder if it's in the rest of the plant? It has to come from someplace. We could get [true] seeds for potatoes, and I thought [that] if I just grew potatoes from a seed – and I couldn't find the inhibitor by grinding up the seed – someplace it had to show up. So I started growing little potato plants. And as the potato plants [germinated], the leaves came out and then a stolen would show up at about the second week. On the end of the stolens, of course, potato tubers would grow.

I was growing a lot of these plants and I was [using] antibodies [to check] for the level of the protein as the plants grew. I couldn't find it in the leaves right off the bat, but all of a sudden, within a day, the leaves began to make the inhibitor. The very next day, the plant would start making stolens. So I thought, well, it's a storage protein, just like in the potato [tuber]. The plant is making more [protein] than it can use [and is storing it] in the leaves. As the stolen [develops, the leaves break down] the protein and [amino acids to] the growing tuber. I thought, if that's the case, I bet if I cut off the leaves, they would continue to make inhibitor and it wouldn't [be broken down]. Well, that happened, and I didn't realize at the time, when I was cutting [the leaves off], that I was wounding the plant.

[I] published [the results] in *Nature,* and that was my first really good publication concerning the physiology of the proteinase inhibitors. I began to study all of the conditions that cause the inhibitor to be in the potato plant – spent several years at that. But I found that it was a very complex system. Then I wondered, [since] a tomato is almost the brother of the potato; in fact [with] some species that are [so close they are] called neolycopersicons, you can't tell the [species by looking]. But the tomato doesn't make tubers and doesn't make stolens. I checked tomato plants to see if the inhibitor was in the leaves and I couldn't find it there. I was growing tomato plants out in the greenhouse, and I was checking [plants in large flats, 200 plants in a flat]. All

of a sudden, there they were – the inhibitor was showing up in the [leaves of some of the plants]. And so I thought, what's going on here? Because [the plants grew] very close together, and some [were producing inhibitor protein and some weren't]. But I noticed the ones that were – after checking lots of them – [they] were the ones closest to the windows. And I thought, I'll bet [some insects or microorganisms were] coming in [the window] and chewing on those or maybe damaging the plants to make them respond.

I had a post-doc [in the lab, Terry Green, who helped study the phenomenon]. We went down and did the crucial experiments. I [approached] a neighbor [who] was growing potatoes, and I [collected some] Colorado potato beetles from [his plot – the beetles also] eat tomatoes. We [placed] the beetles on one set of tomatoes and kept the other set without any beetles. The next day the plants [attacked by the beetles] were just full of proteinase inhibitors. So the beetle, just chewing on the [leaves], very quickly caused the whole plant to respond by making proteinase inhibitors. Then I started to look at the different leaves of the plants. I let one plant grow [large] and I [made] a shield to keep the beetles on just certain lower leaves so that the upper leaves were not damaged. When the beetles chewed on the lower leaves, the upper leaves [produced the inhibitor protein] just as well as the lower leaves. That was a huge discovery, because that was the first demonstration that a plant can send signals throughout the plant [from wounded leaves] to unwounded leaves to tell them that the plant is under insect attack, [causing] the plant [to begin] making defense chemicals to ward off the insect.

JK: What do those chemicals do to the insects?

BR: Well, they make them sick. We've shown that, and others have too. But nobody knew that at the time.

JK: You knew that it was making the chemical, but you didn't know…

BR: Yeah, but we knew if humans ate raw potatoes, they'll get sick. And others had known that [animals can't eat] soybeans, unless the inhibitors in them [are denatured] by boiling. Humans can't either. So you have to get rid of the proteinase inhibitor [activity. Scientists had known] that the proteinase inhibitors were in storage organs, like beans or potatoes, but they had never realized that they could be made in the leaves as well. This meant that the plant was able to actively protect itself with a system that was [turned] off when it wasn't being attacked and then turned on to fight off attacking insects.

We reported those experiments [in the journal *Science*] in 1972. Then we began to look for the signal, and that turned out to be a huge job. Because we worked all through the later [19]70s and on into about 1980, and I think it was 1981 [before] we had isolated a [signaling] component. We could cut [the stems of] little tomato plants with a razor blade without really damaging them very much, [producing] a very low background of inhibitor. So if you take the extract of a wounded leaf and feed it to the little plant [through the cut stem] for just half an hour, and then [place the plant] in water, the little plant will turn on [proteinase inhibitor synthesis]. [This] meant that the signal was some kind of a soluble component.

We [used] little [tomato] plants [to develop] what we called a radial diffusion immunological [assay and] we could assay thousands of plants – making extracts and trying to identify the parts of the extracts by separation techniques that were responsible. We identified a piece of the cell wall, what are called pectin fragments, were turning on the defense genes in tomatoes. [At the same time], a scientist named Peter Albersheim down in Georgia was finding that pectin fragments were turning on defense genes [in plants] against microorganisms. And so we both published that at the same time, that these [fragments were defense] signals.

Then we got a big kick in the tail when about a year later a group in Scotland had radioactively labeled pectic fragments and showed that they didn't move through the plant. So we said OK, we have to go back and start over again. So through the [19]80s we got rid of all the carbohydrates [in the tomato leaf extracts], and then we started to isolate another component that we found was a very powerful [inducer of proteinase inhibitors in leaves of tomato plants]. And it wasn't until 1992 that Greg Pearce, my lead technician who was with me all these years, isolated a peptide [that has the signal]. It was an 18 amino acid peptide, and we called it systemin.

Plants had never been known before to have a peptide hormone regulate anything. It was always thought that plants were entirely different than animals in regulating genes. Animals use polypeptide hormones for just about everything – insulin, pain, development, endorphins for happiness. I mean, just about everything we do is involved with a polypeptide hormone. So [scientists] thought that plants didn't use polypeptide hormones, they just used small [organic] hormones like gibberellic acid and auxin, ethylene, [and other small hormones] to regulate everything.

So when we found this polypeptide was regulating a defense system, this was really quite new. And then other people began to be aware that polypeptide signals might be involved in [regulating plant genes]. There are about twenty [now identified] in plants that regulate [defense], development, reproduction, and probably [many other processes]. Within a year, we [had proven] that this polypeptide was a signal and showed that it could move in the plant. We also discovered the signaling system that it regulated. It causes a cascade of reactions that end up activating the genes after many, many, many steps. So systemin was just the first step in a whole series of reactions [leading to a defense response].

It was a coincidence [that] a post-doc in the lab, [Ted Farmer], had tested plants with a compound called methyl jasmonate. When he put methyl jasmonate on the plants, they turned on the same genes that turned on when [they were] wounded. I [asked] him, "Where does methyl jasmonate come from?" And he said, "There's a group in North Dakota that just figured it out." It's called the octadecanoid pathway, and [it's derived] from a fatty acid that's in the membranes of the plant called linolenic acid. [I knew of] the animal system [in which] cytokines interact [and cause] a series of reactions that cause a lipid called arachidonic acid to be released from the membranes, and it's converted to prostaglandins, which is involved in inflammation. In our system, apparently the systemin causes the release of linolenic acid from the membranes, and it's converted to methyl jasmonate, which is actually very similar in structure to prostaglandins, to turn on this defense [response].

When he [told me of the effect of methyl jasmonate, it triggered a memory of what]a post-doc in the lab, Kay Simmons, [had found]. Kay was looking at all kinds of [chemicals] that might turn on the system. And we had a lipid biochemist by the name of Pappachan Kolattukudy [in the department who] had several pure lipids that he gave us. So Kay had looked at the various sizes of lipids to see if [when] she painted them on the leaves, [they] would turn on the system. Linolenic [acid, C18 with three double bonds], turned on the system and we didn't know why. Kolattukudy had no idea, we didn't know why; we hypothesized all kinds of things. Kay worked on it for a long time, and finally we gave it up because there was no way to know what linolenic acid was doing. And so when Ted Farmer said [the methyl jasmonate] comes from linolenic acid, I said, "There's the pathway" – the linolenic [acid was connected] to methyl jasmonate [and was] turning on the system. So that

really opened up the whole thing. We had not only the polypeptide that was the defense signal, but we had the signaling pathway.

So that was a big time in the laboratory. Since then we've been isolating other polypeptides and looking to see how the polypeptides interact with cells. About 2001, Justin Scheer – who [received his degree] from the same little college in Helena that I did – [joined my group] as a graduate student, and he isolated the receptor for systemin. So now we had the polypeptide, the receptor, and the signaling pathway, and now we're looking [for other signaling peptides]. We've found that there are other [peptides] that act in a similar fashion. The systemin [peptide was only found] in the Solanaceae family, and in fact only in certain [species] of the Solanaceae family, so it didn't look like systemin itself was something that was found [widely] in plant [species]. But now Greg Pearce has isolated some [peptides] that are different in structure [than systemin] but still have some similarities from other plant species. So our goal right now is to see if these polypeptides might be in [many species] of plants and acting as signals for defense. Because now that [we have those peptides] identified, and the [systemin] receptor identified, we can now be thinking about using [their genes] to improve the ability of plants to defend against insects and pathogens, [either] by selecting for those genes and breeding plants that will respond [better, or] eventually [adding] these genes to plants in order to amplify the system [by increasing the] signal [or adding] more receptor to give the plants a better chance to defend themselves.

JK: You're starting to get there, but maybe you can talk a little about the applications.

BR: We've done two types of experiments. We can put the inhibitor [genes] themselves into plants and express them at high levels all the time. And we know that those plants are defended [better] against certain insects, like Manduca sexta larvae. And we know [that they are better defended] against spider mites and thrips. But we're pretty limited here in what we can do in that regard; others have done the work with the thrips and the spider mites. We found that the [peptide] wasn't synthesized by itself – it came from a much larger protein and later was clipped down into the active signal. That's the way virtually every hormone in our systems work – they're made as precursors, like the proinsulin, and then when it's activated it becomes insulin. And like endorphins – there are several endorphins in a precursor molecule and then upon stimulation, that molecule gets broken down into these small

peptides that stimulate the nervous system. And so we knew [when we got] the gene for systemin, we got a big gene, and we could see that systemin was [produced from a larger protein].

We put the big gene back into the tomato plant under what [is called] a constitutive promoter, a promoter that turns [the gene] on all the time, not just when the plant is wounded. In these plants, the gene is [expressed at high levels], and if you look for the messenger RNA and the protein, you find them there. We thought [that this would produce] a lot more signal when the insect bit the plant, and that [we would] get a lot better [defense] response. But it's like so many experiments – it didn't turn out that way. When we put this gene into the tomato plants, it was processed abnormally and the tomato plants' [defense response was] turned on from the time that they were small to the time that they were big. And when they [grew, they produced] very large quantities of the defense [protein]. These [plants have a better] defense against insects than just putting in specific proteinase inhibitors, because what you're doing is turning on all of the defense responses – even some that we don't know about, probably. We could only put prosystemin into a limited number of Solanaceae [species] like potato and tomato. We couldn't put it into like a bean plant, [for example], because there's no systemin receptor there to turn the system on.

We're now looking at other species, in order to get those [signal] precursor [genes from them] and to see if we can put those genes into plants and turn on their defense genes all the time. The key to it is to get those [peptides] and their precursors, because they're the real key to turning on [the defense responses], instead of just turning on this or turning on that, individually. We can [perhaps] raise the defense responses of these plants, and then we can start looking for plants that respond [even] better. I think as a genetic tool, it's going to really be valuable from [a traditional breeding standpoint] as well as from the genetic engineering aspect.

JK: So the idea is that if the plants are creating their own defense, then you need fewer pesticides?

BR: Absolutely. I think there will be a cost to this because I think originally when nature developed the wound inducible response, it's because these plants were growing in a place where they weren't getting a lot of nutrients, and if they turned on defense genes all the time, it would make them less able to defend against, say, microorganisms. So I think they're going to find that in

the field, there probably will be some cost to this in terms of yield – maybe a fraction of a percent, or maybe a few percent. But on the other hand, there has to be tradeoffs. Either you put something in [plants] that's maybe going to cost you a little bit on yield and is safe for the environment, or else you're going to have to spray very costly chemicals on the plants, which is good for their protection, but it's not good often for the environment.

JK: So you use genetic engineering techniques in your work; have you encountered criticism for that from anyone?

BR: I haven't. Nobody's really come after me because none of my genes are out in the field yet. I'm sure if they were out there they would be criticized. But a lot of the criticism now is because of the potency of the genes that are in the transgenic plants. Like the BT toxin is so powerful – it just kills all the insects. So specific genes are being put into plants now because they're economically feasible, and they're so powerful. But I think that eventually, we're going to have to get back to learning more about how the plant protects itself, and to start using those natural systems in order to beef up the plant's ability to protect, rather than the specific genes. But right now the specific genes are the ones that are making money for companies. The people who are interested in our [research] are underdeveloped countries, and these are the people who aren't concerned about making a lot of money for a company. All they want to do is get a better yield for their crops. And so most of the interest on the proteinase inhibitors has come from places like China and India where they have large populations, and actually there are these genes that are in crops in those countries. But as far as the U.S. is concerned, it might be a while before that happens.

JK: So you clearly believe in the promise of genetic engineering.

BR: Absolutely.

JK: What would you say to people who are apprehensive about the whole idea?

BR: Well, I think we're all apprehensive because you can't just go in [blindly]. I'm not one of these people [who say] genetic engineering is the only way to go. I think genetic engineering offers a wonderful promise if it's done correctly. And I think each one of these genes that goes [into plants] has to be tested. We have the safest food in the world, and it's because we have

the USDA that monitors this food and [ensures that it's] good and healthy. They have to monitor these new crops as they come in, and when they do, [if] they find that [they] are good [and safe, then they] can be grown for food.

I think the danger comes where these crops can outcross and get into the natural population. So you don't want to take transgenic potatoes into Peru, for example. But more has to be learned about that. There hasn't been a catastrophe so far, and there's a lot of [transgenic plants] out there. I think people are still learning, people are still testing. It's a slow process. I think the kind of thing that we're doing is probably ten years down the road or more because of the slow process. But we're building a library of information that's going to be available when the time comes that it becomes acceptable and people can see that it's going to be useful in improving crop productivity.

I think it's really important for fundamental [researchers] to understand what plants are all about. We would never have known that plants have [peptide signals] in them unless we just kind of followed incrementally questions about what's going on and [asking], why the plants [are] reacting [the way they do]. I thought when we first saw in the greenhouse that [when] we put an insect on plant and the plant turned on its defenses, "What a simple system." But I'll tell you, it's one of the most complex biochemical systems I've ever seen. [Laughs] We still don't know [a lot], because there are so many facets to it and it's involved with different organelles in the plant – it's involved with transporting different chemicals, packaging different chemicals. It's just amazing, the complexity of the evolution of that system that must have taken place over the past millions of years. It's so close in its basic mechanism to the animal inflammatory response that I'm convinced that we're going to find some variant of this every place we look. We have to look and keep our eyes open for those variants in order to find them.

JK: Let's talk a little bit more about what you've been doing here. You spend a lot of time in the lab, obviously, and you supervise grad students and post-docs, and you're also teaching?

BR: Well, not very much teaching. Through the years I've taught. We don't have a teaching function in IBC [Institute of Biological Chemistry] because IBC came out of [a non-teaching department]. Remember when I told you [about when] I came here, I was in the Ag Chemistry department? Well, the Ag Chemistry department was a service department – it did a lot service work for pesticide [analyses]. Companies began to take over [that function] and it

became very expensive [for our department] to try to establish pesticide [registration] for a farmer.

JK: So it was more applied research?

BR: Yeah, it was in fact almost all applied. So I used to talk to the chairman about that – what are we going to do with this department? Chemistry wanted the budget and Biochemistry wanted the budget. But the budget came out of [the College of] Agriculture. Those two departments were in [the College of] Sciences and Arts, and I was the only plant biochemist on campus. So we decided maybe there should be a stronger biochemistry presence in agriculture; this would really be very good for WSU into the future because that's the future [of agriculture].

[My] chairman, [Romey Legault], convinced the dean that this was what we really ought to do, that we really ought to be [physically located] in agriculture, and that we really ought to replace the applied people [in the department] with fundamental biochemists as they retired. This building was being built [for agricultural research] in 1970; that was just six years after I came here. We had [just] hired Pappachan Kolattukudy from the Ag Experiment Station in Connecticut – he had a wonderful program in plant lipids. So in [19]70 the dean said, "We're building this building and you're going to get the top floor of it." And of course that upset a lot of people in ag because they thought [it was their space]. It was a major decision that [Dean Madson] made.

So each time one of the applied people retired we'd hire another plant biochemist, and so after a few years we had six or seven plant biochemists. The name of the department didn't fit anymore because all the applied people were gone, so we changed the name to the Institute of Biological Chemistry in 1980 – [it] took ten years. It's built up since then. Now we have ten faculty members, and we bring in a huge amount of grant money. There's 150 people now in the institute, and it's all supported pretty much by grant money, although the College of Ag is a very important source of our support. They've been very supportive over the years, right from the very beginning.

JK: So your work day now – do you come in mostly and spend all day in the lab?

BR: Well, I'd like to. That was my thought. But it seems that I spend a lot of time in my office. I try to get out in the lab once in a while, but it's really hard

and I've kind of lost touch [with technologies] in the areas that are really moving in molecular biology. So when I go in the lab I do some of the things I know how to do and I can still do some of those things [pretty well].

JK: So when you work in your office are you reading or…

BR: Well, I try to read. I spend a lot of my time just talking with the people in the lab. We just talk a lot about our research, where it's going and focusing, [about] what's important, because we're small now. We were up to fourteen about five years ago, and now I'm down to five. We're [soon] going to be up to six. I have three people coming in this year – a visiting professor from Japan and another from Taiwan and a graduate student from Thailand – so we're going to get a little bigger. But I really need more people because Greg Pearce is a magician; he just keeps coming up with more of these peptides, faster than we can keep up with him. We have to get people in here to look for the receptors, to get those genes and get them back into plants and look at the ultrastructure of [the plants to see where they reside]. And so I spend a lot of time [discussing]. I guess it comes with the territory, but it seems like I'm writing an awful lot of letters and reviewing a lot of candidates for promotion for other universities. And I do a lot of editing for the *Proceedings of the National Academy of Science* and other journals, and try to really keep up with what's going on [in other labs] so that we can stay at the forefront of this field. And I write. I don't know how I managed to write before I retired, because I'm spending a lot more time on the papers now, and I wish I could have earlier, but it seems like these things take up a huge amount of time.

JK: So how often do you publish things?

BR: We had ten publications last year. We had eight the year before, and I think since I've retired we're averaging about eight a year. It's because so much has been coming along and the people I have have been so productive. I know that's going to drop this year to maybe five. But we do publish a lot. And last year, for example, I was invited to write three articles for encyclopedias – Encyclopedia of Hormones, Encyclopedia of Plants, encyclopedia of something else. And I have two reviews on my desk right now that people want to know about systemin and they want to see up-to-date reviews. I should be writing more of those for things like *Current Opinions in Plant Science*, but there just isn't that many hours in the day.

And I do try to take a little more time off. I have two grandchildren and we like to spend a lot of time with them – they come up and spend time with us. And I try to do a little more golfing, and I love to fish. I grew up fishing in Montana. Last year I got fishing once, so I'd like to do a little bit more of that. I started ice skating with my wife in the mornings – [taking] ice skating lessons on Saturday and we go ice skating three days a week before we go to work in wintertime. So I'm doing a lot more things. I don't feel like I have to go home every night and spend all night reading.

JK: Can you talk about a challenge that you've faced specific to what you do?

BR: Well, through the years there's been some real challenges, right from the very start. I used to try to convince people, even before I did the proteinase inhibitor work in the plants, that the proteinase inhibitors were probably in plants to protect them against insects and microorganisms. The people in the proteinase inhibitor field were all [working] on animal systems. They [didn't] believe it; they just didn't believe it. And that was kind of hard to take.

I remember once even before that, one real challenge was that we had made a derivative of chymotrypsin and we were trying to study how chymotrypsin came together with the inhibitors. There was a fellow from Purdue who had come up with a mechanism, and everybody accepted that mechanism, and every year we'd go to these proteinase inhibitor meetings and that's what people [believed]. Well we had changed one of the amino acids in the active site of chymotrypsin, which killed the enzyme, and when we reacted it with the inhibitor it reacted even better than the active enzyme. That totally was against dogma. And I went to a meeting in, I think it was Atlantic City – this is a long time ago – and the fellow that was the leading proponent of this other mechanism, I met him at a cocktail party. He told me I should quit working in this area because he thought I was wrong and he thought that the work I was doing was wrong.

Within a month, [Robert] Huber from [near] Munich, who was a crystallographer, called and asked if I would send him that modified enzyme. I sent it to him and he reacted it with the inhibitor and did the crystal structure of it. I got this really excited letter saying the gamma oxygen is gone – that was what we thought was gone, and he proved it. What that did was really change the whole idea of the mechanism – [it] didn't involve that oxygen.

Actually Huber won the Nobel Prize a few years later for a different project. So it was really nice to [collaborate with] somebody of that caliber. He invited me to Germany and took me to dinner at his house with this group and toasted me. He said, "I didn't believe you either until you sent me that material and I did the experiment." [Laughs] So that was really pretty encouraging.

The other challenge was really, I think, more serious. There was a woman in England who became a competitor, and also a group at the Max Planck Institute. Some of these groups have so much money and so many people that they look around for people who have made discoveries and then they jump on [their projects]. This woman came up with this data that suggested that systemin wasn't the wound signal at all; it was an electrical signal. And she really convinced a lot of people of this. I reviewed the paper in *Nature* and I said the methodology is wrong. I could see that she wasn't using good assays. Anyway, she dogged [the editor] until he published this paper. It got half a page in the *New York Times*, and then the Germans picked up on it, and then a guy in Nebraska picked up on it. I was walking around [battered] for a year, I was getting people in the audience really giving me a hard time because I wasn't buying this electrical phenomenon.

And we just kept going. I said, it just doesn't work; we have the data. I'm not going to go out there [and confront anyone] – these people have got to realize it themselves. They would never refute that [data] until about three years ago, the guy that worked with this woman in England in one sentence [in an obscure article] said [that they] don't believe that anymore. It really took the emphasis off of my work for a while. That's the challenge of it – you believe in what you're doing, you believe in yourself and are convinced that your work is good and that your data is good, and you just have to work through those things and not let that kind of [nonsense] influence you.

PART II: Tour of Facilities

[tour begins in laboratory]

BR: [These are] HPLC [instruments] and they're not new, they're pretty old, but boy they've been just key instruments in this research.

JK: What's HPLC?

BR: They separate proteins. You don't need very much material for them. Actually you can gear them up, but when you're working on something like these polypeptides that are there in such small quantities, you couldn't do it without this sort of instrumentation. There's a lot more modern types, but these are just the basic workhorses.

JK: This is where a lot of your polypeptide work was done?

BR: This is where it was all done, right here, [by Greg Pearce].

[Location change]

BR: This room was built when we got into the area of molecular biology, where we had to have tissue cultures to transform plants. These are typical transformed plants of various kinds. Several groups from IBC use this.

JK: So what are these plants doing here?

BR: They're grown with different genes inserted in them to see if they will grow, and see what the phenotypes might be, see how the gene is affecting growth and development.

JK: So these are all genetically modified.

BR: I think everything in here is genetically modified, except they'll have controls that aren't.

Over here – [this is] kind of messy. More recently, we've been using tissue culture to assay for the [peptides]. Instead of using intact plants we use the tissue cultures. You can [remove] a piece of the plant and put it into a defined medium, they'll grow like yeast instead of growing like a plant. Then we can use these to assay for our [peptides], and it's much quicker and much more reliable even than the plant itself. So being able to grow these has really simplified our research.

JK: The machines are just mixing everything up?

BR: They just keep them aerated, keep the oxygen in there. Pretty simple stuff.

[location change]

BR: We start our tomato plants here. In the old days, this whole [place] would be full, but [now] we're not using so many plants. Like I say, we're using more tissue cultures. [The greenhouse staff] get them started and then we bring them in here. You can see they're growing. And then there's some more over here that are already [bigger].

JK: So again, these are just different, seeing what grows and what works?

BR: Well, no. We usually grow them because we're going to be testing them for the hormone. Once we get something isolated, then we go back to the plant and make sure that it turns on the defense response.

JK: OK. So these are just standard plants…

BR: These are just tomato and tobacco.

Somebody's got things growing in here.

JK: So are these…

BR: Pretty well controlled – day length, everything, and they're fertilized very specifically with commercial fertilizer.

JK: So if you're trying to grow things more carefully than in a greenhouse, you use these?

BR: Yeah, this is all disease free and insect free here.

JK: What are these called?

BR: Growth chambers. This has really been a nice facility, and we have another [as well]. I'll show you the building, we can walk in there; we have another set of big growth chambers that we use also.

[tour moves to greenhouses]

BR: Last year we had some transgenic potatoes and we had to grow them [here] – in fact, we're growing some in large pots to get the tubers. You can't grow these [easily] in a growth chamber; it's just impossible to have a growth chamber that big. I don't know who all these belong to. Probably Norm Lewis; he's studying lignin formation. Some really pretty plants here, isn't there?

JK: Yeah, lots of different things.

So are the different greenhouses kept at different temperatures or anything?

BR: I don't think they can control that so much except by just blowing air in and out.

These plants all look they're pretty warm climate plants.

[location change]

BR: These are Arabidopsis. They're the model plant [for our work]. They're the smallest genome in the plant kingdom and the genome has been sequenced, so we know just about every gene that there is in these plants. So they make a wonderful plant for people to study just about everything. If you're looking to see what effect a certain gene has, then this is the plant, because it can be grown very quickly. It's a weed actually. Within a [few] weeks you can get a plant, get your data, and toss it out. They're probably just getting seed here.

[location change]

BR: …[nitrogen] fixation in alfalfa. They have different varieties that they're studying. This is the Arabidopsis again. See the little flowers? They are in beautiful shape. We have a wonderful greenhouse group here that just takes care of our plants in unbelievably good fashion. Some of our stuff is probably back here.

Dr. Croteau studies terpine metabolism in conifers, and he also I think without a doubt is further along in getting the enzymes to make Taxol more than anybody else. And these are ewes where the Taxol was first discovered.

There's about thirteen or fourteen steps, and he's got almost every enzyme identified.

Now we finally get back into some of mine. These are some of my plants right here. These plants have got a gene in them that they will be able to visualize because it has a reporter gene on it. So these plants are transformed with this [gene] called GFP, green fluorescent protein. And when that's expressed you can see it visually with UV light.

We used to work with tomato plants like that and now we can work with these. They're called, I think, either Tiny Toms or Ultra Toms or something. They have a mutation in them. Those are perfectly normal tomatoes except for this mutation that makes them grow small. They grow very fast. It's like the Arabidopsis – you can transform them easily, you can get the plants back, you can get seeds from them and get the second generation much faster with these. Micro Toms [is the correct name]. See, you get lots of seeds from them. And so again, these are transformed with various genes. Now this is our basic tomato line here called Castlemart II.

But I don't see our potatoes. They're supposed to be out here somewhere.

[location change]

BR: This is the rest of our facilities here. When we [first] had the greenhouse down here, we just had the one. Then we were able to get a couple more next to it, and we ran out of growth chamber space. Then we got a grant and we were able to build this facility, and then ran out of space again. We built that large greenhouse over there; I don't know how long that's going to last us. We do have the land behind that, so we can build some more if we need to.

JK: Are you running out of space again?

BR: Yeah. You can see, just about everything down here is getting full.

JK: This building has the growth chamber things like we saw in the other building?

BR: Yeah, except these are nicer.

JK: Have there been a lot of changes in technology since you started?

BR: Oh, it's all changed; huge change in instrumentation. When I came here the HPLC was just had been invented and the separation techniques for proteins were all just being really developed, electrophoresis and all these Sephadex ion exchange things – this was all just in a developmental stage during the [19]60s.

JK: Does that change what you do, or just how you do it?

BR: How we do it; it makes it a lot easier. When we first started, say in the late [19]70s, really studying the system, if somebody had told me that by 1984 we would have the gene for the proteinase inhibitors identified, and by the late [19]80s we'd have it in plants, expressed, I would have never believed that. Never believed that. And now it's just a piece of cake.

I had to get permission to plant those transgenic potatoes of ours last year. So this field from here on down is the first transgenic field on WSU's main campus. But unfortunately we got them in late and they hardly grew, so it's kind of a bust.

JK: Was it a problem to get permission to do it? Was it a big deal?

BR: Well no, it wasn't, they made it easy. It was just really simple. The people there were just so helpful, it was really good.

[location change]

BR: This is the arabidopsis plants again. Probably Dr. Browse's.

JK: Looks a lot different – big leaves.

BR: They are probably mutant plants, they're probably transformed plants. Or it might be the conditions in there. I don't know.

That's rice. That's Dr. Okita's.

We're photographing your plants.

These are also Dr. Okita's.

Looks like lots of rice. More rice. I don't think any of my stuff is in here. I don't know what that is. Some kind of a conifer?

Peppermint, all kinds of mints. Peppermint.

JK: So these can all be very specifically programmed, it looks like.

[location change]

BR: That's a big USDA greenhouse up there.

JK: It's huge.

BR: Wheat Commission built that.

JK: This stuff out here, is that just décor or are they…

BR: No, they're studying it. That's new. See that, I think those are ewes, part of Rod Croteau's stuff, and this is probably part of Norm Lewis' stuff. But we just keep growing. Every time I come down here, I see something new.

JK: What do you see as the role of science in agriculture?

BR: The role? Well, to provide fundamental information to develop healthy crops. I think it's just that simple, because there wouldn't be any other reason to [pursue it]. Except [that] some of the crops are being developed to provide [chemical] intermediates. For example, if you can transform a plant to make a specific chemical, [when] that chemical is so complex that it's [too] expensive to make in a laboratory. Plants become really, really important in that respect. The flower industry has used transformed plants a lot in order to develop new flower colors and things like that. There's a [professor] here on campus who's developing a better barley variety that doesn't have certain carbohydrates in it. So in the malting industry, they get this haze, and he's developed [a new] barley [variety]. He used to be the head of the Carlsberg Lab in Copenhagen. They force you to retire over there at 65, so he came here to do his work. He's involved with that, and he's got some really great results. Rod Croteau is involved with the hop industry, for example. He showed from his fundamental research that you can get certain compounds to be in the hops if you water at a certain time, because you have to avoid water

stress or overwatering and underwatering. They gave him an award for that. So [plant research has] either a direct effect on say, breeding programs, or an effect on processing of plants [for] foods or pharmaceuticals or other raw materials. I think that [diversity is] really the great [thing].

JK: I remember reading that some of your discoveries might get turned into appetite suppressants or…

BR: Oh, yeah, I don't even think of my own stuff. The inhibitors [that we discovered] are appetite suppressants, and I think that's one of the reasons that they're in these plants. We've been working with a company in Des Moines, Iowa. They found that if a human takes 15 milligrams – that's just a little bit, one pill – 20 minutes before they eat, it suppresses their desire to eat. Fifteen milligrams, very powerful, and that made me think. We've never studied the effects on insects' [appetites]. I'm going to do those experiments. One experiment I'm going to do is to take some defined media, get these insects growing on it and then put the inhibitor into the medium and let them eat it for maybe two or three hours; then put them on a plant and then see if just that alone doesn't depress their appetite. Because they really devour a plant in a hurry. So maybe that's one of the things that's happening there.

And then we're working with [a scientist] here on campus [on an aspect of carcinogenesis]. It's been known for years [from] some work I did with people at Harvard and at NYU, showing that [potato] inhibitors block carcinogenesis in [human tissue] cultures. They culture the cells and they put a carcinogen on them, or a tumor promoter. You can actually see [the cells] turn carcinogenic. If you put inhibitors on them, just briefly, they don't turn carcinogenic if you hit them with UVB or x-rays. I did some work a couple years ago with a fellow at the Hormel [Institute]; I sent him the inhibitors, and he found that they block a transcription factor [involved with the early stages of cancer]. He put [the inhibitors] on these cells and then measured this factor that's regulating the carcinogenisis – it blocked that. So now we're seeing if we can put the inhibitors into a skin cream, to see if it would go into the skin. If it does, it would make a tremendous difference in the protection against aging and sunlight, so we're really excited about that. In fact, [a representative of] Kemin [Industries from Des Moines, Iowa] was just here [a few] days ago to talk about that. They're giving me some money [to do the research].

But you see, those things are just spin-offs. Total spin-offs. And here it isn't agriculture that's using my stuff, it's human nutrition and human health. So you never know when you do [research how it will turn out]. Plants are an amazing source of chemicals for pharmacies and for health and to protect people. So yeah, these are things that just spin off.

JK: So what other directions – you were saying you're still trying to isolate the different polypeptides in the plants?

BR: Yes. We're looking at Arabidopsis right now and we found some indication [the defense peptide signals] might be there. If they're there, then we can go into things like wheat and rice – things that are really important. We have a woman coming from Thailand that's going to be looking at sweet potatoes and at the latex of the rubber plant. You have to really solidify and understand the system as a model system before you start [looking at other plants], and that's what I meant by focusing. You know, we could have started looking for these [peptides everywhere, but then we could] get lost. So if you can do [the result] in a single plant, then you really understand the system, and when you go to the next plant, you really feel confident when you see something [now, then] that that's the way [it is], that this is what you've got. It's time consuming incrementally.

JK: Do you feel like that's the direction that you're going in the future with research, continuing to solidify the knowledge of the plants and then see if other plants fit that system?

BR: That's right. [Peptide signals]. That's [our whole focus]. But the main thing is, it's just a fun thing to do. I can't think of another profession that's so rewarding and so much fun.

JK: Why is it rewarding for you?

BR: Oh man, it's like hitting a home run when you see these things happen. I mean, you realize that nobody's ever seen this before; you've discovered something that might be useful to mankind and it just drives you all the time. It drives a lot of people. I think most scientists feel an obligation to society. I've had a fantastic life, and the public has paid for that. People, even fellow scientists, don't really grasp that – that Joe Citizen is out there paying his taxes so that I can have fun finding new things [that might be useful to society].

JK: And who benefits from what you do.

BR: Well, I hope so and I think that's [true]. If it wasn't I'd quit right now, because I wouldn't want to take advantage of that. But when you really stop to think about it, that's the bottom line – society allows you to do these things and it's incredible.

[break in taping]

[It's nice that we] have these facilities now. I didn't even have a growth chamber when I started.

JK: Really.

BR: I had to borrow one. A guy from the USDA [was given] some money to buy a new one because his old one wasn't good enough, and he gave it to me. People just didn't understand where we were going, and it was hard to justify giving [me] that much money. But then as each one of us kicks in, then it becomes pretty obvious [to granting agencies] that a lot of people are doing a lot of [new] things, so then we can get funds to build a greenhouse like this.

JK: The program's definitely expanded.

[break in taping]

Is this where someone would come who wants to learn about what you are doing? I mean, are you kind of the person doing the most of that sort of polypeptide work?

BR: I think I've been the only [one], as far as I know. Nobody else has really [developed a program on peptide discovery]. There are people who are trying to use the genomics approaches, but they haven't been successful. It's just too hard. I mean, these are little tiny genes, and how do you know if they're doing anything without a system.

[break in taping]

So, yeah, I would like to think there's a future [in this type of research], but it's not so fashionable as molecular biology, per se, or genomics, and kids want to go where's there's fashion.

JK: Why is it more fashionable – just because it's newer?

BR: Because there's jobs, and that's where you can publish. There's a lot of really great people working in that area [and the kids go to] at major universities, so you can't blame them. A lot of our kids come [here from overseas].

JK: So have a lot of your students gone on to be professors?

BR: Oh yeah. One is a professor in Lausanne, Switzerland, and one is an associate professor at Michigan State; one is a full professor at Bowling Green, another at Michigan State in biochemistry, one is in the plant research labs. I have a professor down at UC Riverside, one in Hawaii. There's quite a few in industry, quite a number in agriculture.

JK: That was my next question, if someone left and went [to work for industry].

BR: Yeah, Alex's mom, and the group leader.

[break in taping]

JK: If there was a kid starting out today, say a high school kid, who wanted to go into what you're doing, how would you tell them to prepare?

BR: I would tell any kid who wanted to get into science, even [while still] a high school student, if they are around a university, go start working in a lab, because we love to have those kids in the lab. It's just really uplifting to have young, enthusiastic kids [learning new things]. When they get into college, they should get into a laboratory and do undergraduate research, or even get in and do some research and get paid – you know, a lot of them can get paid under, what do they call it, this student help…

JK: Work-study?

BR: Yeah, work-study. The main thing is to get into a lab. But for some reason, a lot of kids just don't do it. They don't realize what fun it is. The kids who come in and start doing this stuff, they're bright-eyed and bushy-tailed and excited. That's how you do it, is just get them in there and get them experience. The excitement of science is just there for them to find. It's just really too bad that some of the kids, especially bright kids, don't take the time to go into a lab and spend, even if it's a couple hours a day, a few hours a week. That's how it works.

JK: What do you think the future looks like for the science field? Is it a good field to go into for kids? Is there a lot of opportunity?

BR: Yeah, there's a lot of opportunity. I think there'll be more, especially as this recession that we've been in [comes to an end] and the industry starts to hire again, and money gets back into these industries. Because during this lull, there's a huge amount of information that's been gleaned, both at the universities and in companies, that really needs now to be put to use. And there's opportunities. I have a diagram that I saw a fellow from Monsanto draw one time, and I kind of filled it in, but it goes from fundamental science up at the top, where brand new knowledge is being [discovered], where nobody's ever seen [what's happening] before, all the way down to the farmer, and there's room for bright minds in every single aspect. You don't have to be a genius to be [at the top of the list]; there are geniuses [at the applied level] just as much. If a person could just get in [the labs to] see and understand [the research], the opportunities are just unlimited, [especially], I think, for good people who are willing to work.

JK: Thank you, this was wonderful.

BR: Thanks to you. This has been a lot of fun.

END OF VIDEOTAPE

END OF INTERVIEW OF BUD RYAN ON MARCH 18, 2004