Interview with Ronald Mason, Ph.D.

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RM = Ronald Mason, interviewee
JM = John Maruca, interviewer

RM: Hello, I'm Ron Mason. I'm principal investigator of the Free Radical Biology Group at the NIEHS.

JM: Well, Ron, thank you very much for joining us today and helping us with our project. Have you always been interested in science?

RM: I collected rocks and minerals as a boy, and the books had the chemical empirical formulas. So, I became aware of the periodic table quite early, and it probably started from there.

JM: Were you studying in high school and college? Tell us a little bit about your academic background then.

RM: I was actually a pre-med major when I first went to college in 1962. I'm dyslexic, which means I can't spell, and I have trouble pronouncing words, especially foreign words. So, the challenge of naming all the veins and arteries in the fetal pig, which are in Latin, was well beyond my capability. And I got a C in the pre-med biology and decided that not only was I not good at it, but it was boring.

So, I switched to a chemistry major, because I was doing very well in chemistry, which was also taken at the same time. And I still maintained an interest in biochemistry. I took a semester of biochemistry, one of the few electives I was allowed. We almost had no electives then. I did that my senior year. I applied to three graduate schools: The University of Wisconsin at Madison, Caltech, and Harvard. Harvard was a joint chemistry-biology program of some kind. They didn't accept me, but Caltech and Madison did. Madison offered me a p-chem TA-ship [teaching assistantship in physical chemistry]. Caltech offered me a TA ship teaching their freshmen. Why at the time I thought would be a bit intimidating. I'm probably smarter than I thought I was at that time. In retrospect, it wouldn't have been a problem, but I went with the p-chem TA-ship. I love physical chemistry.

And in that lab, there was an experiment, called electron spin resonance, which is basically a twin of magnetic resonance imaging or NMR, except it is specific for unpaired electrons. Unpaired electron is what defines a free radical. So, all free radicals have an odd number of electrons. So, one electron is unpaired, and its spin is detected by this ESR instrument. So, I was trained in that in graduate school, did actually single crystal ESR. I postdoc for a man named, Jack Freed at Cornell. And he, even then, this would have been '71/'72, he was the most imminent ESR spectroscopist in the world. And he still is, after 50 some years. I was supported by an NIH postdoctoral fellowship. It didn't have much biological content, but I was awarded it anyway for 22 months. At the end of the 22 months, there were no jobs in chemistry and physics.

[President] Kennedy had got us to the moon. There was the Great Society, the Vietnam war, and Nixon wanted to outdo Kennedy and declare war on cancer, because he thought it was an engineering project, in which it was not, obviously. War's still going on, so there was no opportunity in chemistry or physics. My wife typed up, maybe 100 letters, and I applied to 100 schools. I didn't get a single interview, but I still had some interests in free radicals and ESR as applied to biology. And one of the former graduate students of this Jack Freed worked for Varian, which was the American company that made ESR's. And he knew of a Chief of Clinical Pharmacology at a VA in Minneapolis, who had bought an ESR, but knew he had to have somebody that knew what to do with it and that I was available for that position.

So, I took that position at the VA hospital, and that was a very fortuitous move. I was hired to do one thing, but he handed me a review article on drug metabolism. And it described an enzyme named nitroreductase. Many nitrile compounds were known to be reduced, and it was thought that that gave mechanism of action and also toxicity. Well, I figured that there was a radical form in that process, and that was totally unexpected. And I remember very clearly this Jordan Holtzman, had four advanced degrees from the University of Chicago, looks at this ESR spectrum and he says, "Well, how do you know that's nitrobenzene anion radical?" And I realized that in the king of the blind, the one-eyed man is king. So, I kind of took over free radical metabolism in North America.

This work brought me to the attention of a Colin Chignell, who was asked to come down from Bethesda to start the Laboratory of Molecular Biophysics at NIEHS, and I was hired as a Principle Investigator. There's one technician, well actually a 20-hour student, wasn't a technician yet, and one postdoc. And I have prospered ever since. I've done well on every Board of Scientific Counselor review. I was promoted heavily by legendary scientific directors, like Nick Carter, Carl Barrett, and my group grew over the years. It peaked out at four staff and seven postdocs. And then was a decline of funding for intramural. It's been pared down to its present size.

In general, I've been very well supported. And even though I'm a little bit anomalous here, the institute is populated primarily by biochemists and MD's. Although if they took physical chemistry, they struggled with it typically, so I always had great respect from these people because I was a p-chem TA. And, so they realized I understood things that they didn't.

JM: Has your research changed over the years, or is it all the same as you started?

RM: In the beginning, it was purified enzymes and rat liver microsomes, mitochondria, free radical metabolites of drugs and toxic chemicals, and now it's evolved to a whole animal, living animals, even and it's more disease-oriented.

Two of the three postdocs I have now are really working on Parkinson's, and iron overload, and the mechanism of the dopamine oxidation that leads to Parkinson's. So, I've gone from very chemical to whole animals, from toxicity to disease, but it's been a continuality. Some of my early papers are still highly cited, and I even cite some of them myself.

JM: It sounds like there's a range of areas where your work impacts human health. It sounds like there's something with the diseases or also the metabolism of drugs.

RM: Yeah, toxic chemicals. One way to describe my research is I chase electrons in biology. And I don't really care where they're going or what their consequences are. In the beginning, I was detecting radicals. And then you could identify them and quantify them with this electron spin resonance, and then I would work through to what would be the radical reactions with macro-molecules, and then what would be the toxicological consequences of such reactions. So, it's kind of a deductive logic. Well, it's an inductive logic, as opposed to biology, which always is deductive logic. You start with a disease and you take it apart. Where physics and chemistry, especially physics, inductive logic is the way you investigate things. You take particular details, and then try and make a general principle. Physics is full of principles and laws. Biology, not so much.

So, it's a different approach, and I actually use both the inductive and deductive. When you get to disease, that last step, what are the biological, or toxicological, or carcinogenicity consequences, working deductively from the disease is very helpful, as well.

JM: Is there something over the year that the discovery that you've made that's really been surprising, unexpected?

RM: Not so much. As I mentioned earlier on, I'm dyslexic. And dyslexia is an overused term, but it's really a double-edged sword. I have trouble with pronunciation, especially foreign words. Spelling is a total loss, but dyslexics are blessed by a creativity and imagination. In the morning I wake up, I've been thinking about a problem. All the facts I know in my brain that are relevant seem to rise up out of the brain into kind of a space that I can access, and I try and put pieces together. And pieces start to mesh, and maybe there's a second layer of information that's not so obviously related, so I start adding pieces from that. And on a good morning, I'll have an idea for a paper. I know the first four experiments will work, and they do. And there are a couple of more that I'm not so sure about, but my postdocs don't fish. They're following a sequence of experiments, which seem obvious to me, but are actually novel in the literature. So, it's novel enough to publish, and it passes for original.

JM: But it does sound to me like your original concept of analyzing free radicals for medical purposes was unique at the time. Was that like a …

RM: It was, and it wasn't. Electron spin resonance was first published in 1946 by a Russian physicist. There were people doing ESR of hair, which has an ESR signal, a free radical in the melanin, black pigment has a stable signal. It didn't really work. But most of this work was done by chemists and physicists, who frankly were more interested in the spectroscopy than they were the result. And there's still a lot of people in the area that are that way. They have their toys, and their NIH grants are a means by which they get to play with their toys. Where I think where I'm different is I identified as, at first, as a pharmacologist. I'm a member of ASPET, the Pharmacology Association. I thought I'd been badly treated by chemistry, certainly couldn't have supported the family, couldn't have supported myself with my PhD in chemistry, as it was. And so, I actually, turned my back on chemistry for a while, but then the chemists started to recognize me too, and so I forgave them.

But I had self-identified as a pharmacologist. And if you're going to ask me what I was, I'd probably still stay that. The point I'm trying to make is that what you're actually interested in is really different. I'm not interested in using that spectroscopy. In fact, I invented the technique,

called the immuno-spin trapping, where you don't have to use the ESR anymore. You can just use a confocal, or westerns, and an antibody to what is a marker of where the free radical was. And so, any biochemist can now measure free radicals in tissue slices or cells, and there may be 160 papers using that approach. So, my lab doesn't actually use electron spin resonance. It was a means to an end.

JM: Well, the next item here is what advances would you like to see happening? But it sounds like you're making the advances yourself.

RM: Yeah, I'm still quite active, and I'll be retiring in April. I'm going to be 73. I hope to be emeritus, and I probably won't have postdocs, but I'll be able to work through former postdocs, who are now faculty members. I figure if I feed them ideas, they'll be appropriately grateful. And maybe their graduate students would come here as guest workers, and it would be good for everybody.

JM: Is there anything lacking in the techniques, or the equipment, or the analysis that you wish we could do or are trying to develop something new?

RM: This immuno-spin trapping technique, I don't think the full potential of that has totally been realized yet. There's some tweaking, and it can be improved. But there's many, many experiments left to do with that approach, another 20 years easily. The electron spin resonance petered out, not because of any limitations in the technique, other than sensitivity. Every problem that could be done with the available sensitivity was done. But this immuno-spin trapping technique has about a 100,000 times more sensitivity, and so that just opens up a whole world that was not available.

JM: You talked about this earlier but tell us a little bit more about your coming to NIEHS. You were recruited because of your work?

RM: Yes, yes. Colin Chignell was in Bethesda at the Heart, Lung and Blood [Institute], and he was recruited by Dr. Fouts, who was the Scientific Director at that time, to start this Laboratory of Environmental Biophysics. And there was NMR, and mass spec, and me and him, and a couple of people that were already here doing microwave and hearing, so it was a physically-oriented lab. And I met him in the usual way, meetings. Got to know him best at a Gordon conference, actually. And I was selected to give a short presentation after the banquet, which is a mixed blessing, because people had been drinking and eating lobster all evening. And so, keeping their attention after the banquet was a challenge, but he paid attention, and was impressed, and offered me the position.

JM: If that hadn't happened and you hadn't really gotten into science, what would you have done? Would there have been another career path?

RM: I was good in all sorts of chemistry. At Madison, there were 100 graduate students in the chemistry department. Now Wisconsin doesn't need 100 new PhD's in chemistry every year, and actually they only produce 50 a year, because they flunked out 50. But still, it doesn't need 50. That was part of the problem with the oversupply, which is endemic in biomedical science now. But it happened first in chemistry and physics.

JM: A couple of things to wrap up, for students coming along, what is the most important thing you think that scientists should have?

RM: Originality. People can be very good at book work and get good grades in school, but they don't have originality. If they can't do something different than what's been done, they will not be very successful. It'll just be following the trends. And originality is a strange thing, in that you can't test for it. It doesn't show up on an SAT score. So, it's a gift, the one that I had, but not one that you can acquire. It takes a lot of work. I've been working pretty hard for a long, long time. When I was a postdoc, I worked 6 and a half days a week.

JM: Is there's something in the way that your mind works that just things click together.

RM: Yeah, it just clicks. It has to do with dyslexia, and that's a whole fairly new area. The term didn't come into usage until, probably, the early seventies, so I had difficulties. As someone whose dyslexic now, they can be avoided. I remember being taught to read in third grade. I was kept in by the teacher at noon hour and recess. Of course, I hated that being the third-grade boy, but I learned to sight read. Dyslexics don't have phonics, so they can't sound out words.

But I have a very good memory, and we tend to have a good memory, I think, in general. So, we've become sight readers. But you skipped the easy stage. And so sometimes you don't read. In extreme cases, dyslexics never learned to read, but they can be rock stars or artists. They just can't read. But they are still highly original people. Even rock stars in their way are highly original people, and many of them are dyslexic.