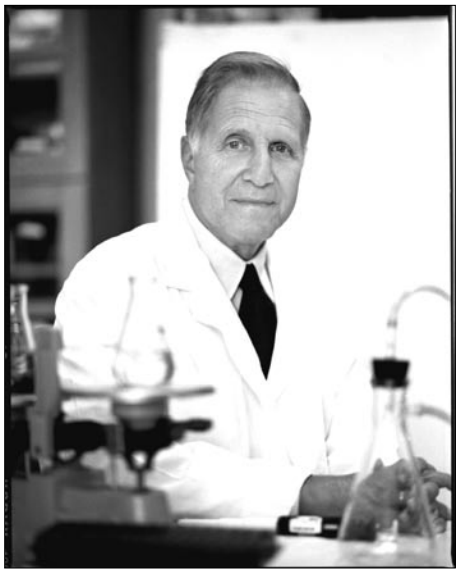

Photo Courtesy of Haig Kazazian

Haig H. Kazazian, Jr., M.D.

Haig H. Kazazian, Jr. is the Seymour Gray Professor of Molecular Medicine in Genetics in the Department of Genetics at the University of Pennsylvania School of Medicine. Dr. Kazazian received a A.B. in Biology from Dartmouth College in 1959 and a medical degree from the Johns Hopkins University School of Medicine in 1962. He also had a post-doctoral fellowship at the Johns Hopkins University School of Medicine. His current research focuses on the population genetics of active L1 retrotransposons in humans.

How did you get interested in science?

I was interested in chemistry and math in college and I was pushing towards medicine. I got into medical school and decided that I should talk to the dean about whether I should work in a hospital. He said no, you should go and do some research with this biochemist. One thing led to another and I got very interested in doing biomedical research.

After my initial experience with the biochemist, I had another experience with a biochemist. I didn't do research while I finished medical school. Then after a couple of years of residency, I went back and decided that genetics was going to be my field. I went to NIH and I worked on some other problems, actually hemoglobin problems, and I worked on those for about 20 years. Towards the end of that time, we had figured out the mutations that caused some of the hemoglobin disorders and this was a very small gene. We thought we would work on a bigger gene and in working on this bigger gene, which was the factor 8 gene involved in hemophilia, we made a finding. We made a finding of a jumping gene that had jumped in and knocked out the factor 8 gene and caused hemophilia in a couple of cases. I decided at that time, now 1988 and so mid-career, I decided that [jumping genes] were what I was going to work on.

What is your research about?

My main topic of interest is retrotransposons, which is just another term for "jumping genes." I work on the biology of jumping genes in humans and other mammals. I'm interested in when they jump and how they do it, what are the problems they cause, etc.

What exactly is a jumping gene?

It's a sequence that is present in fragments or full length copies over 500,000 times in our genome. They're lots of them. They make up about almost 20% of our genome and the full length copies have certain activities that are important in their jumping. They jump through an RNA intermediate, so they are transcribed into RNA and then they get reverse transcribed and inserted into a new site in the genome.

What are the new things on the horizon?

[I am] trying to locate all the potential jumping genes in any one human genome. If I look in your genome or my genome, we easily find how we differ in the location of these retrotransposons or jumping genes. Do we each have one copy per cell or did some of them some of them come in during early development, which we now believe to be the case? And if so, are they important in cancer or other conditions?

What is the future for genomics?

It's heading towards figuring out the etiologies of these very complex diseases. The common diseases are very complex with a lot of genes making small contributions. Let's say if you're susceptible to asthma, you may have a set of ten genes that have these minor changes that make you susceptible, but if I'm susceptible I might have maybe two or three in common with your ten but maybe seven others that are important, so it gets to be very complicated. There may be some genes that have a high impact and others that have a very small impact in producing the common disease. So this is where we are expecting it to go and then there will be the potential for drugs that will alleviate some of those gene problems.

What path should undergraduates take to do similar research?

If they're really motivated, they could go with a PhD, an MD/PhD or a straight MD, but if they did a straight MD, they would have to do a lot of research training after their MD was completed. For most individuals, I would say that training period, even for the straight PhD, for all three pathways, is probably ten to eleven years. It's not an easy road. But I'll tell you, once you're there, it's really great. There are lots to do. There are a lot of frustrations, but the highs are very high. It's a very rewarding career.

What advice would you give undergraduates?

If you are going to end up doing research, you've obviously got to get well-trained. You've got to have a high degree of motivation. You've got to be thinking about the work a lot. You have to be willing to take gambles, gambles that are not outrageous, but gambles. You don't want to work on problems where the chance of success is say 2 to 1. You want to work on problems where the chance of success is say between 5 and 10 to 1. But you don't want to work on problems where the chance of success is 50 to 1. So you're gambling. You have to have a little bit of a gambling spirit besides being highly motivated.

— Interviewd by Matt Canver