

Nazareth Gengozian – Oak Ridge Associated Universities Chief Scientist

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At age 77, Dr. Gengozian retired. He expressed his decision this way, "I had been very fortunate to have had a professional career which I loved very much: The freedom to pursue basic research with only limited time commitments toward activities which can often be counter-productive to research, e.g. teaching and management of laboratories."

His daughter contacted me after reading the Historically Speaking column featuring the ORAU Medical Division. She was encouraged by seeing mention of the Marmosets and wanted to add additional details of her father's work with them.

He describes his career as beginning in 1955 when he worked as a Postdoctoral Fellow in the Biology Division of the Oak Ridge National Laboratory in the Mammalian Recovery program headed by Dr. C. C. Congdon. Dr Gengozian describes his work as, "The mission of this program was to examine the effects of ionizing radiation on mammalian tissues and the potential therapeutic value of marrow infusions in irradiated animals."

This was in the early years of the Biology Division, located at the Y-12 site because there were no large buildings available at the X-10 site of the Graphite Reactor. The Biology Division was begun in 1946 on a small scale at the X-10 site.

However, by February, 1949, Building 9210 (The Mouse House) was converted from a Beta Chemistry Building to a biological research facility. The reason for the "92" designation in the number was that all buildings at Y-12 which processed uranium were assigned numbers beginning with the number "92" – the atomic number for Uranium!).

I must mention an important aspect of the history of the Biology Complex at Y-12. Liane (Lee) Russell and her husband, Bill Russell, were two of the first biologists hired as the Biology Division was being formed.

Later, the biology research was moved from Y-12 to a new facility on the main campus of the Oak Ridge National Laboratory. That nice new biological science facility was named in honor of Bill and Liane Russell.

That was some 60 years after that large vacant building at Y-12 had been taken by Dr. Alexander Hollaender. He had taken that necessary action to house the new Biology Division already growing too large for available space at the X-10 site.

Now back to Dr. Gengozian who continued, "Basic studies in radiation immunology was initiated in collaboration with Dr. T. Makinodan, a senior fellow in this group. Utilizing 250 kVp x-rays, we examined a number of variables affecting the immune response of irradiated mice."

This research led to the successful understanding of bone marrow transplantation in mice. It also determined the critical relationship between the dose of radiation to the host and the number of bone marrow cells injected.

In 1957, Dr. Gengozian received a National Institute of Health Postdoctoral Fellowship to continue his studies at ORNL and was then placed on staff as a Biologist in 1958. While there he coauthored 24 publications, 12 of which he was the senior author.

Dr. Gengozian transitioned from ORNL to the Oak Ridge Institute of Nuclear Studies, which in 1966 became Oak Ridge Associated Universities, where he was given the position of Chief Scientist. His direction was to develop a basic marrow transplant program in collaboration with the clinical staff and explore the feasibility of performing transplants in patients with hematologic malignancies.

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In 1962, he presented an overview, Effects of Ionizing Radiation on Immune Processes, at the Atomic Energy Commission's international conference. This newly forming field of expertise offered Dr. Gengozian opportunities to both learn additional information and to share his knowledge with others.

Because of the limitation of the only available radiation source equipment at ORINS at the time being a Cesium 137 unit with a very low exposure rate, Dr. Gengozian examined the effect of dose rate of radiation on immune processes. By comparing results of earlier shorter exposure and higher radiation doses used at ORNL, he was able to determine that the radiation delivered over a period of a few minutes was more effective for immunosuppression than the same amount of radiation delivered over an hour.

This research led to a protocol deemed suitable for a clinical trial. Ultimately the regime developed led to the first successful clinical marrow transplant in Tennessee of a patient with acute leukemia.

One of Dr. Gengozian's stated goals when arriving at ORINS, was to, "explore radiation/marrow transplants in a small subhuman primate, with the aim of ultimately using information gained to be translated to the human situation." This led to his involvement with the marmosets.

He said, "I had heard of the marmoset, a small South American primate, being used in nutrition studies in a laboratory in Miami, FL." Although Dr. Gengozian was encouraged to explore the feasibility of utilizing a primate in his studies, he was told this would have to be funded entirely through external sources, not with contract monies from the Atomic Energy Commission.

The U. S. Aerospace Medical Division in San Antonio, TX, funded the program from 1961-1964. From 1965-1980, agencies of the National Institutes of Health funded the research.

During the same time period, in 1966, ORINS changed its name to Oak Ridge Associate Universities with mission focus areas in research and education. Later, in 1992 the Oak Ridge Institute for Science and Education was added to focus support for the Department of Energy.

Dr. Gengozian's number of marmosets grew until in 1980 there were 400 of them. The initial intent to use marmosets in radiation studies was limited because of their apparent radiosensitivity.

However, the fact that twinning occurs with a very high frequency (greater than 80 %) and also that blood chimerism (mingling of two or more genomic lineages within an individual is prevalent in the hematopoietic tissues of marmosets) led to other research opportunities. Data on skin and kidney grafts between twins proved them to be tolerated indefinitely.

Another research area was to determine if the frequency of producing twins could be altered and eliminate blood chimerism. Removing an ovary did not result in any change as the remaining ovary evidently adapted to the change to compensate and continue to produce twins with blood chimerism.

In a three-year study ligation of one fallopian tube did result in producing a high frequency of single-born marmosets lacking blood chimerism. This successful procedure advanced the research significantly.

Yet, in 1981, Dr. Gengozian lost funding for the program. Both he and his staff were forced to look for work elsewhere. He was able to connect with Dr. R. A. Good at the Sloan-Kettering Institute in New York and learned they were moving to Oklahoma Medical Research Foundation in Oklahoma City, OK. Dr. Good hired him after reviewing several of his publications, where he worked until 1992.

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During this time Dr. Gengozian's research focused on first the rhesus monkey and then the cat and resulted in "the development of a new technique, the production of monoclonal antibodies, proteins capable of identifying selective populations of cells."

Next Dr. Gengozian returned to the Knoxville area when offered a joint appointment as the Senior Scientist Member at Thompson Cancer Survival Center and a professor at the University of Tennessee.

At the Thompson Cancer Survival Center, Dr. Gengozian's primary responsibility was to establish technical procedures for the successful isolation and storage of blood stem cells. These cells were then used in the treatment of the patient.

He said, "Basically, the protocol was quite straightforward: patients were hooked up to a machine wherein blood cells were isolated over a period of approximately two hours and the cells subsequently frozen at liquid nitrogen temperatures after having been mixed with dimethylsulfoxide, a blood stem cell preservative. "

Dr. Gengozian continued, "This procedure was repeated for two or three days, terminating when it was decided that an adequate number of cells were obtained. Patients with hematologic malignancies of multiple myeloma, Hodgkins lymphomas, were the primary candidates for treatment.

Finally, Dr. Gengozian concluded, "Following extensive chemotherapy to eradicate the malignant cells, the patients then received their own hematologic stem cells which had been frozen in liquid nitrogen.

The procedure was quite successful in the majority of patients, leading to complete recovery and free of any cancer." Don't you think WOW! What a tremendous leap forward in cancer research!

So, as you have seen, from working with marmosets at ORINS/ORAU to successful treatment of cancer patients, Dr. Nazareth Gengozian had a long and significant career. I dare say some of his work with animals have produced results beneficial to many of the people all of us know and love.

The scientific advances made during the period of his career from 1955 – 2006 and now 10 years later are amazing. Where the future may lead us is yet to be determined, but with brilliant minds such as Dr. Gengozian, new discoveries will undoubtedly be continually forthcoming.

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Dr. Nazareth Gengozian (Photo courtesy of Oak Ridge Associated Universities)



Dr. Gengozian holding small marmosets (Photo courtesy of Oak Ridge Associated Universities)

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A group of adult marmosets (Photo courtesy of Oak Ridge Associated Universities)



Two small marmosets (Photo courtesy of Oak Ridge Associated Universities)