

ARAGA RAMESHA RAO

(27 September 1937 - 21 December 2008)

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ARAGA RAMESHA RAO

(1937-2008)

Elected Fellow 1989

INTRODUCTION

ARAGA RAMESHA RAO, born and raised in a small village in Karnataka, took his childhood passion for observing animals and plants to become one of India's leading scientists in the field of Cancer Biology. Professor Rao graduated from Karnatak University Dharwad with Gold Medal and 1st Rank in BSc and MSc and PhD from Rajasthan University. After completing his post-doc at Brookhaven National Laboratory in USA, and a brief stint at Cancer Research Institute, Bombay, he settled in Jawaharlal Nehru University (JNU), New Delhi starting and leading its cancer biology courses and cancer research facilities until his retirement in 2002. Professor Rao published numerous research papers and books, but was happiest when harnessing the boundless energy of MSc and PhD students towards innovative research. Post retirement, Professor Rao was UGC Emeritus Professor at JNU and Mysore University. Apart from academics, Professor Rao loved creating puzzles, writing poetry, playing with his children and grand children, cooking and enjoying food from diverse cultures, entertaining friends and relatives, helping needy students and most importantly, always thinking of new ideas to solve daily problems in any walk of life. Professor Rao died December 21st 2008 in New Delhi. Professor Rao is survived by his wife Sudha, two sons, their wives and 3 grand children.

FAMILY BACKGROUND AND EDUCATION

Araga Ramesha Rao was born on 27th September 1937 in Araga village, Thirthahalli Taluk, Shimoga district, in "Malnad" from Male - Rain and Nadu - region, in Kannada region of Western Ghats in Karnataka State. He was the third child (one each elder brother and sister and a younger brother) of Shri K Bhaskar Rao and Smt. Seethamma. His father an agriculturist, antique jewellery business, was involved in the freedom struggle. His mother was the village problem solver and a practitioner of ayurveda medicine. Early primary school did not interest Ramesha, however something triggered in him in later primary school and he took towards education in such a format that there was no looking back. He was an extraordinarily intelligent and popular student, while a teacher would be absent or busy with some other work Ramesha would take on the task of the substitute teacher, for his junior as well as his own classmates. During exams he would take evening classes for his classmates and



juniors at home. Once in class 7th he had a disagreement with his mathematics teacher on the answer to a problem which led him to write a letter to the author of the book who replied, confirming Ramesha's method of solving as correct. The following day he very proudly showed the letter to his teacher who being magnanimous, praised him in class and came home and congratulated his parents as well. This incident probably taught him to listen to everyone including students and to have an open mind and magnanimity even to juniors (believing that even students can teach you) which he followed for life. In the class 8th exam (that time it was a public level exam) he topped the region with 1st class (a rarity at that time) and was followed by a huge celebration in the village with praise from one and all in the village. Once in middle school under leadership of his elder brother Ganapathi, following the "Quit India" movement of Gandhiji, all the school students went on a protest cutting palm trees and saplings (palm trees were a property of the British Government) as this was a source of revenue to the British and considered illegal.

As there was no opportunity for further education in the village he moved to Shimoga to his elder sister's place to continue his high school (National High School). He continued to excel as a student. He was a voracious reader and literally read anything that crossed him, well outside his school requirements. He got 29th rank in the state at the matriculation exam (Senior School Leaving Certificate Exam, Class X) and realized that he was not in the top 10 due to lower scoring in Kannada language. He joined Sahyadri College, Shimoga for his junior college (preuniversity college, XI & XII) and continued his record in excelling in his studies. He was really interested in biological sciences. Although coming from a conservative family he at this stage only set up a laboratory in his room at home and maintained white rats, guinea pigs, birds, lizards, garden snakes, fish and animal skeletons. He got fascinated by Darwin's theory of evolution and would visit the nearby fields and forest and observe and ponder. In this pursuit he was joined by friend, classmate and relative Manohar who later went on to become a Senior Scientist at Bhabha Atomic Research Centre, Mumbai. At this young age only much ahead of his peers he would read books, experiment and critically analyse biological phenomena and would come with theories. One theory he came up at the time was what he called "Micromorphism" and stated that number of plants and animals that can occur at any given time in the biosphere of this planet would be inversely proportional to their size. He explained this by the fact that larger plants and animals need more food and space as compared to smaller plants and animals. Later when he was studying in graduation and post graduation and reading higher grade books he realized that this concept of his was already described in ecology books. Although he felt disappointed at the time that someone else had described it already, he also felt pleased with himself that he could put together this concept independently at a young age.



Another fact he read about was that rate of digestion is different for different animals. He decided to put this theory up for test in his home lab and he chose a myna and a rat which he fasted overnight. Next morning at a fixed time he fed the myna some killed flies and the rat was fed wheat balls with pieces of fly wings. He waited and collected the droppings containing the undigested fly wings and calculated the food transit time, which was shorter in the bird (myna). When he came for graduation later and while doing other experiments he explained this experiment to his teachers, who decided to include this experiment as a part of the exercise in the physiology practical class.

Another interest of his was the effect of music on the growth of embryos. He collected lizard eggs and divided them into two groups, one group was exposed to radio music (Vividh Bharathi, All India Radio) and the other group had no music. After a couple of days he would cut open the eggs of both groups and compare the size and length of the foetuses. He was pleasantly surprised to find that music had a promoting effect on foetal growth. He further to confirm his findings now used spider eggs. Now he divided them into two groups, one he exposed to Carnatic music on the gramophone while the other was exposed to no music. To his surprise, Carnatic music inhibited the hatching of spider eggs into tiny spiders.

He enjoyed to read books by Sigmund Freud on psychoanalysis and dream analysis and would analyse dreams of himself, family, friends and in fact maintained a record of his analysis. Kannada language impressed him and he took to writing articles and poems. While studying in High School and Junior College (class XI and XII) he was editing a handwritten Kannada magazine "Deevige". He was lucky also to have JR Laxman Rao and UR Ananthmurthy as his teachers at this stage (Dr Ananthmurthy later won the Jnanapeeth award).

His craze for higher learning in science led him to move to Karnatak University, Dharwad for his graduation (Karnatak college) and post graduation studies. Dharwad was an epicentre of higher learning at that time. He quickly established himself again as an excellent student and a popular one too and became a blue eyed boy of his teachers. He was elected as President of the Zoological Society of the college and was busy organizing seminars, discussions, field trips etc. Again here as in school and junior college he was giving lectures and demonstrations to his classmates. He stood first and received a gold medal in his BSc (Hons) (1960).

He decided to pursue his post graduation studies (MSc) in the field of Zoology at the Karnatak University, Dharwad and securing admission to it was simple seeing his earlier performance. He again excelled in studies, with him being the cynosure of his peers and teachers. His favourite teachers were Dr VB Nadkarni, Dr M Gowder, and Dr Desai with whom he involved regularly in discussions well beyond university hours with them fixing a discussion club in the evenings. He proposed a hypothesis on the origin of dorsal and paired lateral fins in the earliest piscine



vertebrates by the local fusion of dorsal and venterolateral ciliary elements in the ciliated ancestral vertebrate larvae for increasing mobility and its further evolution into musculoskeletal dorsal and lateral fins. He also proposed a hypothesis on the origin of paired limbs among land vertebrates, evolving from piscine pectoral and pelvic fins to amphibious limb bearing forms. He also would write to evolutionary biologists in India and abroad and discuss with them. He was the recipient of the then most prestigious "Daxina Fellowship" of Karnatak University. He again secured first rank in MSc (1962) and was awarded the gold medal from the university.

He also got admission for PhD at Minnesota University under the iconic embryologist, Dr Nelson T Spratt, however his parents refused to send him abroad and he did not avail of this opportunity. Being an avid bird watcher he was in contact with Dr Salim Ali who offered him a fellowship and a position under him to do his PhD but he declined the same as he was not keen in a lot of field work which involved travelling in the hills and forests. He secured admission to PhD programme at the Karnatak University, Dharwad with scholarship which was given to the topper in science. He commenced his PhD studies in the field of entomology the only field available for research at that time. However his wish was to work under Professor LS Ramaswami a celebrated zoologist and reproductive biologist who had recently moved from Mysore University to Rajasthan University. He wrote to him and secured admission to the Rajasthan University PhD programme there with a scholarship of Rs125 pm which was less compared to the scholarship of Dharwad University of Rs 200 pm which he accepted gladly (his principle of giving less importance to money as compared to scholarly pursuits continued throughout life).

His parents would not let him go to Jaipur (outside Karnataka state) without getting married and he married Sudha from Mysore. On arrival in Jaipur, on the direction of Professor LS Ramaswami the Head of Department, he met Professor PN Srivastava (Professor PN Srivastava later went on to become the Vice Chancellor of Jawaharlal Nehru University, Delhi; Member, Planning Commission and Chairman National Board of Accreditation, Delhi) Chief of the newly created Radiation Biology Laboratory and registered for his PhD under him. He started his work on the effects of ionizing radiation on male and female reproductive physiology of mammals. As radiation biology was a new subject for him he spent a lot of time reading and understanding the subject and started work on his thesis. He became a master on effects of radiation to mammalian cells and would design experiments for and train other students on germ cell kinetics and dynamics. He got selected as a Lecturer in the Zoology Department while still pursuing his PhD. He completed his thesis (1968) and remembered a comment from his PhD guide (Dr PN Srivastava) who said while signing his thesis "Rao you could very easily have made two theses out of this voluminous data".



PROFESSIONAL CAREER AND RESEARCH CONTRIBUTIONS

Ramesha Rao's research contributions and teaching started well in his school days, but he officially became a teacher when he joined as a Lecturer in the Department of Zoology, Rajasthan University, Jaipur while in the final stages of his PhD programme. He would also go and teach at Maharaja's College (a constituent of Rajasthan University) and quickly became a very popular teacher. When he had to teach in the newly introduced radiation biology course, he would go to his colleagues in the Physics Department of the university and understand concepts about radiation and only then would he go to teach his students. He never even carried a piece of paper to his class and followed this till he took his last class (no transparencies or power point presentations either). He was a master at drawing figures and said in science if you can draw and represent your concept clearly it indicates that you have understood the subject. He believed learning was a continuous process and said "when there is continuous explosion and expansion of knowledge, those who wish to be successful scholars and professionals have no alternative but to be students all the time".

His initial work in radiation biology includes germ cell population dynamics in male murine model system following exposure to internal β radiation, the oocyte depopulation pattern (quantitative analysis) in the ovary of mouse following its exposure to internally deposited P-32, Co-60 and Ca-45 radioisotopes, radioresponse of spermatogonia of mammalian model system exposed to X-radiation in the atmospheres of air, oxygen and nitrogen, discovery that exogenous gonadotropin can augment the germ cell killing action of internal radiophosphorus in male mouse and internal Co-60 irradiation at very low dose levels does not affect the reproductive performance, sequential events occurring in the process of inflammation elicited by radiocalcium released into the testis of gerbil. These works have been profusely cited even in textbooks. He was also the Sectional Editor of the *Indian Journal of Gerontology* for several years while he was at Rajasthan University.

He proceeded to Brookhaven National Laboratory (BNL), Long Island, USA for his postdoctoral work (1970-72) receiving the Fogarty International Postdoctoral NIH fellowship. He worked under the supervision of Professor CJ Shallabereger. He worked there on the areas of radiation and chemically induced mammary carcinogenesis in rats. He developed an ovarian granulosa tumor model using BNL mice. Being an avid learner and going beyond call of duty he learnt electron microscopy and tissue culture. His study demonstrates the paradoxical influence of hyperinsulinism on the process of mammary carcinogenesis elicited by DMBA in female virgin rats, with reduction in number of tumors when exogenous insulin is administered during the initiational phase of carcinogenesis whereas if same is administered during the promotional phase of carcinogenesis the number of tumors increased. He was active to discuss scientific issues with the high and mighty of



science at BNL including the celebrated radiobiologist Professor MM Elkind and Professor Cronkite. In one of his discussions with Professor Elkind he proposed his hypothesis explaining the radioresistance of microbes as compared to mammalian cells. He theorized that as microbes live in an environment full of various chemicals etc they develop a better DNA repair system and hence also are more radioresistant. Professor Elkind impressed by his idea suggested him to further pursue this work but was unable to pursue work on this problem. He later found people were working on this idea and coming to similar conclusions. During this period he also exposed new born mice to UV radiation and found most of the babies dying within 3 days, he prescribed these deaths to immunosuppression. By 1980 he found papers claiming the immunosuppressive properties of UV radiation. He was offered long term job opportunities at BNL however wishing to come back to his home country returned back to India.

He returned to Rajasthan University in 1993, however, he was exploring avenues where he could continue his further research. He was offered a Senior Scientist position at Cancer Research Institute (CRI), Bombay, now Mumbai which had very good labs and since was associated with Tata Memorial Centre had a good clinical material resource. Being from Malnad region (large producer of arecanut) he spent his energy in working on the carcinogenicity and embryotoxicity of arecanut (betelnut). He and his colleagues showed the enhancing effect of betelnut in carcinogenesis. He spent two years at CRI and was a very fruitful period for him as he learnt experimental methods for chemical carcinogenesis and experimental tumor pathology. His interactions with Dr Srinivasan, Dr Ranadhive, Dr Bhise, Dr Anand Rao etc. paved the way for his further work in the field of cancer biology. However the restrictions of working in an institute setup and also the humid Bombay weather which did not suit him made him to look for other opportunities. He was a firm believer in academic freedom and looking for it, found it in Jawaharlal Nehru University (JNU), New Delhi which offered him the post of Associate Professor, in the School of Life Sciences (SLS).

He joined JNU in 1976 and continued there till his retirement. He started the Cancer Biology Laboratory and offered the Cancer Biology course which was the first course in Cancer Biology in any University in India. He was very serious about teaching and research and would not mind missing a departmental meeting but would take his class. His course and lab was very popular with both the course and lab being full of students to the permissible limits. He has guided 29 PhD students to gain doctorates from across the country with him guiding a student from Spain as well. His home was akin to his office where students were free to come anytime for discussions, which led his students to become a part of his family.



His areas of work included radiation biology Cancer Biology, Genotoxicity, Teratology, Immunology and Biochemical Methodology. He has published over 106 papers in peer reviewed international and national journals.

His laboratory had various interests and conducted research in various areas and he was especially interested in the value of naturally available substances. He continued his work further on arecanut and discovered the immunomodulatory potency of arecoline, a major alkaloid of arecanut, showing its capability in inhibiting humoral as well as cell mediated immunity. His studies have shown the carcinogenic, embryotoxic and immunotoxic action of arecanut and its alkaloids. He has further shown that conventional processing operation (boiling as done in south india) removes large amounts of tannins and alkaloids from the arecanut and renders them relatively safe whereas the unprocessed and ripened varieties have weak carcinogenic potency. His lab has also shown the chromosome damaging effects of arecoline *in vivo*. He went further by testing individual ingredients of betel quid (betel nut, betel leaf, tobacco, lime) and has shown that short-term treatments with individual ingredients did not produce any tumors however long term treatments produced tumors only with tobacco and betelnut. Betel leaf in both short-term and long-term studies expressed its inhibitory influence on Benzo(a)Pyrene induced tumorigenesis. There has also been an observed significant increase in the number of sister chromatid exchanges in mouse bone marrow treated with arecaidine, a betel nut alkaloid and further treatment of mice with arecoline has elicited dose-related increase in number of abnormal sperm heads showing its genotoxic potential, fetotoxic potential and transplacental micronucleus inducing ability of betel nuts in mice has also been observed by his team. His laboratory has proved the epidemiological claim that synergistic smoking and chewing habits increases the risk of oral cancer.

His team has further shown the radiosensitizing action of neem (*Azadirachta indica*) oil on cells. Similar radiosensitizing action of camphor on transplantable mammary adenocarcinoma in mice has been observed by his team. Also observed by them was the chemopreventive potential of camphor against chemical carcinogenesis. Camphor also induces in the liver of mice antioxidant defence system and xenobiotic detoxification system.

Ovarian cancer incidence is high in certain populations and the causative or risk factors are not clear. Using murine model systems Dr Rao has shown that loss of oocytes and high proliferation of granulosa cells (due to gonadotropin) contribute to tumors in large numbers which has implications in adolescent age in girls when there is a surge of gonadotropins.

Mammary carcinogenesis and mammary tumor growth are affected by alterations in various hormone levels. Dr Rao has studied the role of Aminoglutethemide (depresses endocrine function) at the initiation and promotion



phase of DMBA induced mammary carcinogenesis in female rats. He has shown a decrease in the number of rats with cancer and number of tumors per rat in a dose dependent manner.

Uterine cervical cancer is one of the most prevalent cancers in India and has been associated with viral, chemical and dietary factors. Dr Rao established a pre-cancerous and cancerous mouse model of cervical cancer. Using this model he determined the role of oral hormonal contraceptives and non-steroidal anti-inflammatory agents (NSAID) and reported that high doses of hormonal contraceptives and indomethacin can enhance the development of cervical cancer.

Dr Rao made his contribution in the area of biochemical methodology also. His laboratory has described two affinity chromatography methods for the purification of Glyoxalase I from organs like liver.

Dr Rao has the credit of development of an experimental ovarian cancer model in a BNL strain of mice. Mice naturally have a very low incidence of ovarian tumors and this is so inspite of experimental exposure to carcinogens. Dr Rao discovered that mice ovaries that are primed with gonadotropin and exposed to chemical carcinogen DMBA yield tumors of granulosa cell type significantly.

With the increasing use of oral contraceptive (OC) pills around the world, Dr Rao decided to look at its effect in cervical carcinogenesis. His team found paradoxical action of OC pills like Noracycline and Overal on MCA induced cervical carcinogenesis. At lower doses comparable to human doses the OC pills significantly inhibited the occurrence of cervical squamous cell carcinoma however at higher doses the tumor incidence tended to be higher.

Dr Rao's team has also shown a profound inhibitory effect of caffeine on the incidence of fibroadenoma and benign mammary cysts. His lab has also shown that oral ingestion of methylxanthines like caffeine or theophylline by ovariectomized mice induced mammary gland lobulo-alveolar development.

His heart lay in the area of chemoprevention of cancer for which he is considered a pioneer in the field and his lab become the hub of research activity in this area with his interest being to evaluate the innumerable number of natural substances. He actively pursued study on these natural phyto compounds for their chemopreventive role. He studied a large number of plants based on their use in Ayurveda or Folklore medicine and his laboratory was the first to discover a chemopreventive action of many of them. The plants which he studied for chemopreventive and chemomodulatory role were Garlic (*Allium sativum*), Mustard (*Brassica compestris*), Betel leaf, Cumin (*Cumin cyminum*), Triphala (a composite Indian drug), *Tinospora cordifolia*, Bitter melon (*Momordica charantia* Linnaeus), Neem (*Azadirachta indica*), Cashew nut kernel oil (*Anacardium occidentale*), Basil leaf (*Ocimum basilicum*), Asafoetida (*Ferula asafoetida*), Henna leaf (*Lawsonia inermis*).



Spirulina platensis, Fenugreek (*Trigonella foenum graecum*), *Andrographis paniculata*, *Aloe vera*, *Adhatoda vesica*, *Aegle marmelos*, *Spirulina fusiformis*, *Ocimum sanctum*, Camphor, Garam masala (Indian spice mixture), Mace (*Myristica fragrans* Houtt.), Cardamom, Celery seed, Coriander, Ginger, Nutmeg, *Zanthoxylum*, Black pepper, Sandalwood oil and Piper betle.

He also explored and studied the chemopreventive and chemomodulatory of several other compounds including Selenium, Magnesium Ascorbic acid, Retinyl acetate, Tamoxifen, Tocopherol, Ergocryptine, Butylated hydroxyanisole, Disulfiram and Dehydroepiandrosterone. He retired from JNU on 27th July 2002 after which he became a UGC Emeritus Professor at JNU and later at Mysore University.

HONOURS AND AWARDS

- Gold Medal for standing first in BSc Zoology Honours, Karnatak University, Dharwad (1960).
- Gold Medal for standing first in MSc Zoology, Karnatak University, Dharwad (1962).
- "Dakshina Fellowship", Karnatak University.
- National Institute of Health (USA) International Postdoctoral Fellowship Award, (1970-72).
- Yamagiwa-Yoshida Memorial International Cancer Study Grant Award (UICC), (1985).
- Fellow, National Academy of Sciences (Allahabad), 1986.
- Fellow, Indian National Science Academy (New Delhi), 1989.

THE INDIVIDUAL AND HIS FAMILY

Professor A Ramesha Rao a man of great virtues was adored by one and all who came in contact with him. He was a person of high integrity, true intellectual, always smiling, kind hearted, helping natured, apolitical, and probably one amongst the very few in the present society who valued money to the minimum extent necessary. He would work day and night in the lab along with the PhD and post doctoral students, research associates, lab attendants and animal house workers, but would feel running to the finance dept to ask for the pending cheques was considered a waste of time. His home at JNU was his second office for his students who were welcome at anytime of the day for discussions. He did not believe in the caste system and never even discussed anything of this sort even with his family, so much so that his children never knew about the castes etc.

He was known to support needy meritorious and poor students by helping them monetarily. One of his students narrated an incident. When the student came to JNU to learn some techniques from his lab and he (student) exhausted whatever



money he had brought was found sitting with a sad face in the lab. Dr Rao enquired about the reason for his sadness thinking that some experiments might have got spoiled. But when he learnt that the reason is his financial crisis, Dr Rao signed a blank cheque and handed over to him which was shocking to the person who received it. Probably he could be one amongst the very few officials who has not submitted LTC and Hometown bills to the University. He (with his family) would rather travel in a second class instead of keeping accounts and maintaining bills etc. which he felt was highly time consuming and distracting. A man, who was genuinely interested in scientific research and believed that societal problems could be solved only with good research. He strongly felt that original research could be done by only those who are not drilled too much while they are growing. Freedom, exposure to problems stimulates the individual to think and solve in an innovative manner. With this in view he supported bright students from rural background in spite of their English language deficiency who later contributed to scientific research in many ways. Today his students are spread all over the world and a large number of them are in USA in well established research labs and universities in good positions.

Born to respectable parents, who were arecanut plantation owners and agriculturists. Father a god fearing individual, though educated only upto 6th standard was active in village affairs and an active participator in the freedom struggle during the British period. Mother, a beautiful lady, though hardly educated up to 5th class only, was a highly intelligent, talented lady and had multiple hobbies. People would come with all their problems in search of her from her which she would solve in an amicable manner, be it a land related or a family concerned. A good counselor and her decisions were respected by one and all in the village. One of her hobbies was treating patients with ayurvedic/herbal medicines which were passed on to her by her parents. She was quite popular in treating infertility, irregular menstruation, jaundice and other ladies concerned diseases. As landlords they supported several poorer families, to the extent that when they decided to shift to the city acres of land was donated to the farmers who tilled their land for several years. Three members of the family even today draw freedom fighter pension. Dr Rao's elder brother Mr Ganapathy is an rice mill, automobile and electrical parts dealer and wife Dr C Nandini is a well known doctor who is involved in charity work in Shimoga even today. Younger brother, Mr Nagaraj a comedian has acted in several Kannada films. Sister Smt Vimalamma a housewife and brother in law A. Ramkrishna was a well known insurance agent who remained a Member of the Chairman's Club at LIC.

Dr Rao married Sudha, eldest daughter of Shri K Ananda Rao a gold and diamond merchant and Smt Sharadamma from Mysore in 1963 while prior to his moving to Jaipur for his doctoral work. Smt Sudha who was just a matriculate (Class X) at the time of marriage, with the full support and encouragement from Dr Rao,



she could not only complete her PhD in educational psychology but also proceeded for her post doctoral studies at Harvard University, Cambridge, USA with the support of Fulbright Scholarship. As a strong supporter of gender equality, ensured that his wife is educated to the maximum extent and enabled her to become Senior Advisor of AICTE, New Delhi and Vice Chancellor of Karnataka State Open University, Mysore. She is presently Head, Department of Education Policy, National University of Educational Planning and Administration, New Delhi. Dr Rao has two sons, the elder being Dr Nitin Rao a Surgical Gastroenterologist specializing in Hepatopancreatobiliary Surgery at Ramaiah Hospitals, Bangalore whose wife Ms Mamata Rao is an Architect, specialized in creativity and design and is on faculty at National Institute of Design R & D campus, Bangalore. Their daughter Snigdha N Rao is presently studying in Class X and is keen to pursue her career in research in biological sciences. His second son Nishit is a Director of Product Management at Oracle Corporation, San Francisco USA, his wife Bharathi is a Principal Engineer with Oracle Corporation, San Francisco USA and they have two sons Tejas who studies in Class III and Yesh who is presently in preschool.

Such was his influence on his students (Dr. Rao considered them family) that his family and students have initiated a Fellowship Program at JNU for meritorious and the economically needy students.

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