



Dr. Virendra B. Mahesh is the 2005 recipient of the SSR Distinguished Service Award (funded by Serono Research Institute), which is given by the Society for the Study of Reproduction in recognition of an individual who demonstrates unselfish service and leadership in advancing the discipline of reproductive biology. In addition to his role as a pioneer in the field of reproductive biology, Dr. Mahesh has a long history of generous service to the scientific community that is matched by few other reproductive biologists and is the perfect embodiment of the definition of distinguished service. Below is a summary provided by Dr. Mahesh describing his scientific career.

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Dr. Mahesh received a B.Sc. degree in Chemistry from Patna University, India, in 1951; an M.Sc. in Chemistry followed by a Ph.D. in Organic Chemistry from Delhi University in 1953 and 1955, respectively; and a D.Phil. in Biological Sciences from Oxford University in 1958. He was a James Hudson Brown Memorial Fellow at Yale University from 1958 to 1959, and in 1959, he joined the Department of Endocrinology at the Medical College of Georgia in Augusta, Georgia, as Assistant Research Professor. Dr. Mahesh progressed through the ranks as Associate Research Professor in 1963, Professor in 1966, and Regents Professor from 1970. He was appointed Robert B. Greenblatt Professor of Endocrinology in 1979 and served as Chair of the Department of Endocrinology from 1972 to 1986. In 1986, he was appointed Regents Professor and Chair of the Department of Physiology and Endocrinology at the Medical College of Georgia. He assumed the rank of Regents Professor and Chair Emeritus in June 1999. During his career, Dr. Mahesh has authored or coauthored 441 journal articles and book chapters, and he has edited 11 books.

Between 1956 and 1959, Dr. Mahesh established that glucocorticoids, which hitherto had been thought to exert biological action by extensive metabolism and interconversion, did not undergo structural changes to exert their biological action. Thus he was the first to report the absence of steroid metabolism for biological action, a finding subsequently extended to estradiol by Dr. Jensen and colleagues, and a concept that led to the current views of steroid hormone action.

Dr. Mahesh has contributed greatly to our understanding and treatment of polycystic ovarian syndrome, a major pathophysiological syndrome that produces anovulation and infertility in women. He demonstrated that excessive androgen production in polycystic ovarian disease patients leads to hirsutism and virilism. He went on to show that the excessive androgens were both adrenal and ovarian in origin, and that the excessive androgens were primarily weak androgens such as dehydroepiandrosterone and androstenedione. He next showed that, in the human, these weak androgens were converted to the more potent androgen, testosterone, through peripheral conversion. Subsequent work by Dr. Mahesh's group showed that the high ovarian androgens present in patients with polycystic ovarian disease were due to a relative decrease in aromatase and/or the enzyme  $3\beta$ -hydroxysteroid dehydrogenase-4,5-isomerase. Dr. Mahesh and his group next confirmed that the weak androgens were responsible for the pathophysiological symptoms of polycystic ovarian disease by demonstrating that administration of dehydroepiandrosterone to immature rats produced polycystic ovaries, ovulatory failure, and abnormal gonadotropin and steroid secretory profiles.

Dr. Mahesh and coworkers were the first to show that clomiphene citrate was effective in inducing ovulation in anovulatory women. Clomiphene citrate remains today a "front-line" weapon in the arsenal of the practicing physician for inducing ovulation. Dr. Mahesh also

showed the effectiveness of the first antiandrogen tested,  $17\alpha$ -methyl- $\beta$ -nor-testosterone, for the treatment of hirsutism in polycystic ovarian disease patients.

Dr. Mahesh has advanced our understanding of key physiological events in reproductive biology through his work on explaining the mechanisms underlying the preovulatory gonadotropin surge. Using discrete animal models, he demonstrated that while estradiol is the trigger for the preovulatory gonadotropin surge, activation of progesterone receptors is important for the precise timing and full expression of the surge because it leads to enhanced gonadotropin-releasing hormone (GnRH) release, inhibition of GnRH degradation, modulation of estrogen receptors in the anterior pituitary, and increased anterior pituitary sensitivity to GnRH. Since the majority of published work shows that the GnRH neuron does not contain steroid receptors, Dr. Mahesh and coworkers conducted studies demonstrating that glutamate neurons in the hypothalamus mediate steroid effects on GnRH neurons and play an essential role in the steroid-induced, preovulatory gonadotropin surge. These glutamate neurons surround the GnRH neurons and, among other actions, activate nitric oxide synthase resulting in the release of nitric oxide, which in turn stimulates the GnRH neuron to release GnRH.

Dr. Mahesh has served on numerous NIH Advisory Committees, including the Reproductive Biology Study Section from 1977 to 1981; and the Human Embryology and Development Study Section from 1982 to 1986, 1990 to 1993, and as Chair from 1991 to 1993. He has served on numerous editorial boards for scientific journals including the *Journal of Clinical Endocrinology and Metabolism*, *Endocrinology*, *Journal of Steroid Biochemistry and Molecular Biology*, *Steroids*, *Assisted Reproductive Technology/Andrology*, *Maturitas*, *Archives of Andrology*, and the *Journal of Endocrinological Investigation*. He also served as Editor-in-Chief of *Biology of Reproduction* from 1999 to 2004 and is currently serving as Consulting Editor to the journal.

Dr. Mahesh has received international recognition for his contributions to science; he received the Rubin award in 1963 for his work on polycystic ovaries and the Billings Silver Medal in 1965 for his work on gonadal dysgenesis. In 1986, he received the Albert Einstein International Academy Foundation Bronze Medal; in 1989, the Distinguished Scientist Award of the Association of Scientists of Indian Origin in America; and in 1996, the Carl G. Hartman Award of the Society for the Study of Reproduction. In 2005, he received the SSR Distinguished Service Award.

Dr. Mahesh has contributed extensively to the education of medical students, graduate students, and postdoctoral fellows. He has been recipient of Best Teacher Award and Outstanding Faculty Award from the School of Medicine and the School of Graduate Studies at the Medical College of Georgia, the life time achievement award, and Excellence in Research Award as Faculty Advisor on twelve different occasions at the Medical College of Georgia. In 1965, he was instrumental in setting up a Ph.D. program in reproductive biology at the Medical College of Georgia. The program was funded by an NIH Training Grant in 1965 with Dr. Mahesh as Program Director. The training grant was funded for 34 years, making it the longest training grant at the Medical College of Georgia. The program produced 14 M.S. students and 45 Ph.D.s, with Dr. Mahesh serving as major advisor to 10 M.S. and 22 Ph.D. students. In addition Dr. Mahesh contributed to the training of 59 postdoctoral fellows from around the world.