

Valerio Monesi, a pioneer of modern Reproductive Biology

GREGORIO SIRACUSA^{*,1} and MARIO STEFANINI²

¹Dept. of Public Health and Cell Biology, University of Rome Tor Vergata and ²Dept. of Histology and Medical Embryology, University of Rome La Sapienza.

Valerio Monesi was born in Milan, Italy, in 1928 and died of a sudden heart attack in 1979 at the age of 51. His untimely death deprived reproductive biology of an active and brilliant scientist who had made relevant contributions to the understanding of spermatogenesis in mammals. He was fascinated by the study of cell differentiation and of cell cycle control, and he approached these problems during twenty five years of active research with an uncommon capability of cultural and methodological renewal. He was ahead of his time in bringing together autoradiographic and biochemical techniques to study testis biology.

In 1953 he gained his M.D. degree at the University of Pavia. During his early post-doctoral years he stayed at that University, with its associations with Sertoli and Spallanzani, mainly studying the differentiation of hemopoietic and chromaffin cells in organ cultures of the chicken embryo. In 1959 he moved to the Biology Division of the Oak Ridge National Laboratory, Oak Ridge, Tennessee, where, under the supervision of A. Hollaender, he spent two years studying cell cycle and cellular radiosensitivity, using mammalian spermatogenesis as a model. Back to Italy in 1961, he was appointed head of the Embryology group at the Laboratory of Radiobiology of the National Committee for Nuclear Energy (Rome) and then, from 1965, Director of the same laboratory. In 1968 he obtained the chair of Histology and Embryology at the University of Siena and the following year he was appointed to the same chair at the University of Rome, position that he held until his death. The main contributions of Monesi's research deal with the regula-

tion of mammalian spermatogenesis and in particular with the characterization of the spermatogonial cell cycle, the study of meiotic and post-meiotic macromolecular syntheses and the role of cyclic nucleotides in the differentiation of the male gamete.

In the early 60's with the use of autoradiographic techniques he was able to evaluate, in the mouse, the number of spermatogonial generations occurring between A1 and B spermatogonia. He showed that spermatogonial proliferation is characterized by a constant generation time, a gradual increase in the duration of the S phase and a parallel shortening of G2 (Monesi, V., *J. Cell Biol.* 14: 1-18, 1962). He showed that the radiosensitivity of spermatogonia increases with differentiation, and correlated these data with the gradual increase of the S phase during spermatogonial proliferation (Monesi, V., *Radiation Res.* 17: 809-838, 1962). To explain spermatogonial stem cell renewal, in 1962 he proposed a model which postulated that in the mouse A1 spermatogonia are stem cells capable to produce, by bivalent mitoses, stem cells and differentiated A2 spermatogonia.

Of fundamental interest are his early autoradiographic studies, later confirmed by biochemical techniques on purified populations of germ cells at the same differentiative stages. These showed that in the mouse, the stages of mid-late pachytene spermatocyte and of round spermatid are the most active in the synthesis of ribosomal and messenger RNA. He showed that at least part of the RNA synthesized during meiosis and early spermiogenesis is still present in the cytoplasm of more advanced stages of differentiation, thus

*Address correspondence to: Gregorio Siracusa, Dept. of Public Health and Cell Biology, University of Rome Tor Vergata, 00173 Rome, Italy. TEL: 39 06 7259 6156. FAX: 39 06 7259 6172. e-mail: g.siracusa@uniroma2.it



Fig. 1. Valerio Monesi shortly before his death (1979), beside the Greek temples of Syracuse (Sicily).

suggesting that haploid germ cell differentiation may be controlled by the diploid as well as the haploid genome (Monesi, V., *J. Cell Biol.* 22: 521-532, 1964).

During these studies he showed that the XY bivalent is invariably genetically inactive throughout meiotic prophase. He studied the pattern of protein synthesis during male gamete differentiation, and showed that during late spermiogenesis a new histone, characterized by higher basicity and much higher arginine content, replaces the previous lysine rich "meiotic" histones (Monesi, V., *Exp. Cell Res.* 36: 683-688, 1964).

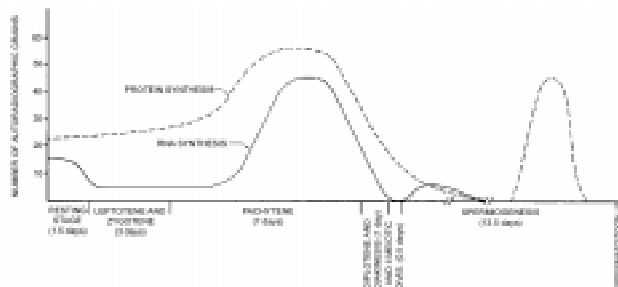


Fig. 2. Macromolecular synthesis in mouse germ cells at various stages of spermatogenesis (from Monesi, 1967, modified). This graph, based on Monesi's autoradiographic observations from the early sixties, has represented for decades a milestone for scientists interested in the biochemistry and molecular biology of mammalian spermatogenesis.

In his final work he was involved in the study of cyclic nucleotide-dependent pathways in differentiating germ cells. The early results of his involvement in this field lead to the demonstration of changes in isoenzymes of cAMP-dependent protein kinase during spermatid maturation.

Valerio Monesi greatly contributed to the growth of Developmental Biology in Italy by attracting numerous scientists to this field and firing their imagination and enthusiasm. Under his leadership, his laboratory became a major developmental and reproductive biology research centre and his scientific legacy is still alive and bearing fruit. Among the main research lines of Monesi's School are the study of the mechanisms which regulate gametogenesis in mammals, with special emphasis on the role of cellular interactions, the pathways of signal transduction active in gonadal cells and on the cellular responses. These studies have yielded important results, with possible practical applications. The mechanisms responsible for the differentiation of somatic cells of mesoderm origin have also been studied. This area includes noteworthy studies on skeletal myogenesis and gonadal smooth muscle cells. Most recently work on the development of paraxial mesoderm, which focuses in particular on the signaling molecules and relative receptors that allocate cells of the somite to their specific fate, has yielded important results.

Monesi was a strenuous catalyst of developmental and reproductive research in Italy: his active and successful lobbying for financial support from public and private sources greatly contributed to a quantum growth of such research fields in Italy. Finally, he was one of the founders, together with other major scientists, including Alberto Monroy, Baccio Baccetti, Luciano Martini and Giovanni Giudice, of the first Italian scientific society for reproductive and developmental biology (SIBRES).

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