



## IN MEMORIAM

### *Professor Dr. Marlena Anastassova-Kristeva*

On the 14<sup>th</sup> of January 2022, Professor Doctor Marlena Anastassova-Kristeva passed away at the age of 98 at her home in Los Angeles, USA.

Marlena Anastassova-Kristeva was born on the 17<sup>th</sup> of December 1923 in Berlin, Germany. She graduated Medical Faculty, Vienna University, (1944), as well as Higher Dental School (1948) and Higher Medical School (1952) at Medical Academy, Sofia, Bulgaria. In 1955 she started work as a researcher in histology and embryology, and later on, as a senior scientist at the Institute of Morphology, Bulgarian Academy of Sciences till 1979. Prof. Kristeva organized and managed research laboratories for Histochemistry, Tissue Cultures, Histoautoradiography and Karyotyping.

Between 1982 and 1990 Prof. Kristeva was honored as a professor in histology and developmental biology at the California State University Northridge (CSUN), USA. Between 1990 and 1994 Prof. Kristeva organized and managed Central Lab on AIDS research. She conducted research on BSL 3 Mouse-Human Chimeras at Core Faculty in Hematology-Oncology at University of California Los Angeles (UCLA). Since 1996 till 1999 Prof. Kristeva was teaching histology as a part time professor at School of Medicine, Department of Cell and Neurobiology, University of Southern California (USC).

Prof. Kristeva was Honorary Member of the Bulgarian Academy of Sciences (2006), The New York Academy of Sciences (1982) and Sigma Xi, USC (1981). She was a member of Union of Scientists in Bulgarian and European Cell Biology Organization, France. Since 2001 she was an official adviser in embryology for Journal of Chemotherapy and Stem cell Research, now renamed Stem Cells and Development.

Prof. Kristeva dedicated more than 50 years to students, graduated and post-graduate students. Her scientific work includes over hundred of publications and hundreds citations in journals with high impact factor.

Prof. Kristeva's major scientific achievements contributed to several areas of research: First priority was reproduction, particularly the origin of the primordial germ cells (PGC) in undifferentiated gonads, cell differentiation of germ and somatic cells, development and maturation of germ cells and meiosis. With her wide background in the field of embryology, cellular and molecular biology, Prof. Kristeva transferred her scientific activity in genetics, introducing modified method for human chromosome karyotyping. She described for the first time the changes in nucleolus that occurred during mitotic cycle in humans. She created nucleolar test for evaluation the number of satellite chromosome in plants and animals, widely cited and applied in molecular biology and pathology.

After retirement at 2000, Prof. Kristeva was completely devoted on theoretical science and published many articles in prestigious scientific journals. In 2003 she published an article entitled: "The origin and development of immune system with a view to stem cell therapy" in "Journal of Chemotherapy and Stem Cell Research". She reported her new concepts about hemopoiesis, lymphopoiesis and macrophage-monocyte systems. Comparative study on lymphopoiesis, hemopoiesis and macrophage system during phylogeny and ontogeny showed her contemporary concept that lymphocytes and macrophages originate in the bone marrow from a common hematolymphoid precursor.

In the paper "The secret of epigenetics and its implication for cell therapy" (2007), Prof. Kristeva postulates that since the morphogens selectively unlock new genes, it will be possible production of morphogens and selective trans-differentiation of adult patient cells *in vitro*.

Obtaining pluripotent embryonic cells from patient cells *in vitro*, and production of such nutrient medium, named "cloning medium" will be indisputably very profitable.

On the basis of her erudition and fundamental knowledge in embryology, cell differentiation and genetics, she published few articles in journal Stem Cells and Development, entitled: "Morphogens Reveal the Appearance and Function of lncRNAs" (2015) and "Correspondence on: A Hyaluronic Acid-Rich Node and Duct System in which Pluripotent adult Stem Cells Circulate" (2016). She hypothesized that the nuclear HOX proteins bind the mRNAs and suppress translation turning them into lncRNAs. This new compound (HOX protein + mRNA) is a morphogen, which explains in a very elegant manner the molecular mechanism of cell differentiation and the great and multifaceted repertoire of RNAs. According to Prof. Kristeva this scientific data open great possibilities for further research in the field of gene engineering giving the manner of producing morphogens *in vitro* for cell therapy. In this article she concluded that the transcripts of each gene may be coding or non-coding, depending on the proteins they bind. The morphogenesis (mRNAs bind with HOX proteins) in the embryonic cells (blastomere) are synthesized in the oocyte and during the cleavage

segregate in a special order in the blastomere, determining the body plan of the future embryo. The morphogens make the early embryo cell pluripotent. The two elements – HOX proteins and non-coding RNAs applied separately cannot work as morphogens.

Prof. Kristeva declared the great discovery she made studying the meiosis. She knew that her hypothesis will face extreme opposition within the scientific community. However, on the basis of her half-century-long scientific career, she was obligated to share her knowledge with younger scientists to achieve a deeper insight into the evolution of the immune system.

A remarkable Editorial's note on her last article was: "She was an accomplished embryologist who maintains a vigilant survey of the interpretation of key results in the field of phylogeny and ontogeny of hematopoietic, lymphopoietic and macrophage systems as well as of stem cell research".

Nevertheless, working in United States for many years, Prof. Kristeva always published her articles on behalf of Institute of Morphology, Bulgarian Academy of Sciences, thus presented our science in the world. She never lost her connections with all her former students and collaborators. With her vitality, enthusiasm, goodwill and encyclopedic knowledge, Prof. Kristeva never will be forgotten. By her death Bulgarian Academy of Sciences as well as Bulgarian Morphological School lost a great scientist.

*Yordanka Martinova*