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Modern Trends and Scientific Contributions of IEMAM—BAS to Modelling of the Life Processes *in Vitro*

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The article presents the history and the development of the ideas in the field of the modelling of the life processes in vitro during the last 68 years in the Institute of Experimental Morphology and Anthropology with Museum (IEMAM) — Bulgarian Academy of Sciences in Sofia.The aim of the authors is to systematise, analyze and discuss the modern trends and scientific contributions published in the scientific works in the IEMAM—BAS. In Bulgaria the method of tissue cultures was introduced by academician A. I. Hadjioloff in 1938. Later his Bulgarian scientific morphological school created many original methods and obtained important results for the theory and practice.

Key words: tissue cultures, growth factors, monoclonal antibodies, biotechnology.

The modelling of the life processes in vitro is an important and actual medico-biological problem. In the Institute of Experimental Morphology and Anthropology with Museum in Bulgarian Academy of Sciences (IEMAM — BAS) these investigations have nearly 68 years history.

The aim of the present study is to systematize, analyze and discuss the modern trends and scientific contribution in the field of the modelling of the life processes in vitro, published in the scientific works in the IEMAM — BAS during the last 68 years.

In our research the development of these conceptions and ideas were arbitrary divided into four periods: The first period is period of origin of the ideas —since 1938 till 1965. The method of tissue cultures was introduced in Bulgaria by academician A. I. Hadjioloff in 1938 [7]. In 1955 professor J.Jordanov suggested a new method for using the vitelline membrane as a sole for cultivation of tissue fragments and tumor cells. He has first used the yolk membrane of hen egg and other artificial semi-permeable membranes (collodion) in tissue cultures. In 1959 professor J. Jordanov developed a new original method for preparation of nutritional media based upon yolk dalysates [8, 9]. In the first period academician A. I. Hadjioloff and his Bulgarian scientific morphological school created many original methods and obtained important for the theory and practice results.

Second period is empirical — since 1966 till 1976. In 1966 Professor J. Jordanov developed an original modification of New's method, using celoidin membranes.

Later Professor J. Jordanov and P. Angelova applied in 1974 agar organ cultures upon celoidin membranes. They studied the impact of drugs upon the differentiation of bird and mammalian gonads in vitro. The scientific investigations and contributions of Dr. P. Angelova, Dr. L. Kancheva, professor J. Jordanov, Y. Martinova, professor M. Anastasova-Kristeva and academician A. Hadjioloff concern the morpho-functional differentiation of avian and mammalian embryonic, pubertal and adult gonads, in vivo and in vitro. Their works in the field of tissue culture are related especially to the mechanisms of regulation of the gonado- and gametogenesis [1, 10].

The third period is biotechnological - since 1977 till 1992. Professor J. Jordanov, P. Angelova, A. Boyadjieva. M. Kristeva cultured in vitro mammalian gametes and zygotes. They showed the important and original criteria of viability of the oocytes and zygotes for the in vitro fertilization and after cryoconservation. P. Angelova and M. Davidoff demonstrated the cellular localization of substance P and neuron-specific enolase-like immunoreactivity of mammalian Leydig cells in tissue sections and cell cultures. They observed that substance P has a modulatory effect on steroid production by foetal, immature and mature gonads of both sexes. A comparison of these results with data obtained in vivo and in vitro suggests that Leydig cells may be related to the APUD — or the diffuse neuroendocrine system [2].

Professor I. Goranov, E. Nikolova, M. Bratanov and A. Rusinova introduced in IEMAM—BAS the hybridoma biotechnology for production of monoclonal antibodies [12, 14]. They developed the methods for production of monoclonal antibodies against certain viruses and ricketsiae that caused the tick encephalomyelitis and yellow fever. The authors generated monoclonal antibodies against lymphocyte membrane markers involved in the recognition and presentation of the cells of the immune system.

M. Christova and E. Zaprianova investigated myelination and demyelination in tissue cultures. Their comprehensive studies into the same brain structures in vivo and in vitro suggest that myelinogenesis in tissue cultures has one of the same duration and periodicity as in vitro. Tissue cultures from the central nervous system are suitable model for studying the pathogenesis of demyelinating diseases and the important problems of neurobiology [5].

The last period is period of intensive development and broad application of in vitro biotechnology in biology and medicine - since 1993 and during 21st century. A. Rusinova, L. Kancheva, N. Atanassova generated new monoclonai antibodies against rat testicular antigens. They showed that the synthesis and cell specificity of antigens depend on the testicular development [3, 16]. L. Kancheva et al. demonstrated the expression of different proteins from cultured Sertoli cells of the mammals during different stages of the prepubertal period [11]. The effect of the vasoconstrictive peptide endothelin — 1 (ET-1) synthesized by and release from porcine granulosa cells on the ovarian steroidogenesis (progesterone production) was examined in vitro by R. Denkova et al. The authors elucidated the putative role of the neuropeptide in the regulation of the steroid secretion. Their findings suggested that ET-1, present in the follicular fluid may play an important role in the local regulation of progesterone production [6]. E.Yaneva et al. showed that ET-1 suppressed basal and FSH-stimulated progesterone production by ovarian granulosa cells, but this effect is not mediated by prostanoids [19]. K. Baleva - Ivanova et al. investigated the direct toxic effect of the Lindane on embryonic chick gonads during ontogenesis in organ culture [4].

D. Kadiysky et al. showed original results for in vitro cellular interrelationships between nervous and immune system [20].

Prof. E. Nikolova et al. studied the development of the systemic and mucosal

immune systems and the morphogenesis of the digestive tract in organ and cell cultures with application of milks' liquid and cellular factors [13].

V. Ogneva et al. established that the biologically active substances: fibroblast growth factor, epidermal growth factor, cholecystokinine stimulated the proliferation of the epithelial pancreatic cells during embryonic and postnatal development [15].

E. Zvetkova et al. determined the influence of haematopoietic growth factors and biologically active substances stimulating the formation of bone marrow colonies [18]. E. Nikolova, E. Zvetkova et al. reported an enhanced cell activation and basal cell proliferation of human and mouse peripheral blood T-lymphocytes in vitro and in vivo by using Vietnamese Crinum latifolium (L.) extracts [17].

During the last 68 years the most outstanding Bulgarian morphologists worked in IEMAM-BAS with their wide interests, original ideas and international recognition in the filed of modeling the life processes *in vitro*.

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