

Introduction

It is a great pride and privilege that we can present this special issue of *Physiological Research* as a representative publication of the Institute of Physiology (Academy of Sciences of the Czech Republic, Prague) to the 50th anniversary of its foundation (January 1, 1954). Actually, the Institute belongs to the leading institutions for biomedical research in the Czech Republic. In the course of its fifty-year-history has developed its priorities represented by numerous projects in the field of **neurophysiology**, **cardiovascular physiology** and **molecular and cellular physiology**. A marked shift in experimental approaches from the system and organ levels to the molecular and cellular levels is apparent in all these research directions. This shift reflects the worldwide trends influenced by rapid development of molecular biology, particularly by the techniques of genetic engineering applicable not only in the basic, but also in the clinical research. This fact is also reflected in the composition of teams, which currently consist not only of physicians and biologists, but also of molecular biologists, physical chemists and mathematicians. The final goal of all research groups is to incorporate the new findings into the theoretical basis of human medicine.

It can be documented that many specific topics, currently investigated in the Institute, reach the level of European quality. Two research directions, belonging to absolute top level in the world, can be found among the number of unique technical approaches developed in the Institute. The first direction, based on a long-lasting history of the Institute, is the ontogenetic approach to questions connected with pathogenesis of serious civilization diseases, such as ischemic cardiac disease, metabolic syndrome, hypertension and obesity. The term "critical developmental period" was established in the world scientific literature by researchers of the Institute in the sixties of the last century. This approach currently represents a general biological law – the theory of "developmental time windows", which explains, why influencing the organism in the earliest phases of its

development (both prenatally and postnatally) can determine many changes detected in the adulthood. It is evident that mutual interaction of the genetic and environmental factors plays a crucial role in this process. The second top approach is systematic development of unique biomodels, which can help to generate various therapeutic and preventive approaches applicable in human medicine. A very unique position from the global perspective is assumed by a set of inbred recombinant rat strains, derived from the F₂-generation of hybrids between the spontaneously hypertensive rat (SHR) strain and normotensive Brown Norway (BN) rats. The original genetic material created in this way is used for mapping the genes not only in the Institute, but also in collaborative projects with many prominent laboratories in Europe, U.S.A. and Canada. In addition to this the Institute owns a number of other biomodels, which are used in physiological and pathophysiological studies and serve for preparation of tissue cultures or isolated organs.

In the field of **neurophysiology**, the most important results come from the experimental work investigating the structure, function and pharmacological properties of membrane receptors (chemically activated ionic channels and receptors coupled with G-proteins). At the system level this research considerably extended the current knowledge of the role of these receptors in transmission of information from the peripheral to the central nervous system and about their involvement in the genesis of pathological changes in the central nervous system. This applies to the relationship between the vanilloid receptor function and perception of pain, to the role of metabotropic and ionotropic glutamate receptors in the mechanisms of epileptogenesis and to the prevention of neurodegeneration accompanying their disrupted functioning. The contribution of research into the role of muscarinic receptors in the pathogenesis of the Alzheimer disease is widely recognized. Unique findings were obtained in research concerning 1) circadian synchronization of the biological clock, 2) rhythm of

body functions, 3) mechanisms of memory trace formation and 4) central nervous system structures involved in spatial orientation and navigation.

Studies in *cardiovascular physiology* concentrate on the genetically or hormonally induced changes in the metabolism of lipids, leading to pathogenesis of many serious cardiovascular complications such as metabolic syndrome, hypertension and atherosclerosis. Particularly significant are the findings of protective influence of chronic hypoxia on the resistance of myocardium to the decreased supply of oxygen and the ontogenetic studies, yielding high-priority information for pediatric cardiosurgery. Closely related to these problems is the chemical analysis of the protein structure during aging and hypertension and three-dimensional reconstruction of the vascular bed with confocal microscopy. It is a complex research, connected with a number of university laboratories and research institutes. The most recent findings from the field of searching the candidate genes and chromosomal *loci* relevant for hypertension can be compared to findings of other world groups studying this problem. Moreover, these findings emphasize the problem complexity and the importance of the genetic background on which the influence of a particular gene is studied. The next priority is presented by studies in the field of influence of physical and chemical factors on the adhesion of vascular smooth muscle cells as well as of sexual differences in the reactivity of these cells to the vasoactive substances.

Many important results are also obtained in the field of *molecular and cellular physiology*. Particular attention is paid to the energy metabolism, where a prominent place is assumed by the study of the role of mitochondria in the synthesis of assembler proteins, which enable diagnosis of currently intractable mitochondrial diseases, and of uncoupling proteins, potentially applicable in the treatment of obesity. Study of the role of uncoupling proteins belongs to the most significant programs of the Institute, which is documented by the number of publications. The most recent results include findings about the role of these proteins in the protection of cells against free oxygen radicals. Substantial attention is also

paid to membrane receptors coupled with G-proteins, which play an important role in the development of the brain and myocardium. The crucial theoretical result is the determination of the complete molecular structure of the ATP-binding site of the Na⁺, K⁺-ATPase.

In cooperation with the universities, the Institute serves as educational and training center for pregradual and postgradual students in biomedicine and other associated fields. Considerable efforts of the management are directed towards transformation of the Institute in such a way that it will represent an institution where the theoretical basis of modern integrated medicine will be assembled and which will be able to offer to new coming scientists the possibility to practice their laboratory work. This is one of the major practical contributions of the Institute. Recently, the Institute became the principal investigator of the large Grant PhD Project (Grant Agency of the Czech Republic), which brings together PhD students of the Institute and the universities. At the same time the Institute is the principal investigator of the Center for Cardiovascular Research, where clinically relevant cardiovascular dysfunctions are studied from the point of view of diagnostics, therapy and prevention. In this center the specialists from the Institute closely collaborate with those from the Second Medical Faculty of the Charles University and the Institute of Clinical and Experimental Medicine. The Institute is also a co-investigator of two other centers, namely the Center for Genomics and Center for Neuropsychiatric Studies.

In addition to these scientific activities, the Institute guarantees the Animal facilities, Scientific Information Center, Department of Biomathematics and Department of Radiology. These departments provide services to the applicants from academical and non-academical institutions. The Institute is an administrator of internet network for the whole campus Krč and for some external users.

I would like to express special thanks to all my colleagues who have actively contributed to this special issue. I am glad that this issue presents the recent work of our Institute.

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Director