From genes to development: phenogenetic contributions to developmental biology in Soviet Russia from 1917 to 1967

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"To put the problem in an extreme form, if we had access to all genetic information in the egg and knew all the genes in detail, could we compute the animal to which it will give rise?".

L. Wolpert (1993)

Introduction

At present, the sentence "genes control development" is trivial. Genetics deal with how genes are passed on from parents to offspring, and we already know about the basic molecular and genetic mechanisms governing this process. Although much less well understand is how genes regulate embryonic development, morphogenesis and cell differentiation, we know at least about the so-called master genes, controlling the development of different organ systems in many organisms (see Gehring, 1996).

At the beginning of the 20th century, genetics appeared to new generations of biologists as the most popular biological discipline

of the time. However, the physical nature of genes and the mechanisms of gene action in development were completely unknown. An analysis of gene action using traditional genetics required accumulation of the mutants that affect well-defined ontogenetic processes. Such approach to early embryonic development in vertebrates was difficult because amphibians, the most popular experimental animals in embryology at that time, were non-starters for genetic analysis owing to their large genome sizes and long generation time. Sea urchins or chickens, were also non-starters in genetic terms. Among vertebrates, the mouse had certain advantages. However, mutations in key genes controlling early mouse development often produced embryonic lethal phenotypes which could not easily be studied in the 1920s-1930s.

For an integral genetic and developmental study, the fruitfly, *Drosophila melanogaster*, had many beneficial advantages. For these reasons, *Drosophila* has been introduced as a model organism on which a large-scale screen of mutations disrupting embryonic development could be carried out. *Drosophila* has been intensively used in research and over a short time a number of

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Fig. 1. Nikolai Konstantinovich Kol'tsov (1872-1940). As a scientist, N. K. Kol'tsov excelled in several fields of study: he not only launched a new era of molecular genetics (hypothesis about molecular structure and replication of "hereditary molecules") and helped to focus scientific attention on phenogenetics, but also pioneered and supported research in developmental genetics and developmental physiology in Russia.

"developmental" mutations have been observed and the mutants collected. However, work with *Drosophila* has shown that it was not possible to deduce the developmental program from expression of individual traits (genes) alone (note that the geneticists of that time could only work with mutants which were viable as adults). Some features of *Drosophila* gene expression that were not seen in vertebrates suggested that genes and genetic pathways involved in fruitfly development were not deployed during embryogenesis in other species. The situation was made more complex by general genetic background extending from the T. Morgan Genetic School. Scientists in the two fields (i.e., genetics and embryology) had different ways of thinking, speaking, and experimenting (Gilbert *et al.*, 1996). Because of this confusion, the embryologists concentrated their attention on morphogenetic interactions, patterns of organogenesis, morphogenetic fields, etc.

Although we cannot point to one single genius determining the conceptual development of experimental embryology in the 20th century, it is necessary to note Spemann's Nobel prize-winning discovery, the so-called "organizer experiment", which was the dominant tool in developmental biology during the 1930s-1950s (see Saxen and Toivonen, 1962; Tiedemann, 1978; Mikhailov, 1984) and is, at present, starting a renaissance period (Mikhailov, 1988; Jessell and Melton, 1992; Harland, 1994; Wilson and Hemmati-Brivanlou, 1997). Since the late 1980s, molecular studies have identified many of the gene products necessary for embryonic induction of mesoderm and neural tissue. Genetic

analysis has been instrumental in identifying the molecules that function downstream of the inducing agents and their receptors (see Lemaire and Kodjabachian, 1996). However, the problem is not so simple. For example, the parent T-box gene, *Brachyury* (Greek for "short tail" or "tail"-T) has been studied for more than 70 years and yet it is still not clear how the factor encoded by *Brachyury* alters mesoderm induction and differentiation (see Smith, 1997).

In the 1920s-1930s, H. Spemann and his colleagues focused on identification and analysis of the tissues with axis-inducing activities. Embryological manipulations demonstrated that communications between the mesoderm and ectoderm were required for normal embryonic development and patterning. Moreover, these studies identified specialized signaling centers that "organize" a patterning of the embryo. In spite of all this, the thinking was generally based on the concept of "morphogenetic fields" that had been introduced by A. Gurwitsch (1923; see also Beloussov et al., 1997 in this volume). As a result, many researchers at the time, including several Russian embryologists, concentrated upon experimental embryology (mechanics of development) and were skeptical of genetic approaches for analysis of embryonic development (from a modern point of view, it is surprising that genetic ideas and methodology were of no importance in the work of embryologists).

Meanwhile, in the 1920s, the problem of genetic mechanisms underlying individual development, i.e. ontogenesis, already attracted the attention of prominent Russian geneticists.

Our commentary is dedicated to the N.K. Kol'tsov' and B. L. Astaurov' scientific Schools which have been leaders of what is generally regarded as the foremost research groups in the Soviet Russia working on phenogenetic aspects of embryonic development. The purpose of our short paper is not to trace the genetic



Fig. 2. N. V. Timofeev- Ressovskii (1900-1981).

studies in that time in detail. Our task consists in writing a commentary on developmental genetics in Russia from 1917, the year of organization of the Institute of Experimental Biology by N.K. Kol'tsov, to 1967, when the Institute of Developmental Biology was founded by B.L. Astaurov. More recent works and names of Russian developmental geneticists are already well-known internationally.

Phenogenetic investigations in the USSR in the 1920s-1930s

With the emergence of the first genetics groups in Moscow and Leningrad, the problem of genetic control of ontogenesis became a most important topic in Russian biology. B. L. Astaurov (1972) noted: "... as distinct from Drosophila geneticists of the American School of T. H. Morgan, all of whose attention was fixed (and in this lies their great merit) upon the development of the chromosome theory of inheritance, upon the genes themselves and their chromosome localization, upon the regularities of hereditary transmission, the interest of our first geneticists was, to a significant degree, concentrated on the regularities of manifestation and expression of the genes in the phenotype, and consequently on the questions of the effect of the gene on development". In the early to mid 1900s, many Russian geneticists were internationally noted for numerous contributions to phenogenetics and developmental genetics. In Europe, the famous German geneticist R. Goldschmidt, against the influence of the T. Morgan School, also developed ideas towards the ontogenetic role of genes (see, Goldschmidt, 1927).

The first scientific center, which became the focal point of investigation into the genetic mechanisms of ontogenesis, was organized in Moscow in 1917; this was the "Kol'tsov's" Institute of Experimental Biology, which in 1920 was affiliated to the State Department of Public Health ("Narkomzdrav"). Its director, a corresponding member of the St.-Petersburg Academy of Sciences, Professor N. K. Kol'tsov (1872-1940; Fig. 1), who headed the Institute up to 1939, was a founder of genetics in our country. In 1938, owing to political pressure, N. K. Kol'tsov was made to leave his post, and the Institute was transferred to the USSR Academy of Sciences and renamed as the Institute of Cytology, Histology and Embryology. This meant that the genetic profile of the Institute started to fade, and was gradually replaced by broad cell biological investigations. However, some phenogenetic studies initiated by N. K. Kol'tsov were continued in the Institute until the notorious "VASKHNIL" (the V. I. Lenin All-Union Academy of Agricultural Sciences) Session (1948) and the coming of T. D. Lysenko to power in Soviet biology. Note that, in spite of communistic distortion of social and intellectual life, for a long time (1917-1937) the "Kol'tsov's" Institute characterized by its stimulating human and scientific atmosphere, attracted students and scholars from many parts of the country who made important contributions to experimental genetics, phenogenetics and embryology. In addition to N. K. Kol'tsov and his collaborators, there were D. P. Filatov, the famous Russian embryologist, who was working on the problems of the so-called "mechanics of development" (Filatov, 1941; see also Dettlaff and Vassetsky in this volume) and his students (among others, T.A. Dettlaff and G. V. Lopashov) who followed the footsteps of their mentors and did creditable works in experimental and comparative embryology (Lopashov, 1936; Dettlaff, 1940).

Kol'tsov's student, N. V. Timofeev-Ressovskii (Fig. 2), who obtained a number of important data on the genetics of *Drosophila*



Fig. 3. P. F. Rokitskii (1903-1977).

development, played an essential role in the formation of phenogenetic research in our country (see Timofeev-Ressovskii, 1934). He showed that the genotype, in the process of its "realization" during ontogenesis, acts as an integral system. In particular, he demonstrated the influence of temperature on the phenotype manifestations of vti mutation in D. funebris development. Sharp changes of temperature at various stages of ontogenesis provoked a broad variation in phenotype manifestation of the trait: from its elimination to its complete restoration. N. V. Timofeev-Ressovskii and his collaborators formulated such fruitful concepts as "gene expressivity" and "penetrance of the gene" and explained phenotype variability in the trait manifestations by influence of genesmodifiers (see Timofeev-Ressovskii and Ivanov, 1966). Studying vti mutation, they described numerous cases of coincidence and non-coincidence in the manifestation of different bilateral traits, a problem to which B. L. Astaurov made afterwards a great contribution. As it has turned out, all these cases could be classified in the following manner: (1) symmetry: the trait is equally manifested on both sides (high positive correlation may be observed); (2) dyssymetry: there is an incomplete positive correlation between the trait manifestations on the right and on the left; (3) asymmetry: equally probable one-side manifestation of the trait(s) can only be observed; (4) dys-anti-symmetry: manifestation of the trait on one side reduces the degree of its manifestation on the other; and (5) anti-symmetry: the manifestation of the trait on one side excludes its manifestation on the other (as a result, complete negative correlation is observed). The data obtained by N. V. Timofeev-Ressovskii and B. L. Astaurov on phenotype variability of inherited traits harmonized with interesting studies performed by E.I.



Fig. 4. I. I. Shmal'hausen (1884-1963).

Balkashina at the end of the 1920s. She discovered the important morpho-physiological *arispopedia* mutation, i.e., the transformation of the arista into a leg with a claw (Balkashina, 1928); later, such mutations were widely used in developmental genetics.

P.F. Rokitskii (Fig. 3), who demonstrated that the development of an individual trait in *Drosophila* is controlled by many genes, i.e., by sequential genetic interactions, which manifest themselves in concrete environmental conditions, found that the effect of gene, in various body segments/parts, had different phenotypic (developmental) significance. On the basis of these and related results, he introduced the concept of "field of gene action" in developmental genetics.

It can be said that the idea, according to which development of the trait is determined by interactions between a "basic" gene and genes-modifiers, has been experimentally confirmed in the works of N. K. Kol'tsov, S. S. Chetverikov, the husband and wife, N.V. and E.N. Timofeev-Ressovskii, N. K. Belyaev, P.F. Rokitskii, as well as, D.D. Romanov, E. I. Balkashina, A. N. Promptov, and S.R. Tsarapkin. As a result of their analyses, two general principles were formulated: (1) each gene has influence on all traits of the organism (although its influence on certain traits may be very small), and (2) any trait of the organism depends on the "common" genotype as a whole (although the trait dependence on certain genes may be practically insignificant) (see Astaurov, 1968; Korochkin and Konyukhov, 1987).

After the initiative of N. K. Kol'tsov, studies on sex regulation in the silkworms were started in the 1930s. Subsequently, the silkworm became a favorite experimental subject of B.L. Astaurov, who achieved outstanding results. B.L. Astaurov solved the problem of artificial parthenogenesis in these animals and succeeded to obtain exclusively females. Moreover, the use of artificial parthenogenesis made it possible to produce triploid and tetraploid silkworms. These tetraploids were the first artificially obtained tetraploid animals capable of reproduction in the course of several generations (Astaurov, 1940, 1967).

N. K. Belyaev, who worked in close collaboration with B.L. Astaurov in the 1920s-1930s, was among the first ones to study the integrate "genetic/physiological" mechanisms of phenotype trait variability in the course of ontogenesis. Studying pigmentation in the caterpillar, *Spilosoma lubriciped* Esp., he demonstrated that the intensity of pigmentation depended on temperature. He also found that the effect took place only at temperature-sensitive stages of development which coincided with moulting. N.K. Belyaev suggested that temperature changes could provoke a "chronological discordance" with respect to timing of development and pigmentation: at moult stage, relatively high temperature accelerated moulting, but not pigmentogenesis, as a result of which coloration was lightened (Belyaev, 1926).

The idea about genetically conditioned temporal discordance of individual development was developed by a student of A.N. Severtsov, I.I. Shmal'hausen (Fig.4). According to the Shmal'hausen's conception of correlation systems, morphogenetic changes are often associated with effects of mutant genes, and an adequate chronological ontogenic correlations, which were formed in the course of evolution between the developmental pattern formation of different tissues/organs, are disrupted. Domestication of animals, when the previously existing natural correlations are lost and new correlations are established instead, is an example of such "chronological" disintegration. Smal'hausen always noted the significance of communications between embryonic cells of different origin and different developmental history (including embryonic inductions) for normal organized development and suggested that differential gene activity could be based on the different developmental states of the target (responding) tissue (Smal'hausen, 1937, 1982).

Among the Leningrad geneticists, the group headed by the famous geneticist Yu.A. Filipchenko (N.N. Medvedev, M.E. Lobashev, Yu.M. Olenov, Yu.Ya. Kerkis, P.P. Kanaev, V. M. Isaev, Ya.Ya. Lusis, and others) concentrated on the key problems of human genetics, genetic bases of animal and plant selection, and phenogenetic aspects of ontogenesis. Yu.A. Filipchenko suggested that the differences between two organisms could be determined at different genetic levels, namely: (1) by tissuespecific traits (genes) which are usually activated at the advanced stages of development and can be detected using the methods of Mendel's analysis, and (2) by a whole genome (or, to be more precise, nuclei and cytoplasm of the gametes) controlling the earliest stages of individual development (see Filipchenko, 1932). Such dualistic point of view on genetic regulation of development has been criticized by N. N. Medvedev. Studying the development of Drosophila 's eye, N. N. Medvedev showed that genes control the earliest stages of organogenesis, and the size of a future organ is genetically determined at the moment of its anlage formation. In our country, N.N. Medvedev was a pioneer in using the method of imaginal disc transplantation (originally developed by G. Beadle and B. Ephrussi) in phenogenetic and ontogenetic investigations. Using this technique, he obtained very interesting data about genetic factors of pigment cell determination (see Medvedev, 1935).

Yu.Ya. Kerkis described in detail the rate of growth of gonads in Drosophila males and females. He also demonstrated that size-



Fig. 5. I. A. Rapoport (1912-1990).

reduction of the gonads in hybrid (*D. melanogaster* x *D. simulans*) males can cause their infertility (Kerkis, 1931, 1933).

One of the Kol'tsov's students, M. M. Zavadovskii, on the basis of his analysis of hormonal regulation of development, formulated the principals of genetic/endocrine theory of ontogenesis. Together with his collaborators (B. A. Kudryashov, L. V. Krushinskii, M. S. Mitskevich) he, already in the 1920s-1930s, was working on the endocrine mechanisms of animal development. In his monograph (1922) "Sex and the Development of its Traits", he concluded: "Equally potential male/female tissues are differentiated in the male ones under the action of testis hormone which we name "masculinizing", and in female ones under feminized action of ovary hormone, "feminizing". Just as the other students of N. K. Kol'tsov, M. M. Zavadovskii clearly recognized the fruitfulness of combining the ideas of genetics and embryology to solve the problems of pattern formation and organogenesis.

Interesting investigations on phenogenetics of development were carried out in the 1930s by I.A. Rapoport (Fig. 5). These studies demonstrated that, despite the intervening and overlapping of the effects of different genes, individual gene systems behave in many ontogenetic situations as a single whole (see Rapoport, 1941). At the end of the 1930s, I.A. Rapoport, on the basis of his investigations of *Drosophila* embryogenesis, prepared a book about genetic mechanisms of embryonic development, tissue determination and cell differentiation (see Rapoport, 1992-1993).¹⁾

The results of phenogenetic investigations in the 1920s-1930s were summarized by N. K. Kol'tsov in the article : "The Role of the Genes in Physiology of Development" in which the necessity of uniting genetics and embryology was specially pointed out: "... Unification of these two sciences with each other, as well as with

cytology and biochemistry, will create a single Science, which will be able to resolve general biological problems." (Kol'tsov, 1935).

Thus, the studies on the genetics of development had taken a great stride in our country already in the 1920s-1930s. Moreover, the results justified the expectations of further rapid progress of Russian genetics towards elucidation of complex problem of genetic regulation of individual development. However, this (the moment of triumph for genetic research in our country) coincided with a decline in such type of investigations. This was not due to dwindling of national or international interests to the problem, but to the forces of a much stronger nature. At the end of the 1930s, the intensifying intervention of the Soviet political ideology into biological science, as well as, legal or, in many cases, outlaw prosecutions of outstanding Russian geneticists as "carriers of reactionary (i.e., bourgeois) theory by A. Weismann and T. Morgan" (the socalled, "Weismannism-Morganism") subsequently modified the way of thinking of our biological community that resulted in stagnation of the Russian Genetic School. However, the negative political influences of the 1930s-1940s could not completely destroy genetics in our country. Although the financial and research conditions were miserable, and most students had to turn to studying classical embryology and morphology, some genetic research, in a masked form, continued. The rapid process of genetic revival in the 1950s could not have occurred without such a background.



Fig. 6. Boris L'vovich Astaurov (1904-1974). B. L. Astaurov was one of the most outstanding Russian researchers crossing the "gulf" between genetics and developmental biology. His trajectory demonstrated that not only talents and excellent experimental skills but also good luck and drive were needed to succeed in an interdisciplinary area, especially with little institutional infrastructure to support it.

¹¹ This book was not published at the time, and only in 1992-93, on the initiative of O.G. Stroeva, the manuscript entitled:»Phenogenetic Analysis of Independent and Dependent Differentiation» was published in «Ontogenez» (ATM).



Fig. 7. N. N. Sokolov (1902-1975).

Revival of genetics and phenogenetics in the USSR

The monopoly of T. D. Lysenko in biological science, and the general political atmosphere which existed in the post-Second World War USSR, had an extremely negative effect on the state of phenogenetics. After the 1948 Session of the "VASKHNIL" (Agricultural Academy), the genetic laboratories were closed and studies on genetics of development were practically prohibited.²)

Note that among the causes for the decline of genetic investigations, the Second World War and its aftermath in the USSR, as well as the subsequent years of distress and isolation from the international scientific community played only a subordinate role. This situation is part of our history and the history of our biology, but it had not only a historical impact. Developmental genetics in our country has never recovered from the loss of many outstanding geneticists. A gradual revival of genetics, including developmental genetics, began only at the end of the 1950s.

Brilliant investigations were carried out on the silkworm (1957-1970) by B. L. Astaurov (Fig. 6). For the first time, interspecific androgenic individuals, constituting unique "nucleo-cytoplasmic" hybrids, were obtained (their cytoplasm belonged to one parental species, and the nucleus, to the other). According to all morphoiogically and physiologically registered traits, such androgenic organisms were similar to the species from which the nuclei were transferred; no data about any influence of "maternal" cytoplasm upon the traits were obtained. The latter indicated the leading role of the nucleus in morphogenesis in higher eukaryotes (Astaurov and Ostryakova-Varshaver, 1957). Later, Kol'tsov's and Astaurov's ideas about sex regulation in animals were developed by V. A. Strunnikov. Using the method of artificial androgenesis, genetically identical copies of silkworm were obtained, and the androgenetic clone was converted to the ambisexual homozygotic line (see Strunnikov, 1971).

Analyzing *D. virilis* x *D. littoralis* hybrids, N. N. Sokolov (Fig. 7) showed that cytoplasmic characters reflected the features of the nuclei which were previously in it or are currently present in it. The species-specific properties of the cytoplasm are labile and they are altered in the course of development; gene products, received by the cytoplasm from the given species, are dispersed in F1 hybrids during early stages of their development, and they could not be restored in the previous (initial) form by the nucleus of the hybrid (Sokolov, 1959).

The morphogenetic function of the nuclei during early vertebrate development, now called midblastula transition, was discovered by A. A. Neyfakh. Using irradiation and/or PNA inhibitors, he obtained interesting data on the periodicity of the morphogenetic activity of the nuclei in the fish embryos (Neyfakh, 1962, 1970).

A group of phenogenetics was formed at the Institute of Medical Radiology of the USSR Academy of Medical Sciences in Obninsk under the direction of N. V. Timofeev-Ressovskii. Most his students (V. I. Ivanov, E. K. Ginter, V. A. Mglinetz, and others) came later to work at the Institute of Medical Genetics (founded in 1970 in the system of the USSR Academy of Medical Sciences), where they carried out investigations into phenogenetics of homeotic mutations in *Drosophila*.

The Institute of Cytology and Genetics was organized in 1958 in the Siberian Division of the USSR Academy of Sciences, and the investigations on the mechanisms of genotype-environment determination of fertility and viability of mammals were started in the



Fig. 8. D. K. Belyaev (1917-1986).

²⁾ At the time, a doctrine of the so-called «living substance» by O.B. Lepeshinskaya dominated oficially in the Soviet embryology and cytology. In the book» Cell: Its life and its Origin» published by «Goskul'tprosvetizdat» (Moscow) in 1952, Stalin proze laureate O.B. Lepeshinskaya wrote (pp.22): «...Academician T.D. Lysenko demonstrated that hereditary traits are transmitted (to offspring, ATM) not only by the chromosomes but also by any particles of the cell. Our works confirm this concept of T.D. Lysenko...Thus, individual development (ontogenesis) of the cell is realized, through several stages, from non-cellular living substance or from the living substance of maternal cells» (ATM).



Fig. 9. B.L. Astaurov (left) and D.K. Belyaev (right) at the 1st All-Union School on developmental genetics (July, 1969, Novosibirsk).

Laboratory of Evolutionary Genetics headed by D.K. Belyaev (Fig.8; see Belyaev, 1977). Later (in 1965) at this Laboratory, a developmental genetics group was organized (under the direction of L.I. Korochkin), and studies on genetics of behavior and developmental neurobiology were carried out. Using synthesis of malespecific esterase in the ejaculatory bulbs of *Drosophila* and of lactate dehydrogenase in erythroid cells of mammals as model systems, it was demonstrated that tissue-specificity of gene expression could be determined not only by differential activity of structural genes in different tissues/organs but also by specificity of the action of genes-modifiers (see Korochkin, 1977a, b).

In Leningrad, at the All-Union Institute of Experimental Medicine, investigations on the cytogenetics of mammalian development were initiated by A.P. Dyban. As a result, it was demonstrated that the chromosomal aberrations, which play an important role in pathogenesis of spontaneous abortions and developmental anomalies in humans, have a much more modest impact in embryonic mortality in mice and rats. A difference in the pre-zygotic selection of male/female gametes was found in mice. Male gametes with a chromosome deficiency either die or do not participate in fertilization; female gametes transit to their progeny various chromosomal aberrations. In the latter, however, monosomy is more rarely encountered in mouse embryos than trisomy (see Dyban, 1952, 1972).

Practically at the same time (in 1958), research into genetics of mammalian development was also begun by B.V. Konyukhov at the Institute of Experimental Biology of the USSR Academy of Medical Sciences. B.V. Konyukhov and his co-workers, studying the effect of mutant genes in mouse ontogenesis, obtained interesting results on the mechanisms of genetic control of eye morphogenesis. With the aid of mutant genes which block the growth of optic vesicle or retina, they demonstrated that lens-inducing activity of the optic vesicle/cup can provoke the activation of tissuespecific genes in lens presumptive ectoderm (see Konyukhov and Sazhina, 1962; Konyukhov, 1968).

At the Institute of Developmental Biology of the USSR Academy of Sciences which was organized in Moscow in 1967 on the initiative and under the direction of B.L. Astaurov, genetic investigations on the mechanisms of ontogenesis were especially expanded. In 1968, the Institute included laboratories: developmental cytogenetics (B.L. Astaurov); genetics ((B.N. Sidorov); experimental karyology (N.N. Sokolov); polyploidy (V.V. Sakharov); biology of reproduction and sex control (V. A. Strunnikov); biochemical embryology (A.A. Neyfakh); experimental embryology (T.A. Detlaff); organogenesis (G.V. Lopashov); hormonal regulations (M. S. Mitskevich), the "Kropotovo" biological station, etc. The station had been a part of "Kol'tsov's" Institute and in 1967 it was affiliated to the Institute of Developmental Biology, serving as the base for applied studies on sex control, parthenogenesis, androgenesis, experimental polyploidy, etc. In 1970, the journal "Ontogenez" was founded by academician B.L. Astaurov (at present, it is translated into English under the title "Russian Journal of Developmental Biology"). A lot of papers by Russian and foreign scientists on phenogenetics and developmental genetics have been published in the Journal.

In 1969, the first school on developmental genetics was organized in Nobosibirsk by Prof. L.I. Korochkin (as the president of the organizing committe) where leading scientists lectured on current problems of genetics and developmental biology (Fig.9).

In 1971 (July 8) at the session of the Section of Chemical, Technical and Biological Sciences of the Presidium of the USSR Academy of Sciences, academician B. L. Astaurov formulated the main directions of further investigations into molecular and genetic mechanisms of development (for the shorthand report, see Astaurov, 1989).

In 1976 the Institute was officially named after N. K. Kol'tsov -"the circle was locked", and it seemed to us that Russian developmental genetics does not belong to the arena of politics and policy. We will end here, leaving the characterization of the last 20-30 years of the Soviet/Russian developmental genetics to other contributors of this issue.

References

- ASTAUROV, B.L. (1940). Artificial Parthenogenesis in Silkworm. USSR Acad. Sci. Press, Moscow-Leningrad.
- ASTAUROV, B.L. (1967). Experimental alterations of the development: Cytogenetic mechanisms in mulberry silkworms. Adv. Morphogen. 6: 199-257.
- ASTAUROV, B.L. (1968). Developmental Cytogenetics of Silkworms and its Experimental Controlling. Nauka Press, Moscow.
- ASTAUROV, B.L. (Ed.). (1972). Problems of Developmental Genetics. Nauka Press, Moscow.
- ASTAUROV, B.L. (1989). Perspectives of the investigations into molecular basis of developmental biology. Ontogenez (Russ. J. Dev. Biol.) 20: 5-21.
- ASTAUROV, B.L. and OSTRYAKOVA-VARSHAVER, V.P. (1957). Complete heterospermic androgenesis in silkworms as a means for experimental analysis of the nucleus. *Cytoplasma Probl.5*: 449-462.
- BALKASHINA, E.I. (1928). Case of heredity homeosis (gene variation). Aristopedia in D. melanogaster. J. Exp. Biol. (Russ.) Ser.A, 4: 93-106.
- BELOUSSOV, L.V., OPITZ, J.M. and GILBERT, S.F. (1997). Life of Alexander G. Gurwitsch an his relevant contribution to the theory of morphogenetic fields. Int. J. Dev. Biol. 41: 771-779
- BELYAEV, D.K. (Ed.) (1977). Problems of Experimental Biology. Nauka Press, Moscow.
- BELYAEV, N.K. (1926). Experimental study of variability of coloration in the caterpillar, *Spilosoma lubricipeda* Esp. (Aritudae, Lepidoptera). J. Exp. Biol. (Russ.). Ser.A, 2: 157-219.
- DETLAFF, T.A. (1940). Peculiarities of Anuran ectoderm. Proc. USSR Acad. Sci. (Dokl. Akad. Nauk SSSR) 28: 669-672.
- DYBAN, A.P. (1953). The Essays on Human Pathological Embryology. Medgiz, Leningrad.

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- DYBAN, A.P. (1972). Cytogenetic aspects of normal and pathological embryogenesis in mammals. In *Problems of Developmental Genetics*. Nauka Press, Moscow, pp.62-85.
- FILATOV, D.P. (1941). On the historical approach to the events of developmental mechanics and its importance. J. Gen. Biol. 2: 3-18. (Russian).
- FILIPCHENKO, YU. A. (1932). Experimental Zoology. "Medizdat"; Moscow-Leningrad.
- GILBERT, S.F., OPITZ, J.M. and RAFF, R.A. (1996). Resynthesizing evolutionary and developmental biology. *Dev. Biol.* 173: 357-372.
- GEHRING, W.J. (1996). The master control gene for morphogenesis and evolution of the eye. Genes to Cells 1: 11-16.

GOLDSCHMIDT, R. (1927). Physiologische Theorie der Vererbung. Springer; Berlin.

- GURWITSCH, A. (1923). Versuch einer synthetischen Biologie. Schaxeis Abh. Z. Theor. Biol. 17: 1-77.
- HARLAND, R.M. (1994). Neural induction in Xenopus. Curr. Opin. Genet. Dev. 4:543-549.
- JESSELL, T.M. and MELTON, D.A. (1992). Diffusible factors in vertebrate embryonic induction. *Cell* 68: 257-270.
- KERKIS, YU. YA. (1931). The growth of the gonads in Drosophila melanogaster. Genetics 16: 212-224.
- KERKIS, YU. YA. (1933). Development of the gonads in hydrids between D. melanogaster and D. simulans. Genetics, 26: 177-502.
- KOL'TSOV, N.K. (1935). The role of the genes in physiology of development. Biol. J. 4: 753. (Russian).
- KONYUHKOV, B.V. (1968). Biological Modeling of Human Hereditary Diseases. Meditzina, Moscow.
- KONYUKHOV, B.V. and SAZHINA, N.V. (1962). Eye development disturbance in a line of mice with microphthalmia (Blind mutation). J. Gen. Biol. 23: 256-264. (Russian).
- KOROCHKIN, L.I. (1977a). Gene Interactions in Development. Nauka Press, Moscow (English translation by Springer, 1981).
- KOROCHKIN, L.I. (1977b). Phenogenetic studies of the laboratory of genetic basis of individual development of the Institute of Cytology and Genetics (Siberian Division of the USSR Academy of Sciences). Ontogenez (Sov. J. Dev. Biol.) 8: 91-95.
- KOROCHKIN, L.I. and KONYUKHOV, B.V. (1987). Genetics of animal development. Genetics (Moscow) 23: 1762-1769.
- LEMAIRE, P. and KODJABACHIAN, L. The vertebrate organizer: structure and molecules. *Trends Genet.* 12: 525-531.

LOPASHOV, G.V. (1936). Eye-inducing substances. Biol. J. 5: 463-488. (Russian).

MEDVEDEV, N.N. (1935). Genes and development of the traits. Proc. (Trudy) of

Genetic Institute 10: 120-151.

- MIKHAILOV, A.T. (1984). "Morphogens": Experimental illusion or reality? Ontogenez (Sov. J. Dev. Biol.) 15: 322-350.
- MIKHAILOV, A.T. (1988). Embryonic Inducers. Nauka Press, Moscow.
- NEYFAKH, A.A. (1962). The Problem of Interactions of the Nucleus and Cytoplasm in Development. Inst. Animal Morphol., Moscow.
- NEYFAKH, A.A. (1970). Functions of the genes in development and the mechanisms of their activation. J. All-Union Chem. Soc. D. I. Mendeleev 15: 612-634. (Russian).
- RAPOPORT, I. YA. (1941). On the law of distribution and extinguishing of gene action. Proc. USSR Acad. Sci. (Dokl. Acad.Nauk. SSSR) 31: 392-395.
- RAPOPORT, I. YA. (1992-1993). Phenogenetic analysis of independent and dependent differentiation (Laboratory of Cytogenetics). Ontogenez (Russ. J. Dev. Biol.) 23 (Nº 3-6) and 24 (Nº 1-2).
- SAXÉN, L. and TOIVONEN, S. (1962). Primary Embryonic Induction. Logos Press; London.
- SMAL'HAUSEN, I.I. (1937). Actual problems of phenogenetics. News (Izvestiya) of the Dept. Math. Natur. Sci. of the USSR Acad. Sci. Ser. Biol. 3:895-906.
- SMAL'HAUSEN, I.I. (1982). Organism as a Whole During Individual and Historical Development. Nauka Press, Moscow.
- SMITH, J. (1997). Brachyury and the T-box genes. Curr. Opin. Genet. Dev. 7: 474-480.
- SOKOLOV, N.N. (1959). Interactions Between the Nucleus and Cytoplasm in the Process of Remote Hybridization. USSR Acad. Sci. Press, Moscow.
- STRUNNIKOV, V. A. (1971). Actual and further problems in the using of genetic methods in silkworm breeding. In *Practical Aspects of Genetics in Agriculture*. Nauka Press, Moscow, pp. 343-360.
- TIEDEMANN, H. (1978). Chemical approach to the inducing agents. In Organizer. O. Nakamura and S. Toivonen (eds.). Elsevier, Amsterdam, pp. 91-118.
- TIMOFEEV-RESSOVSKII, N.V. (1934). Uber den Einflu (des genotypischen Milieus und Aubenbindungen uaf die Realization des Genotyps. Nachr. Ges. Wissensch. Göttingen Biologie. N.F. 1: 53-106.
- TIMOFEEV-RESSOVSKII, N.V. and IVANOV, V.I. (1966). Aspects of the phenogenetics. In Actual Problems of Modern Genetics. Moscow Univ. Press, Moscow, pp.114-130.
- WILSON, P.A. and HEMMATI-BRIVANLOU, A. (1997). Vertebrate neural induction: Inducers, inhibitors, and a new synthesis. *Neuron 18*: 699-710.
- WOLPERT, L. (1993). The Triumph of the Embryo. Oxford Univ. Press, p.3.
- ZAVADOVSKII, M.M. (1922). Sex and the Development of its Traits. Medizdat, Moscow.