A new perspective on Darwin’s Pangogenesis

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Received 24 July 2006; revised 10 December 2007; accepted 22 January 2008

ABSTRACT

In 1868 Charles Darwin proposed Pangenesis, a developmental theory of heredity. He suggested that all cells in an organism are capable of shedding minute particles he called gemmules, which are able to circulate throughout the body and finally congregate in the gonads. These particles are then transmitted to the next generation and are responsible for the transmission of characteristics from parent to offspring. If any cells of the parent undergo changes as a result of environmental change, they will consequently transmit modified gemmules to their offspring. Soon after Darwin’s pangenetic theory was published, Francis Galton designed a series of blood transfusion experiments on differently pigmented rabbits to test its validity. He found no evidence in support of the existence of Darwin’s gemmules and the concept of Pangenesis was largely abandoned. In this article, recent reports of successful induction of heritable changes by blood transfusion are reviewed. Detection of circulating nucleic acids and prions in plant sap and animal blood is considered as fresh evidence for the existence of gemmules. It is now apparent that a considerable revision of views on Darwin’s Pangenesis must occur before a new comprehensive genetic theory can be achieved.

Key words: Darwin, Pangenesis, genetics and evolution, blood transfusion, circulating DNA/RNA, prions.

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I. INTRODUCTION

Pangenesis is the mechanism proposed by Charles Darwin (1868) to explain heredity. He suggested that all cells in an organism are capable of shedding minute particles, or gemmules, which migrate through the body and finally congregate in the gonads, from where they are transmitted to the next generation. Whereas his theory of Natural Selection is now widely accepted, Pangenesis has been largely thought to be wrong and thus was excluded from the expanding science of genetics for more than a century, being now only of historical interest. Early blood transfusion experiments designed to test it (Galton, 1871) found no evidence for the existence of gemmules. During the 1950s and 1970s, however, several independent groups of biologists in the Soviet Union, France and Switzerland
found evidence for heritable changes induced by blood transfusion and DNA injection. More recent detection of circulating DNA and RNA in plant sap, as well as in the plasma and serum of healthy and diseased individuals has seemingly indicated the existence of gemmules. Thus it is timely to reconsider Darwin’s Pangenesis and to reassess its relevance to a comprehensive genetic theory.

II. DARWIN’S PANGENESIS: A DEVELOPMENTAL THEORY OF HEREDITY

Hippocrates (c. 400 B.C.), the father of medicine, is thought to have been the first to propose a pangenetic explanation for inheritance (Moore, 1993). Darwin built on Hippocrates’s ideas and extended them by specifying that gemmules were responsible for hereditary transmission, and applying Pangenesis to classes of facts unknown to the old philosopher (Darwin, 1888, p.82).

Darwin recognized that cells multiply by division, and that in so doing they preserve essentially the same nature. He considered that this rule forms the basis of heredity, but that it could not explain all of the observable phenomena such as the effects of use and disuse, the inheritance of acquired characters, graft hybridization, xenia, telegony, variation, development, regeneration, reversion or atavism, etc. In order to include all these phenomena, Darwin assumed that, in addition to cell division, there was another means of transfer of hereditary characters. He proposed that cells not only grow by means of cell division but are also capable of “throwing off” minute particles or molecules (gemmules) that are self-replicating, can move through the body, can vary in response to the environment and are capable of dormancy. He suggested that all cells of the body throw off gemmules throughout development and these gemmules are able to circulate throughout the body and enter the buds and the sex cells. In sexual reproduction, the transmission of characteristics from parent to offspring was explained as a consequence of the incorporation of these gemmules into gametes, and their development in the offspring. Cases in which the characteristics of one parent dominate he believed to be a consequence of that parent’s gemmules having some advantage in number, affinity, or vigour over those derived from the other parent. Thus Pangenesis explained Mendelian inheritance. Further, if the cells of one part of the body underwent change as a result of environmental change, they would consequently throw off modified gemmules, which could then be transmitted to the offspring. Thus Pangenesis can explain the inheritance of acquired characters or Lamarckian inheritance. Gemmules released in a stock plant would be transferred into a graft and incorporated into the sex cells and meristematic cells of the scion, resulting in heritable changes in the scion and its progeny; thus explaining graft hybridization, the subject of Michurinist Genetics.

Gemmules, like seeds or spores, are capable of transmission in a dormant state to successive generations, allowing a character to be expressed after several generations. Thus reversion is explained as a consequence of long-dormant gemmules becoming active. A reserve of gemmules in the tissues allows regeneration when parts are lost; malformations and monstrosities are due to gemmules reaching the wrong destination in the offspring. The fact that mutilations are not transmitted by inheritance is accounted for by the presence of sufficient gemmules from previous generations. In the case of xenia (the belief that previous matings of a female influence her later offspring by another male), it is the diffusion, retention, and action of the gemmules included within the spermatzoa of the first male that cause features of this male to manifest in offspring resulting from later matings with other males.

Characters that appeared only at a certain stage of development were explained as resulting from interactions between the developing cells and gemmules: “the organic units, during each stage of development throw off gemmules, which, multiplying, are transmitted to the offspring. In the offspring, as soon as any particular cell or unit in the proper order of development becomes partially developed, it unites with (or, to speak metaphorically, is fertilized by) the gemmules of the next succeeding cell, and so onwards” (Darwin, 1868, p.165).

In this way Pangenesis was used to explain observations pertaining to inheritance, variation and development.

Darwin's Pangenesis was based on the presence of gemmules but he had no real evidence for their existence (Moore, 1963). Darwin (1868, p.452) wrote that “the existence of free gemmules is a gratuitous assumption, yet can hardly be considered as very improbable, seeing that cells have the power of multiplication through the self-division of their contents”. No one had detected a gemmule; yet he was convinced that they must exist, because then the diverse and often puzzling phenomena of inheritance “jumped together” into a single explanatory scheme (Endersby, 2003).

Darwin proposed Pangenesis to explain how the variations arose upon which natural selection acted. When The Variation of Animals and Plants Under Domestication (Darwin, 1868) appeared, he was concerned how his readers would react to the theory. To Charles Lyell he wrote in 1867: “I have been particularly pleased that you have noticed Pangenesis. I do not know whether you ever had the feeling of having thought so much over a subject that you had lost all power of judging it. This is my case with Pangenesis (which is 26 or 27 years old), but I am inclined to think that if it be admitted as a probable hypothesis it will be a somewhat important step in biology” (Darwin, 1888, p.72). He assured Asa Gray that “The chapter on what I call Pangenesis will be called a mad dream, ...but at the bottom of my mind I think it contains a great truth” (Darwin, 1888, p.73). To Edwin Ray Lankester he wrote, “I was pleased to see you refer to my much despised child, ‘Pangenesis’, who I think will some day, under some better nurse, turn out a fine stripling” (Darwin, 1888, p.120).

III. CRITICISM OF PANGENESIS: GALTON’S EXPERIMENTS

Francis Galton greeted Darwin’s Pangenesis with enthusiasm, and set out to test the prediction that hereditary
particles circulate in the blood by using transfusion experiments on rabbits. In a first experiment, he injected defibrinated blood from a common lop-eared into a silver-grey rabbit. The transfused silver-grey rabbits then were allowed to breed; out of 36 offspring, 35 were silver-grey and one was silver-grey with a white foot. Galton then conducted a second series of experiments, in which a cross circulation was established between the carotid arteries of common rabbits and silver-grey rabbits, the transfused rabbits being allowed to breed with their own kind. Out of 38 offspring of transfused common rabbits, all were like their parents and none was silver-grey. Out of 50 offspring of transfused silver-grey rabbits, 49 were silver-grey and one was Himalayan (sandy with black tips); Galton’s stock of silver-grey rabbits was known to produce the occasional Himalayan in the absence of treatment, so this could not be attributed to the transfusion (Galton, 1871; Bulmer, 1999).

Galton concluded that Darwin’s Pangenesis was incorrect: “I have now made experiments of transfusion and cross circulation on a large scale in rabbits, and have arrived at definite results, negativing, in my opinion, beyond all doubt the truth of the doctrine of Pangenesis” (Galton, 1871). Darwin (1871) responded in a letter to Nature: “In the chapter on Pangenesis in my ‘Variation of Animals and Plants under Domestication,’ I have not said one word about the blood or about any fluid proper to any circulating system... It does not appear to me that Pangenesis has, as yet, received its death blow; though from presenting so many vulnerable points, its life is always in jeopardy”. In order to discredit the findings of Galton, Pearson (1900) wrote that Pangenesis “is no more disproved by the statement that ‘gemmules have not been found in the blood,’ than the atomic theory is disproved by the fact that no atoms have been found in the air”.

IV. RECENT EVIDENCE FOR HERITABLE CHANGES INDUCED BY BLOOD TRANSFUSION AND DNA TREATMENT

(1) Blood transfusion

Sopikov (1950) reinvestigated the effect of blood transfusion on hereditary traits, inspired by the investigations carried out by Michurin and others on plant graft hybridization. Repeated transfusion of blood of Black Austalorps roosters to White Leghorn hens, and subsequent mating of these hens with White Leghorn roosters yielded progeny with modified inheritance. Injections (2.5-3 ml blood per kg live mass) were given twice weekly for two and half months before the fertilized eggs were laid. Some of the progeny had several black feathers (8-40 per bird) in their white plumage. When a similar experiment was made with White Leghorn donors and Black Austalorp recipients, some of the progeny had white feathers (5-25 per bird) in otherwise black plumage. Compared with purebred controls, the experimental birds showed an increase in body mass, larger neck and body size, longer legs and abnormal leg pigmentation. The shell colour of some of the experimental White Leghorn resembled Black Austalorps. These changes increased in each successive generation of birds in which the treatment was continued. In the third generation plumage was white, white with black feathers, light-grey to grey, or black like that of the Black Austalorp donors. When the blood of Chuvash geese was injected into White Leghorn recipients and Khaki Campbell ducks, or the blood of Bronze turkeys was injected into White Leghorn recipients, similarly abnormal characters were observed in the progeny (Sopikov, 1954). The blood transfusion technique was found to increase viability, productivity, reproductive efficiency and body mass of recipients and their progeny; to eliminate the adverse effects of inbreeding, to facilitate hybridization between species, and was used in the development of new breed groups (Sopikov, 1966). The Leningard White and Leningard Black breed groups were created by blood transfusion between White Leghorns and Black Australorps over three generations, followed by interbreeding and selection (Sopikov, 1967). A heavy type of Leningard White fowl with males weighing 4-5 kg and females 3-3.5 kg was also produced in this way (Sopikov, 1980).

During the 1950s and 1970s, Sopikov’s observations were confirmed by many Soviet researchers (Golubev, 1966; Golubev & Balukova, 1967; Gromov, 1970; Gromov et al., 1974; Kushner, 1957b, 1958; Kurbaiov & Golubev, 1970; Tolokonnikova, Moiseeva & Bogatyreva, 1961). Golubev & Balukova (1967) injected 332-380 ml of blood from Barred Plymouth Rock chickens into Australorps over an 11 month period. Two control groups were bred: non-injected Australorps and Australorps injected with blood of the same breed. Plumage colour changes in birds of the experimental group were seen in 0.9-2.2% and 5.0% of F1 and F2 birds, respectively. No birds in control groups had plumage changes. When unchanged F1 males were mated with F1 females with plumage changes, 10% of the progeny showed changes. When changed males were mated with changed females, 17.5% and 64.2% of F3 and F4 progeny, respectively, showed changes.

In order to produce white-feathered guinea-fowl, Gromov et al. (1974) transferred blood from Moscow White cocks into grey-speckled guinea-fowl weekly at the rate of 4 ml per kg body mass, each bird receiving a total of 150 ml. By the fifth generation all vegetative hybrids had some white feathers distributed over the body, and by the eighth and ninth generations white plumage areas equal to 1/2 and 2/3, respectively, of the total plumage surface were obtained. The skin had also altered from dark coloured to light yellow. The new vegetative hybrids had higher egg production than the common grey guinea-fowl.

Reports of the success achieved by Soviet biologists in inducing hereditary changes in poultry by blood transfusion have received considerable attention among geneticists. The first summary of this work to an international audience was presented in 1956 at the International Genetics Symposium held in Japan (Kushner, 1957b). Two years later Kushner spoke at the 10th International Congress of Genetics in Montreal (Kushner, 1958). Lerner (1957) argued that should the experiments be found to be repeatable with purebred material outside the Soviet Union or its allied countries, no geneticist anywhere would be able to ignore it. Such
experiments were then conducted in France, Switzerland and elsewhere. J. Stroun et al. (1963) reported that birds of a White Leghorn strain repeatedly injected with blood from grey guinea fowl produced progeny with some grey or black-flecked feathers in the second and later generations. Leroy (1962) injected whole or fractionated guinea fowl blood into a strain of Rhode Island Red chickens and obtained progeny in the first and second generations with extensive changes in the quantity and distribution of melanin pigment visible in the plumage. The transmissibility of modifications continued to the seventh generation after a single series of injections of guinea fowl blood (Leroy & Benoit, 1966; Leroy et al., 1966). Some investigators failed to induce heritable changes in chickens by blood transfusion (Lowe, Carson & King, 1963; Lowe, Kinney & Wilson, 1968; Kosin & Kato, 1963).

The question arises why Galton (1871) failed to observe heritable changes in his experiments, whereas many others obtained positive results. Darwin himself admitted that Galton’s experiments were extremely curious, and that he deserved credit for his ingenuity and perseverance (Darwin, 1871). It is not known whether Galton encountered transfusion incompatibilities due to blood group differences, although species differences and transfusion method, frequency, duration and blood volume are known to be important factors. Also, as Sopikov (1964) pointed out, heritable changes may be easier to detect in poultry than in rabbits; they usually take place in the first or second generation, and become clearer in subsequent generations.

As will be discussed below, if the variable of interest in the transusions is the DNA content, bird and animal blood differ in that bird erythrocytes are nucleated, and contain DNA: 1 ml of avian blood constitutes a larger source of foreign DNA than 1 ml of rabbit blood. There is evidence that heritable changes in rabbits can be induced by blood transfusion when an accumulated total of 200–400 ml of blood is injected into each recipient (Sopikov, 1964). A careful analysis of Galton’s (1871) report reveals that his recipients only received a total of 100–150 ml blood. It should be mentioned that Bondarenko & Ostroumova (1968) also failed to induce heritable changes in fur colour when the blood of a Vienna Blue rabbit was transfused into a White Down. However, Taranov (1960) demonstrated that, of 32 progenies of Black-Brown rabbits transfused with the blood of White Giants, six showed areas of depigmentation of the fur, although the progeny of the White Giants transfused with the blood of Black-Brown rabbits did not show abnormal fur colour, indicating variety differences.

The method of parabiosis (surgical union of anatomical parts of two animals, usually involving exchange of blood) was used to investigate heritable changes in rabbits: Boriachok-Nizhnik (1951) surgically connected a pair of rabbits so that they had a common blood supply. A 50-day old Angora female was parabiosed with a Flanders female of the same age for 36 days. One month after separation, the Angora female was mated to an Angora male and seven young rabbits were born, of which only one had Angora long hair, the other six having Flanders-like short hair. Despite the fact that both parents possessed the recessive character, long hair, most of the litter had short hair, a dominant character. At the age of five months the young rabbits weighed an average of 3020 g, compared to the mean mass of 2330 g for normal Angora rabbits under similar conditions. The progeny of the parabiosed rabbit, the “vegetative hybrids” as the author called them, clearly were more vigorous than controls, and had undergone certain morphological changes.

Among 50 reports on blood transfusion I collected, 45 obtained positive results and only five obtained negative results (see Table 1). There is thus a considerable body of experimental evidence for animal vegetative hybridization by blood transfusion, which cannot be disregarded simply because several scientists have had negative results.

(2) DNA treatment

Avery, Macleod & McCarthy (1944) were the first to describe the induction of transformation in bacteria by exogenous DNA extracted from other bacteria. Later, Sopikov (1954) discussed the possibility that DNA may be involved in the results of his transfusion experiments. A subsequent report of successful induction of heritable changes in the Pekin duck using DNA from the Khaki-Campbell stimulated further interest in this problem: Benoit et al. (1960) not only found evidence of vegetative hybridization in the progeny of ducks treated with erythrocytic DNA but also found the parent to be affected. They extracted DNA from Khaki Campbell ducks and injected it into Pekin ducklings. The majority of the treated birds and their offspring developed a range of characters (pigmentation of beak, morphology of feathers, shape of head, size and conformation of body) apparently derived from the donor breed. Hereditary modifications of morphological characters in ducks as a result of DNA and RNA injection from other breeds of ducks were reported by Novikov (1966) and Benoit et al. (1966).

In recent years, there is increasing evidence that DNA injection can induce heritable changes. Tsukamoto et al. (1995) reported that a single intravenous injection of expression plasmid: lipopolymine complexes into pregnant mice resulted in successful gene transfer into the embryo. The transgenes thus introduced were expressed in the foetuses and newborn progeny. Schaubert et al. (1998) demonstrated that, following prolonged feeding of M13 or plasmid pEGFP-C1 DNA to mice during pregnancy, the orally ingested foreign DNA could be detected by fluorescent in situ hybridization (FISH) in cell clusters in several organs, both in foetuses and in newborn mice.

It has been suggested that genetic material (i.e. DNA) from the donor can become integrated into the chromosomes of the ovary of the recipient (Freeman & Messer, 1985). In recent years, many researchers have detected circulating DNA/RNA in the plasma of healthy and diseased individuals. It is clearly possible that when DNA-rich avian blood cells are transfused to other members of the same species, the transferred DNA can be expressed. The ability to integrate foreign DNA into the host genome and its expression in the progeny, provides a mechanism for horizontal gene transfer from one animal to another following blood transfusion.

V. IN SEARCH OF DARWIN’S GEMMULES

(1) Gemmules, pangens and genes

According to Ghiselin (1975), the term “gemma” or bud, hence meaning ‘little bud’. Darwin described gemmules as self-replicating, corpuscular and numerous. They were flexible, produced mainly in the organs whose generation they directed, passed from the somatic tissue to the reproductive organs or buds, and controlled morphogenesis through strictly chemical interactions.

In his theory of “Intracellular Pangenesis”, de Vries coined the new term “pangen”: “To the smallest particles, of which each represents one hereditary characteristic, I shall give a new name and call them pangens, because with the designation ‘gemma’ is associated the idea of a transportation through the whole organism” (de Vries, 1910). According to de Vries (1910), pangens only move between the nucleus and the cytoplasm within a cell, and can be in two different states, either active or inactive.

Johannsen (1909) realized that there was no satisfactory term for the “something” in the gametes and zygote, which determines or very substantially influences a character in an organism. He pointed out that de Vries’ (1910) term “pangen” might be used but objected to it on the grounds.

Table 1. Experiments investigating the effects of blood transfusion on the transmission of heritable characteristics

<table>
<thead>
<tr>
<th>Donor/recipient</th>
<th>Results</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Leghorn chicken/Black Australorp chicken</td>
<td>Heritable changes in plumage colour, body mass and egg production observed in F1-F3 generations.</td>
<td>Sopikov (1950, 1954, 1962, 1964)</td>
</tr>
<tr>
<td>Black Australorp chicken/White Leghorn chicken</td>
<td>Heritable changes in plumage colour, body mass and egg production observed in F1-F3 generations.</td>
<td>Gromov (1959, 1966); Gromov &amp; Feoktistov (1956); Sopikov (1966, 1967, 1972, 1980); Stroun (1965); J. Stroun et al. (1958, 1963); M. Stroun et al. (1962)</td>
</tr>
<tr>
<td>New Hampshire chicken/White Leghorn chicken</td>
<td>Heritable changes in plumage colour detected in F1-F3 generations.</td>
<td>Kushner (1957a, b, 1958); Kushner et al. (1959); Piko &amp; Suschka (1956)</td>
</tr>
<tr>
<td>Bronze turkey/White Leghorn chicken</td>
<td>Heritable changes in plumage colour and body mass were observed in F1-F2 generations.</td>
<td>Gromov (1959); Gromov &amp; Feoktistov (1956); Nestorov et al. (1958); Sopikov (1954)</td>
</tr>
<tr>
<td>Moscow White chicken/grey guinea-fowl</td>
<td>Heritable changes in plumage colour, body mass and egg production observed in F1-F9 generations.</td>
<td>Gromov (1970); Gromov et al. (1974, 1975); Sergeev &amp; Skorik (1979)</td>
</tr>
<tr>
<td>Barred Plymouth Rock chicken/Black Australorp chicken</td>
<td>Heritable changes in plumage colour, body mass and egg production observed in F1-F5 generations.</td>
<td>Balukova &amp; Golubev (1971, 1972); Golubev (1965, 1966); Golubev &amp; Balukova (1967, 1974); Kurbaoov &amp; Golubev (1970)</td>
</tr>
<tr>
<td>Guinea-fowl/Rhode Island Red fowl</td>
<td>Heritable changes in plumage colour detected in F1-F4 generations.</td>
<td>Leroy (1962, 1968); Leroy &amp; Benoît (1963, 1966); Leroy et al. (1964, 1966)</td>
</tr>
<tr>
<td>New Hampshire chicken/Russian White chicken</td>
<td>Heritable changes in plumage colour detected in F1 generation. Certain metabolic changes detected in F1 generation.</td>
<td>Lebedev (1963); Tolokonnikova et al. (1961); Penionzhkevich et al. (1962)</td>
</tr>
<tr>
<td>Bronze turkey/Russian White chicken</td>
<td>Heritable changes in plumage colour detected in F1 generation.</td>
<td>Pavlichenko (1972)</td>
</tr>
<tr>
<td>Russian Large White pig/Russian Large Black pig</td>
<td>Heritable changes in hair and skin colour detected in F1 generation.</td>
<td>Tong &amp; Geng (1956)</td>
</tr>
<tr>
<td>Lou Island Red chicken/Shou Kuang chicken</td>
<td>Certain changes in egg production and egg shell colour detected in F1 generation. Depigmentation of the fur detected in F1 generation.</td>
<td>Taranov (1970)</td>
</tr>
<tr>
<td>White Giant rabbit/Black-Brown rabbit</td>
<td>Heritable changes in body mass detected in F1 and F2 generations. No change in fur colour found.</td>
<td>Bondarenko &amp; Ostroumova (1968)</td>
</tr>
<tr>
<td>Vienna Blue rabbit/White Down rabbit</td>
<td>No heritable change in plumage colour detected over three generations.</td>
<td>Lowe et al. (1963); Lowe &amp; Wilson (1963); Lowe, Kinney &amp; Wilson (1968)</td>
</tr>
<tr>
<td>Rhode Island Red fowl/White Leghorn chicken</td>
<td>No heritable change in plumage colour and body mass detected in three-year study.</td>
<td>Kosin &amp; Kato (1963)</td>
</tr>
<tr>
<td>New Hampshire chicken/White Leghorn chicken</td>
<td>No evidence of hereditary modification found.</td>
<td>Buschinelli (1962)</td>
</tr>
</tbody>
</table>
that it was a compound word, proposing instead the latter half, “das Gen.” The first reference in the English language to Johannsen’s “Gen” was in a paper by Shull (1909), who later introduced the anglicized spelling “gene” (Shull, 1912; Riley, 1952).

So de Vries’s pangens remained intracellular; we now know that genes have fixed positions on the chromosome and that “jumping genes” can move within a chromosome and between chromosomes. Only Darwin’s gemmules can circulate throughout the whole organism. Most biologists now accept that certain genes routinely move within and between chromosomes and within and between species. In a letter to Hooker, Darwin suggested that gemmules might live outside the body and “multiply under proper conditions” (cited in Ghiselin, 1975), foreseeing, perhaps, the now widely used polymerase chain reaction (PCR) and reverse-transcriptase polymerase chain reaction (RT-PCR) techniques, used to make a huge number of copies of a gene in vitro. It has been suggested that Darwin’s gemmules could include RNAs, circulating DNA, mobile elements, prions or as yet unknown molecules (Steele, Lindley & Blanden, 1998; Forsdyke, 2001; Van Dierendonck, 2004; Liu, 2004, 2005).

(2) Circulating nucleic acids in plasma or serum

As described in Section IV, J. Stroun et al. (1963) induced hereditary changes in the domestic chicken by blood transfusion. The same team, after three generations of grafting between two varieties of aubergine (Solanum melongena), succeeded in obtaining hereditary modifications of the recipient plants, which acquired some of the characteristics of the donors (Stroun, Mathon & Stroun, 1963; Stroun and Anker, 2006). Recent work on bacteria, plants, animal cells and organs, and human cells, blood plasma and serum led them to suggest that nucleic acids are released by living cells and circulate throughout the whole organism (Stroun & Anker, 2005).

Over the past several decades, detection of circulating DNA/RNA in the plasma and serum of healthy and diseased individuals has resulted in substantial interest and hundreds of publications in the medical literature (Anker, Mulcahy & Stroun, 2003). Early suggestions that such circulating DNA is of endogenous origin have been widely accepted (Ziegler, Zangemeister-Wittke & Stahel, 2002). It has been shown that substantial amounts of degraded genomic DNA are present in the blood plasma and fluids surrounding cells, arising from cells in the body that have died. This circulating DNA binds to receptors on the surface of living cells and is taken up and transported to the cell nucleus (Yakubov et al., 2002). It is also shown that DNA can move laterally from apoptotic bodies to normal cells, and that the uptake of DNA from apoptotic cells that carry oncogenes might cause transformation of a healthy cell (Holmgren, Bergsmehd & Spetz, 2002). Reports of uptake by mammalian sperm of DNA and RNA and of reverse transcriptase activity in sperm provide a mechanism for movement of somatic gene sequences to the germ line (cited in Steele & Blanden, 2000). The detection of circulating DNA/RNA in plasma and serum provides evidence for the existence of Darwin’s gemmules.

Darwin explicitly stated that gemmules were “inconceivably minute and numerous as the stars in heaven”. In fact, RNAs—specifically, tiny RNAs with high binding specificity known as “small RNAs” or “microRNAs”—do control plant and animal gene expression. In plants, miRNAs are transported between tissues in the network of phloem tubes that carry sap (Lucas, Yoo & Kragler, 2001). To investigate whether small RNAs are carried in the phloem, plant biologists analysed sap from several plant species and identified a population of small RNAs of 18-25 nucleotides, providing strong support for the suggestion that small regulatory RNAs are induced in response to a variety of external stimuli and transported via the phloem to exert non-cell-autonomous control over diverse processes in plant growth and development (Sunkar & Zhu, 2004). The precise number of small RNA genes in the human genome is still unknown, but current estimates range from 500 to 1000. In invertebrates, small RNAs control developmental timing, neuronal differentiation, tissue growth and programmed cell death. Functional studies in zebrafish (Danio rerio) and mice suggest important roles for small RNAs during morphogenesis and organogenesis. Small RNAs might regulate viral infection and human cancer (Miska, 2005). Finally, it has been indicated that more than a third of the worm (Caenorhabditis elegans) microRNAs are differentially expressed during larval development, suggesting they have a role in mediating larval developmental transitions. Most are present at very high steady-state levels—more than 1000 molecules per cell, with some exceeding 50,000 molecules per cell (Lam et al., 2003).

(3) Inherited prions as genetic elements

Just as nucleic acids can carry out enzymatic reactions, proteins can be genes (Wickner et al., 2004). The prion model promotes the revolutionary idea that proteins can transmit certain information directly from one protein molecule to another. According to the prion concept, the infectious agent is a protein in an altered conformation (called a prion protein) that can reproduce itself by converting the target cellular protein of the same amino acid sequence into the prion conformation. It has been established that prions can traverse between, and exist stably in, many functionally distinct conformations, at least one of which is self-replicating. Prion conformers operate as a template for other conformers to acquire the prion conformation, and these, in turn, are templates for others, creating a protein-folding chain reaction. This self-replication of conformational information enables prions to act as genetic elements with the ability to transmit disease, encode heritable phenotypic traits or encrypt molecular memories (Shorter & Lindquist, 2005). Now most biologists accept the existence of prions and increasing evidence indicates that this may well be a form of protein-based information flow, which seems to be important in various biological processes ranging from the establishment of long-term memory to the
adaptation of organisms to new environments. It has been suggested that the prion anomaly may challenge the central dogma of molecular biology and evoke a scientific revolution (Bussard, 2005). Recently, Saa, Castilla & Soto (2006) detected a misfolded prion protein biochemically in the blood of Syrian Golden hamsters (Mesocricetus auratus) infected with scrapie during the presymptomatic phase of the disease. At early stages of the incubation period, the misfolded prion protein detected in blood is likely to be from the peripheral replication of prions, whereas during the symptomatic phase, the misfolded prion protein in blood is more likely to have leaked from the brain. Van Dierendonck (2004) believed that prions provide evidence for Darwin’s Pangenes, though he did not suggest that prions perfectly fit the concept of gemmules.

VI. CONCLUSIONS

(1) Darwin’s Pangenes is a developmental theory of heredity, which explains dominance inheritance, graft hybridization, reversion, xenia, teleony, the inheritance of acquired characters, regeneration and many groups of facts pertaining to variation, inheritance and development. Darwin felt a deep conviction that Pangenes would eventually be generally accepted.

(2) The main reason why Pangenes was disregarded was that Galton’s blood transfusion experiments designed to test it had negative results; no evidence was found for the existence of Darwin’s ‘gemmules’.

(3) During the 1950s to 1970s, blood transfusion experiments were found to alter hereditary traits of the offspring in poultry and rabbits.

(4) Over the past several decades, detection of circulating DNA/RNA and prions in plant sap and in the plasma and serum of healthy and diseased individuals has provided evidence for the existence of Darwin’s ‘gemmules’.

(5) It is now apparent that Darwin’s Pangenes contains a great truth and needs to be reconsidered; whether it can serve as the basis for a new comprehensive genetic theory is another question.

VII. ACKNOWLEDGEMENTS

I am deeply indebted to Dr Anne McLaren for translating the main content of Boriachok-Nizhnik’s Russian article into English and to Dr Donald Roy Forsdyke for providing me with valuable research materials. I am also very grateful to the referees and editors for their valuable comments and suggestions.

VIII. REFERENCES


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