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POINT OF VIEW

Valentin Haecker (1864–1927) as a pioneer of phenogenetics: Building the bridge between genotype and phenotype

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ABSTRACT
Valentin Haecker is one of the forerunners of experimental biology, genetics, and developmental physiology. Haecker introduced the term *Phänogenetik* (phenogenetics) in 1918 in *Entwicklungsgeschichtliche Eigenschaftsanalyse* (Evolutionary Analysis of Characters), in which he described the earliest stages in the development of the phenotype.[1] His major objective in this publication was to integrate the 2 most important concepts of Mendelian genetics—phenotype and genotype—within a well-articulated theory. Haecker realized that a proper analysis of how the genotype gives rise to the phenotype requires the integration of knowledge of morphology, physiology, and experimental embryology.

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Introduction

The 2016 Louisa Gross Horwitz Prize was awarded to Dr. Howard Cedar and Dr. Aharon Razin, of the Hebrew University of Jerusalem, and Dr. Gary Felsenfeld, of the National Institutes of Health, on September 6, 2016 to commemorate their research, which led to the formation of the field of epigenetics. As the chair of the Horwitz Prize Committee and chair of the Department of Genetics and Development at Columbia University Medical Center states: "These researchers laid the foundation for an important new field of study. As our cells divide and become more specialized they need instructions on which genes to use and which to ignore. Epigenetics adds these annotations to our biologic textbook; it is a process that is crucial to our development and continues throughout our lives."[2]

Epigenetics is defined as "the study of emergent properties in the origin of the phenotype in development and in modification of phenotypes in evolution."[3] Thus, as these 21st century pioneers in the field of epigenetics are being honored for their contribution to the field, it seems appropriate to acknowledge the work of another pioneer, Valentin Haecker, who began to bridge the gap between genotypes and the origin of phenotypes almost 100 y ago and coined the term *Phänogenetik* (phenogenetics) in 1918 in an attempt to integrate the 2 most important concepts of Mendelian genetics—phenotype and genotype—within a well-articulated theory. In doing so, Haecker integrated knowledge from the fields of morphology, physiology, and experimental embryology to analyze how the genotype gives rise to the phenotype.

Although Haecker's contributions may have been overshadowed by more recent scientific progress and discovery in the field of genetics, his impact during the first half of the 20th century was so monumental that when Conrad Hall Waddinton coined the term "epigenetics" in 1942 he made a direct reference to Valentin Haecker's work in 'phenogenetics'.[4] Here we take a look at this incredible man, his life, his work, and his legacy.

Life

Ferdinand Carl Valentin Haecker was born on September 15, 1864 in Ungarisch-Altenburg (today Mosonmagyaróvár, Hungary) as the son of Professor of Agriculture Christian Ludwig Haecker. During his childhood, Haecker showed an early interest in the natural sciences. He began school at the Volksschule in Altenburg in 1870 and had to change schools in 1874 when his family moved to Stuttgart following the sudden death of his father in 1873. In 1879 he attended a Convent School in Maulbronn (Neckarkreis) and 2 y later his class moved to Blaubeuren (Swabian Alb), where he passed a difficult university qualification on August 15, 1883. After school, Haecker served a mandatory year in the German army as a lieutenant. In the fall of 1884, together with his brother Walter, he enrolled first at the Convent of Tübingen (Stift), and later at the Tübingen University to study mathematics and natural sciences. At the Tübingen University Valentin attended lectures by Theodor Eimer (1843–1898), a founder of the orthogenesis theory. He then studied for a while in Straßburg and graduated in the spring of 1889 from Tübingen University. After receiving his PhD (1889) with Eimer as his doctoral advisor (his thesis focused on the colors of bird's feathers), he spent a decade in Freiburg with August Weismann (1834–1914), the co-founder of neo-Darwinism, first serving as an assistant and later (after defending his second thesis or habilitation) as a Privatdozent. In 1895 he became an extraordinary Professor of Zoology. Based on the research Haecker conducted in Freiburg, he published his first book *Praxis and Theory in the Cell and*

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Fertilization Studies (1899).[5] Two other books he published later in his career, *Bastardization and the Formation of Gametes* (1904)[6] and *About the Memory, Heredity and Pluripotency* (1914),[7] were dedicated to Weismann for his 70th and 80th birthdays respectively.

In 1900, when Haecker was 36 y old, he became the Chair of Zoology at the Technische Hochschule in Stuttgart as the successor of Carl Benjamin Klunzinger (1834–1914). In Stuttgart, he gave lectures on agriculture and veterinary medicine and also became increasingly interested in Mendelism. During his time in Stuttgart, Haecker evaluated the Radiolaria collection from the Valdivia-expedition (1898–1899) with Karl Chun (1852–1914). In 1903 Haecker married Johanna Lucia Anna Kühn. The couple had 2 children: a daughter, Hertha, and a son, Rudolf. In 1908 Haecker joined the editorial board of the newly founded journal *Zeitschrift für Induktive Abstammungs und Vererbungslehre* (Journal for Inductive Evolutionary and Genetic Research). In 1909, he moved to Halle as an Ordinarius (Full Professor) of Zoology at the Philosophical Faculty. He was elected as a member the Leopoldina Academy in 1910.

While teaching at the University of Halle, Haecker supervised Bernhard Rensch (1900–1990) and Gerhard Heberer (1901–1973), 2 PhD students who later became leading figures of the Modern Synthesis (Synthetic Theory of Evolution) in Germany.[8] Among all of Haecker's students, Rensch was especially well trained in the analysis of speciation and phylogeny. Rensch recognized early the potential and the great theoretical importance of new systematics. His studies significantly contributed to the new field of genetics created by Haecker, the so-called *Phänogenetik* (phenogenetics).

The goal of phenogenetics was to analyze the developmental processes that caused different phenotypic characters. During their work together, Rensch and Haecker were not always in agreement. While Haecker was convinced that there was strong evidence in favor of non-genetic, Lamarckian mechanisms of modification, Rensch did not. As Rensch put it: "He also thought that the geographic color differences of birds and mammals—more brownish in Western and more grayish in Eastern Europe—were non-genetic modifications, whereas I was convinced of their genetic nature".[9] In 1912, the first edition of Haecker's *Allgemeine Vererbungslehre* (General Genetics) came out of print [3rd ed., 1923] and in 1918 his major work *Phänogenetik* (Developmental Genetics) was published. Finally, Haecker summarized his analysis of Goethe's morphological views in the book *Goethes Morphologische Arbeiten und die neuere Forschung* (Goethe's morphological works and new research agenda, 1927).[10] In 1926 Haecker became the rector of Halle University. His inaugural lecture was entitled *Umwelt und Erbgut* (Environment and Heredity).[11] On December 12, 1927, he died suddenly of a stroke in Halle.

Work

A short historical background on the development of genetics in Germany

Barthelmess and Harwood have shown that the interest in Mendelism grew rapidly in Germany around 1900.[12] The 'rediscovery' of Mendel's laws in 1900 is seen worldwide as a turning point in the development of modern genetics. During the first half of the 20th century, it was generally held that the 'rediscovery' took place several times. Four European biologists independently and simultaneously rediscovered Mendelian laws—the German plant physiologist Carl Correns (1864–1933), the Dutch botanist Hugo de Vries (1848–1935), the Austrian plant breeder Erich von Tschermak-Seysenegg (1871–1962), and his brother, the Austrian physiologist Armin von Tschermak-Seysenegg (1870–1952).[13] In the years immediately following the rediscovery and before the start of the First World War, the 3 Mendelian laws[14] were modified and supplemented to explain more complex patterns of inheritance. The quantitative analysis of inheritance was extended to include both plants and animals. The Danish geneticist Wilhelm Johannsen (1857–1927) coined the term "gene" in his *Elemente der exakten Erblichkeitslehre* (Elements of Exact Theory of Heredity) to refer to discrete hereditary units located within the cell. The terms "phenotype" and "genotype" were also first introduced by Wilhelm Johannsen.[15]

In 1901 Carl Correns began to teach the new Vererbungswissenschaft (Science of Heredity) in Tübingen, later in Leipzig and then in Münster. Other German biologists such as Erwin Baur (1875–1933), Richard Goldschmidt (1878–1958), and Valentin Haecker began to follow him starting in 1910.[16] It was also during this time that German biologists published several textbooks on genetics: Johannes Paulus Lotsy (1867–1931) with *Vorlesungen über Deszendenztheorie* (Lectures in Evolutionary Theory, 1906, 1908),[17] E. Baur with *Einführung in die experimentelle Vererbungslehre* (Introduction into the Experimental Genetics, 1911),[18] R. Goldschmidt with *Einführung in die Vererbungswissenschaft* (Introduction into the General Genetics, 1911),[19] Haecker with *Allgemeine Vererbungslehre* (General Genetics, 1911),[20] Ludwig Plate (1862–1937) with *Vererbungslehre* (Genetics, 1913),[21] Arnold Lang (1855–1914) with *Die experimentelle Vererbungslehre in der Zoologie seit 1900* (Experimental Genetics in Zoology since 1900),[22] Heinrich Ernst Ziegler (1858–1925) with *Die Vererbungslehre in der Biologie und in der Soziologie* (Genetics in Biology and Sociology, 1918)[23] and Johannes Meisenheimer (1873–1933) with *Vererbungslehre* (Genetics, 1923).[24]

Moreover, several new German biologic journals were founded such as *Archiv für Rassen- und Gesellschaftsbiologie* (Archive for Race and Social Biology; *Archiv für Zellforschung* (Archive for Cell Research; Leipzig, 1908–1923), *Zeitschrift für Pflanzenzüchtung* (Journal of Plant Breeding Research; Berlin, 1913) or *Zeitschrift für induktive Abstammungs und Vererbungslehre* (Journal for the Inductive Study of Evolution and Heredity; ZIAV). As a result of this development, several geneticists with an interest in botany or zoology acquired chairs at different German universities. Haecker moved to Halle (1909), Correns went to Leipzig (1902) and, later, to Münster (1909). Plate, since 1909, became Haeckel's successor in Jena as a chair of zoology,[25] while Baur received a chair in genetics in Berlin (1911).

As a zoologist at Halle University, Valentin Haecker was a key figure in the development of genetics of that time. In addition to genetics, he was also interested in other various fields of biology such as ornithology, animal physiology, marine biology,

developmental genetics, and philosophy.[26] Along with R. Goldschmidt (see for instance his later book *Physiologische Theorie der Vererbung*—Physiological Theory of Inheritance, 1927),[27] he was the second German geneticist interested in the early stages of ontogenesis. Haecker evidently influenced Conrad Hall Waddington (1905–1975), who credited Haecker's work in phenogenetics when he coined the term "epigenetics" in 1942 and explained his new concept of the "epigenotype",[28] which is still used as the basis for the modern concept of epigenetics.[29]

Haecker's take on Lamarckism

Many German biologists, in particular zoologists and paleontologists, defended Lamarckian evolutionary mechanisms between 1900 and 1940. They believed in the inheritance of acquired characteristics and a direct effect of the environment on organism's inheritance. For example, the zoologist and geneticist Ludwig Plate (1862–1937) campaigned for a revival of the original Darwinism. His research program, which he labeled "old-Darwinism," advocated the synthesis of selectionism with "moderate Lamarckism" and orthogenesis.[30] Plate defined the inheritance of acquired characteristics as follows: "The inheritance of an acquired characteristic means only that a newly occurring characteristic was somatogenic in the first generation whereas it becomes blastogenic in the subsequent generations".[31] In modern terms, this means that there are a variety of features, which have been phenotypic in a certain generation and became inheritable in all subsequent generations.[32] Plate attached great importance to the idea that inheritance of acquired characteristics should not necessarily be combined with the Lamarckian idea of use or disuse of a certain organ as he stated: "It does not matter whether somatic modifications are caused by a use or disuse of an organ or by temperature, nutrition or other factors".[33]

Haecker, as well as Plate, advocated Lamarckian evolutionary mechanisms but, in contrast to Plate, he concentrated on the description of the phenotype and paid little attention to selectionism; in fact, there is not a single reference to natural selection in Haecker's 1918.

Haecker acknowledged the importance of chromosome theory but remained dissatisfied with several of its features throughout his life: "Many of his criticisms were also voiced by Bateson: the cytological evidence for crossing-over was inadequate; vastly different kinds of organisms sometimes possessed the same number of chromosomes; sex chromosomes were less likely to be the cause of sex differences than merely indicators of the real cause; and the evidence for purity of the gametes was unconvincing."[34]

In his *Allgemeine Vererbungslehre* (General Genetics) Haecker postulated that speciation was caused by the natural selection of hereditary varieties in August Weismann's sense. Haecker was convinced that the inheritance of acquired characteristics must be regarded as improbable, because a chain of causal events which phenotypically altered the soma and, thereafter, the genes could never be identical to a causal chain leading from altered genes over embryonic stages back to the characteristics of soma.[35] In this, Haecker argued: "If one assumes that different 'virtual possibilities of individual development' exist, then 'a parallel activation' (*Parallelaktivierung*) of latent general potentialities in genetic and somatic cells by means of the altered chemical processes takes place."[36] He also believed that 'constitutional concussion' of genetic and somatic cells could cause a parallel reduction of the resistance against illness. Therefore, he postulated, in 1918, that a 'parallel induction' of somatic and germ cells would be possible only "when characteristics acquired by the parents already preexisted in the virtual potential of the plasma".[37] Haecker saw the so-called "parallel-inductions" (simultaneous impact of environment on soma and germ cells) as possibilities for neo-Lamarckian evolutionary mechanisms (*gleichzeitige Beeinflussung der Körper und Keimzellen*) as well as the "ideocynesis" (Influence of external stimuli on the ideoplasm).[38] Haecker remained the champion of Lamarckism throughout his career.

Haecker's Phänogenetik

One of Haecker's objections to the Mendelian chromosome theory was its failure to bridge the gap between hereditary units and phenotypic traits. His research program, which he called *Phänogenetik* (phenogenetics), set out to build a bridge between genotype and phenotype. He outlined this program in a study in 1918. In the preface, Haecker described a new research field that should explore "in terms of morphogenetics and developmental physiology" the appearance of organism's "external characteristics."[39] According to Haecker, phenogenetics always begins with the so-called *Differentialdiagnose* (Differential Diagnostics), i.e., with histological, morphological, and physiologic studies of differences between species or races. This "phenoanalysis" is followed by a "phenogenetic-descriptive" investigation of variations of a certain trait. The traits in question are traced back to the point of bifurcation, i.e., to the developmental stage manifesting in the initial divergence of the trait. Haecker calls this stage a "phenocritical phase." Phenogenetics in the narrow sense is the study of diverging developmental pathways. It must penetrate into the deeper causes (phenocritical causes) of the observed divergence.[40] This process can proceed epigenetically or autonomously and in that sense phenogenetics is a sub-discipline of *Entwicklungsmechanik* (Developmental Mechanics) and *Entwicklungsphysiologie* (Developmental Physiology). All of Haecker's phenogenetics investigations were descriptive, whereby in various chapters of *Phänogenetik* he described the differences among subgroups of mammals, axolotls, birds, and plants, according to coloration (ch. 7–13) as well as the stripe patterns in various species (ch. 14), the growth of the skin (ch. 16–18), and so on.

From today's viewpoint, Haecker's phenogenetics appears to be an experimentally based science that used methods to analyze the physical result of alteration or switching off and on certain genes. In doing so, phenogenetics examines reactions of various organs to differing genetic compositions.[41]

The problem of Pluripotenz

The study of the manifestations of pluripotency and its evolutionary causes was one of the main focuses of phenogenetics. Hacker first used the term *Pluripotenz des Artplasmas* (Pluripotency of Species Specific Plasm) in his

book *Über Gedächtnis, Vererbung und Pluripotency* (On Retention, Heredity and Pluripotency; 1914)[42] and explained his hypothesis in detail in 1925 in his work *Pluripotenzerscheinungen* (On the Manifestation of Pluripotency).[43] In general, Haecker's theory of pluripotency postulated a relatively plastic concept of hereditary material that allowed for variety in the inheritance of acquired characters.[44] In 1925, he published the most complete definition of the term: "In a narrow (evolutionary) sense, I understand pluripotency as an essential ability of every organism (not only of species and races, but also of any individual germ and any cell on the embryonic stage of any individual) to develop in directions *deviating from the basic type* under certain circumstances. Insofar, pluripotency is understood as the presence of greater numbers, *although not unlimited numbers*, of potencies or developmental possibilities than determined by a *property grounded in a normal, material, structural constitution of a species specific—but for the most part common to many species—plasm*."[45]

Haecker used the term *Artplasma* (Species Specific Plasm) to describe hereditary material in the very broad sense, while he believed germ plasm to be identical to the nuclear substance of germ cells and germ line cells. According to Haecker pluripotency exists when the species-specific plasm moves from one state of equilibrium to another. If pluripotency exists in germ cells, it is said to be a germ plasmatic pluripotency. If pluripotency occurs, on the other hand, during ontogenesis of embryonic organs, it is called somatic pluripotency. In that sense, Haecker maintained that transitions from heritable variations of germ cells to non-heritable variations of soma were in fact possible.[46] The importance of the concept of pluripotency for evolution manifests itself in the parallel development of various species.

Figure 1. Valentin Haecker as Rector at Halle University (University Archive Halle, Rep. 40, Nr. I, HI 36).

Haecker and epigenetics

Haecker's dissatisfaction with the simplicity of Mendelian chromosome theory, led to his theory of phenogenetics, which established the idea that the phenotype is not dictated merely or solely by the genetic makeup of an individual. He recognized that both genetic and environmental factors affect the phenotype of an organism. This idea is the cornerstone of epigenetics. Building upon Haecker's ideas, biologists began to focus on this bridge between genotype and phenotype, leading to the development of the field of epigenetics. Moving forward on the basis of Haecker's phenogenetics theory, Waddington defined epigenetics as "causal interactions between genes and their products which bring the phenotype into being".[47] Forty years later Medawar and Medawar defined the modern use of "epigenesis" as all processes that are involved in the implementation of genetic instructions within a fertilized egg.[48]

Now, almost 100 y after Haecker's proposed ideas about phenogenetics, it is clear that multiple mechanisms are involved in regulating genes, such as gene products (e.g. transcriptions factors) and environmental factors (e.g., uterine conditions, population density, temperature, or presence of a predator). Yet, the exact means by which phenotypic variations can become heritable genetic factors over time was unknown to Haecker and discovering the exact method of inheritance of epigenetic states has become an important research agenda in the field of epigenetics.[49] Now, through advances in the field of genetics, the transmission of epigenetic states of inheritance has been demonstrated through means of cortical inheritance, maternal cytoplasmic control, and, more recently, patterns of DNA methylation.[50] Cortical inheritance occurs through the transmission of information via organelles in the cortical cytoplasm, while maternal cytoplasmic control refers to the process by which early embryonic development is controlled, primarily, by products from the maternal genes deposited into the egg during oogenesis and not the embryo's own genome. The most recently discovered mechanism of epigenetic is DNA methylation, which describes the process by which a methyl group is added to cytosine DNA residues causing the highly methylated DNA to be less transcriptionally active than less methylated DNA.[51]

It is clear that Haecker's idea of phenogenetics ignited an impulse in biology to discover the mechanisms that affect the phenotype beyond the simple makeup of individual chromosomes. Decades of research provided not only more insight into the truth of the complex nature of phenotype development but also divulged the exact means by which epigenetic

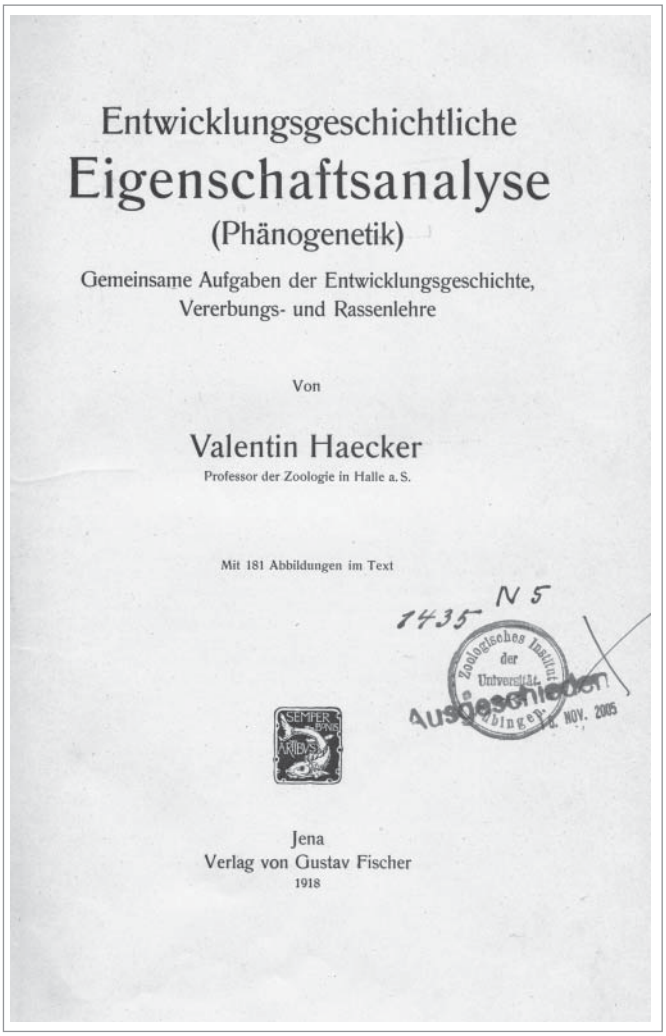

Entwicklungsgeschichtliche
Eigenschaftsanalyse
(Phänogenetik)
Gemeinsame Aufgaben der Entwicklungsgeschichte, Vererbungs- und Rassenlehre
Von
Valentin Haecker
Professor der Zoologie in Halle a. S.
Mit 181 Abbildungen im Text
Jena
Verlag von Gustav Fischer
1918

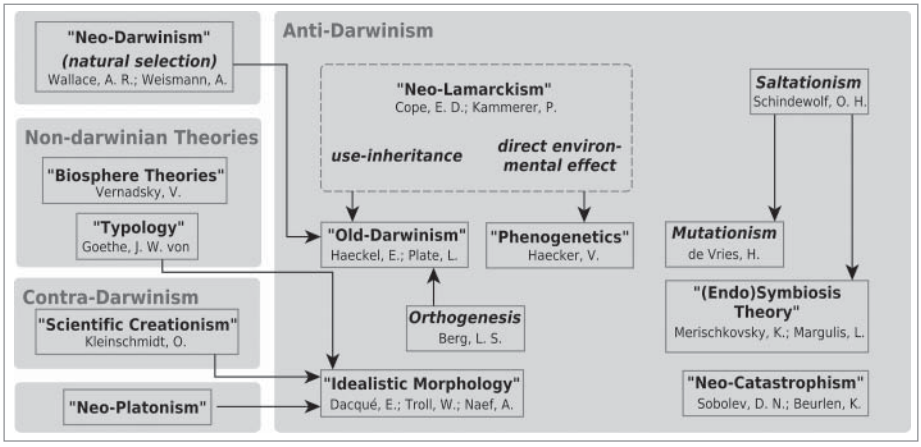
Figure 2. Title pager of Haecker's book "Evolutionary analysis of traits (phenogenetics)" published in Jena in 1918.

inheritance is possible. This scientific pursuit made it possible not only for scientists to understand the complex nature of epigenetics, but also to know the exact means by which it occurs. Interestingly, it was Howard Cedar's work on DNA methylation that won him the Louisa Gross Horwitz Prize this year. Cedar's research illustrated the capacity of changes in DNA methylation to switch on and off the triggers that control gene activity, thus allowing for the potential development of personalized treatment of patients suffering with cancer and other genetic diseases.[52] Cedar's work has truly illustrated the importance of cumulative scientific interest and research. Looking back over the last century, it becomes clear that Haecker's early interest in understanding the bridge between genotype and phenotype led to other scientists' interest in the discovery of the pathway of inheritance of epigenetic states, which was exposed through decades of research. Remarkably, this knowledge was then applied to create life-altering treatments.

Legacy

From phenogenetics to evo-devo

Valentin Haecker counts as one of the crucial figures in the history of German genetics in the first half of the 20th century along with Richard Goldschmidt, Erwin Baur, and Ludwig Plate. His 2 main contributions to the field of genetics were the theory of phenogenetics and the concept of pluripotency that he developed. His theory of phenogenetics merged various biological disciplines and discoveries and answered questions regarding the relationships between the phenotype and the genotype that provided the basis for future work in developmental genetics. Insofar, Haecker's theory of phenogenetics was not only indispensable for the future acquisition of knowledge in epigenetics but also in the fields of evo-devo. Today, evolutionary developmental biology (evo-devo) addresses the means in which development can affect evolutionary explanations.[53] The relationship between development and evolution in this sense focuses on the fact that development structures the phenotypic variations upon which natural selection works.[54] Many developmental tendencies that create or suppress variation arise from mechanisms with epigenetic origins.[55]



Scheme 1. "Evolutionary Theories in the 1st Third of the 20th century:" Various evolutionary mechanisms were advocated in the 1st third of the 20th century. The scheme contextualizes Haecker's theory among other evolutionary theories of that time. As many other contemporaries Haecker looked for a compromise between Darwinian and Lamarckian evolutionary mechanisms. He did not believe in heritability of purely somatic variations, but maintained that a "parallel induction" (environmental influence on both somatic and germinal tissue) may lead to inheritance of acquired characters.[56]

Disclosure of potential conflicts of interest

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References

1. Haecker V. Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik). Gemeinsame Aufgaben der Entwicklungsgeschichte, Vererbungs- und Rassenlehre. Jena: Gustav Fischer 1918.
2. "Pioneers in Epigenetics Awarded Horwitz Prize" CUMC Office of Communications (06 September 2016) http://newsroom.cumc.columbia.edu/blog/2016/09/06/pioneers-epigenetics-awarded-horwitz-prize/
3. Hallgrímsson B, Hall BK. Epigenetics. Linking Genotype and Phenotype in Development and Evolution. Berkeley and Los Angeles: University of California Press 2011, p. 1.
4. Waddington CH. The epigenotype. Endeavour 1942; 1:18-20.
5. Haecker V. Praxis und Theorie der Zellen- und Befruchtungslehre. Jena. Gustav Fischer 1899.
6. Haecker V. Bastardierung und Geschlechtszellenbildung. (Ein kritisches Referat). Zool. Jb., Suppl. 7 1904, pp. 161-260.
7. Haecker V. Über Gedächtnis, Vererbung und Pluripotenz. Jena: Gustav Fischer 1914.
8. Hoßfeld U. Ruderfußkrebse (Copepoden) - ein Versuchsobjekt der klassischen Vererbungszytologie zu Beginn des 20. Jahrhunderts. Biologisches Zentralblatt 1996; 115(2):91-103; Hoßfeld U. (1997): Gerhard Heberer (1901–1973) - Sein Beitrag zur Biologie im 20. Jahrhundert. Jahrbuch für Geschichte und Theorie der Biologie, Suppl.-Bd. 1, Verlag für Wissenschaft und Bildung, Berlin; Hoßfeld, U. (2016): Geschichte der biologischen Anthropologie in Deutschland. Von den Anfängen bis in die Nachkriegszeit. 2. Auflage, Stuttgart: Franz Steiner Verlag; Hoßfeld, U., T. Junker (2000): Bernhard Rensch (1900–1990) - Evolutionsbiologe, Ornithologe, Malakologe und Biophilosoph. Zum Gedenken an seinen 100. Geburtstag am 21. Januar 2000. Blätter aus dem Naumann-Museum 19: 78-89; Junker, T., U. Hoßfeld (2009): Die Entdeckung der Evolution. Eine revolutionäre Theorie und ihre Geschichte. 2. Aufl., Wissenschaftliche Buchgesellschaft Darmstadt; Levit G. S., Simunek M., Hoßfeld U. (2008) Psychoontogeny and Psychophylogeny: The Selectionist Turn of Bernhard Rensch (1900–1990) through the Prism of PanpsychisticIdentism. *Theory in Biosciences*, 127:297-322; Reif, W.-E., T. Junker, U. Hoßfeld: The synthetic theory of evolution: general problems and the German contribution to the synthesis. Theory in Biosciences 119 (2000), pp. 41-91.
9. Rensch B. Historical Development of the Present Synthetic Neo-Darwinism in Germany. In: Mayr E, WB Provine (eds.) The evolutionary synthesis. 4th ed., Cambridge, MA/ London: Harvard University Press 1998, pp. 284-303.
10. Haecker V. Goethes morphologische Arbeiten und die neuere Forschung. Jena: Gustav Fischer 1927.
11. Haecker V. Umwelt und Erbgut, Rede (gehalten beim Antritt des Rektorats der Vereinigten Friedrichs-Universität Halle-Wittenberg am 12. Juli 1926). Halle (Saale) 1926.
12. Barthelmess A., Vererbungswissenschaft. Freiburg/ München: Karl Alber 1952; Harwood, J. Styles of scientific thought. The German Genetic community 1900–1993. Chicago and London: The University of Chicago Press 1993
13. Simunek, M, Hoßfeld U, Thümmler F, Breidbach O. (eds.) THE MENDELIAN DIOSKURI. Correspondence of Armin with Erich von Tschermak-Seysenegg, 1898–1951. Praha: Pavel Mervat 2011a; Simunek M, Hoßfeld U, Wissemann V. 'Rediscovery' Revised – the cooperation of Erich and Armin von Tschermak-Seysenegg in the context of the 'rediscovery' of Mendel's Laws in 1899–1901. Plant Biol 2011b; 13:835-841; Hoßfeld U, Jacobsen H-J, Plass C, Brors B, Wackernagel W 2016. 150 years of Johann Gregor Mendel's "Versuche über Pflanzen-Hybriden." Molecular Genetics and Genomics (MGG); http://link.springer.com/article/10.1007/s00438-016-1254-4
14. 1) The Law of Segregation: Each inherited trait is defined by a gene pair. 2) The Law of Independent Assortment: Genes for different traits are sorted separately from one another. 3) The Law of Dominance: An organism with alternate forms of a gene will express the form that is dominant. (Mendel, G.: Versuche über Pflanzen-Hybriden. In: Verhandlungen des Naturforschenden Vereines in Brünn. 4/1866, pp. 3-47.).
15. Johannsen W. Elemente der exakten Erblichkeitslehre. Jena: Gustav Fischer 1909
16. Harwood J. Styles of scientific thought. The German Genetic community 1900-1993. Chicago and London: The University of Chicago Press 1993, p. 35
17. Lotsy JP. Vorlesungen über Deszendenztheorie. Jena: Gustav Fischer 1906, 1908
18. Baur E. Einführung in die experimentelle Vererbungslehre. Berlin: Borntraeger 1911
19. Goldschmidt R. Einführung in die Vererbungswissenschaft. Leipzig: W. Engelmann 1911
20. Haecker V. Allgemeine Vererbungslehre. Braunschweig: Vieweg & Sohn 1912
21. Plate L. Vererbungslehre. Jena: Gustav Fischer 1913
22. Lang A. Die experimentelle Vererbungslehre in der Zoologie seit 1900. Jena: Gustav Fischer 1914
23. Ziegler HE. Die Vererbungslehre in der Biologie und in der Soziologie. Jena: Gustav Fischer 1918
24. Meisenheimer, J. Vererbungslehre. Jena: Gustav Fischer 1923
25. Levit GS, Hoßfeld U. The Forgotten "Old-Darwinian" Synthesis: The Theoretical System of Ludwig H. Plate (1862–1937). Internationale Zeitschrift für Geschichte und Ethik der Naturwissenschaft, Technik und Medizin (NTM) 2006; N.S. 14:9-25; http://dx.doi.org/10.1007/s00048-005-0233-3
26. Haecker R. Das Leben von Valentin Haecker. Zoologischer Anzeiger 1965; 174:1-22; Immelmann K. Die ornithologischen Arbeiten Valentin Haeckers Teil 1. Zoologischer Anzeiger 1965a; 174:53-74; Immelmann K. Die ornithologischen Arbeiten Valentin Haeckers Teil 2. Zoologischer Anzeiger 1965b; 174; 450-67; Rensch B. Valentin Haeckers tierpsychologische Arbeiten. Zoologischer Anzeiger 1965; 74:445-50; Osche G. Über latente Potenzen und ihre Rolle im Evolutionsgeschehen. Zoologischer Anzeiger 1965; 174:411-40; Heberer G. Valentin Haecker – Klassiker der Genetik. FAZ vom 15. September 1964; Heberer G. Valentin Haecker und das Problem der Chromosomen-Reduktion, unter besonderer Berücksichtigung der Copepoden. Zoologischer Anzeiger 1965; 174:91-116; Kosswig C. Valentin Haeckers Vererbungslehre aus dem Jahre 1911. Zoologischer Anzeiger 1965; 174:441-5
27. Goldschmidt R. Physiologische Theorie der Vererbung. Berlin: Julius Springer 1927
28. Waddington CH. 1942. The epigenotype. Endeavour 1942; 1:18-20. "The epigenotype." Endeavour. 1: 18–20. "For the purpose of a study of inheritance, the relation between phenotypes and genotypes […] is, from a wider biological point of view, of crucial importance, since it is the kernel of the whole problem of development. Many geneticists have recognized this and attempted to discover the processes involved in the mechanism by which the genes of the genotype bring about phenotypic effects. The first step in such an enterprise is – or rather should be, since it is often omitted by those with an undue respect for the powers of reason – to describe what can be seen of the developmental processes. For enquiries of this kind, the word 'phenogenetics' was coined by Haecker [1918, Phänogenetik]. The second and more important part of the task is to discover the causal mechanisms at work, and to relate them as far as possible to what experimental embryology has already revealed of the mechanics of development. We might use the name 'epigenetics' for such studies, thus emphasizing their relation to the concepts, so strongly favourable to the classical theory of epigenesis, which have been reached by the experimental embryologists. We certainly need to remember that between genotype and phenotype, and connecting them to each other, there lies a whole complex of developmental processes. It is convenient to have a name for this complex: 'epigenotype' seems suitable."

29. Hallgrímsson B, Hall BK. 2011. Epigenetics. Linking Genotype and Phenotype in Development and Evolution. Berkeley and Los Angeles: University of California Press
30. Rensch B. The abandonment of Lamarckian explanations: the case of climatic parellism of animal charcteristics. In: Grene, M. (ed.): Dimensions of Darwinism. Cambridge: Cambridge University Press 1983, pp. 31-42; Rensch B. Historical Development of the Present Synthetic Neo-Darwinism in Germany. In: Mayr, E., W. B. Provine (eds.) The evolutionary synthesis. 4th ed., Cambridge, MA/ London: Harvard University Press 1998; Harwood J. Styles of scientific thought. The German Genetic community 1900–1993. Chicago and London: The University of Chicago Press 1993; Levit GS, Hoßfeld U. The Forgotten "Old-Darwinian" Synthesis: The Theoretical System of Ludwig H. Plate (1862–1937). Internationale Zeitschrift für Geschichte und Ethik der Naturwissenschaft, Technik und Medizin (NTM), N.S. 14 2006
31. Plate L. Vererbungslehre. Jena: Gustav Fischer 1913, p. 439
32. Levit GS, Hoßfeld U. The Forgotten "Old-Darwinian" Synthesis: The theoretical system of ludwig H. Plate (1862–1937). Internationale Zeitschrift für Geschichte und Ethik der Naturwissenschaft, Technik und Medizin (NTM), N.S. 14 2006; http://dx.doi.org/10.1007/s00048-005-0233-3
33. Plate L. Vererbungslehre. Jena: Gustav Fischer 1913, p. 440
34. Harwood J. Styles of scientific thought. The German Genetic community 1900–1993. Chicago and London: The University of Chicago Press 1993, p. 42
35. Rensch B. The abandonment of Lamarckian explanations: the case of climatic parellism of animal charcteristics. In: Grene, M. (ed.): Dimensions of Darwinism. Cambridge: Cambridge University Press 1983, p. 32
36. Haecker V. Allgemeine Vererbungslehre. Vieweg & Sohn, Braunschweig, 1921, p. 154
37. Haecker V. Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik). Gemeinsame Aufgaben der Entwicklungsgeschichte, Vererbungs- und Rassenlehre. Jena: Gustav Fischer 1918, p. 324
38. Haecker V. Allgemeine Vererbungslehre. Braunschweig: Vieweg & Sohn, 1921, p. 150ff, 163ff
39. Haecker V. Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik). Gemeinsame Aufgaben der Entwicklungsgeschichte, Vererbungs- und Rassenlehre. Jena: Gustav Fischer 1918, p. 4; Deichmann U. Biologists under Hitler. Harvard: Harvard University Press 1996, p. 164
40. Haecker V. Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik). Gemeinsame Aufgaben der Entwicklungsgeschichte, Vererbungs- und Rassenlehre. Jena: Gustav Fischer 1918, p. 4 ff
41. Freye H-A.: Valentin Haecker (1864 bis 1927) – Leben und Werk. Hercynia 2 (1965a), pp. 327–337; Freye, H.-P.: Valentin Haecker (1864–1927) und die Phänogenetik. Zoologischer Anzeiger 174 (1965b), pp. 401–410
42. Haecker V. Über Gedächtnis, Vererbung und Pluripotenz. Jena: Gustav Fischer 1914, p. 40
43. Haecker V. Pluripotenzerscheinungen. Synthetische Beiträge zur Vererbungs- und Abstammungslehre. Jena: Gustav Fischer 1925
44. Harwood J. Styles of scientific thought. The German genetic community 1900–1993. Chicago and London: The University of Chicago Press 1993, p. 131; Haecker V. Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik). Gemeinsame Aufgaben der Entwicklungsgeschichte, Vererbungs- und Rassenlehre. Jena: Gustav Fischer 1918; Haecker V. Vererbungslehre. Jena: Gustav Fischer 1911, 3rd ed. 1921
45. Haecker's italics: Haecker V. Pluripotenzerscheinungen. Synthetische Beiträge zur Vererbungs- und Abstammungslehre. Jena: Gustav Fischer 1925, pp. 1-2
46. Haecker V. Pluripotenzerscheinungen. Synthetische Beiträge zur Vererbungs- und Abstammungslehre. Jena: Gustav Fischer 1925, p. 3
47. Waddington CH. 1942. The epigenotype. Endeavour 1:18-20; Waddington CH. The evolution of an evolutionist. Ithaca, NY: Cornell University Press 1975
48. Medawar PB, Medawar JS. Aristotle to Zoos. A philosophical dictionary of biology. Cambridge, MA: Harvard University Press 1983
49. Hall BK, Pearson R, Müller GB. Environment, Development, and Evolution: Toward a Synthesis. Cambridge, MA: MIT Press 2004
50. Hallgrímsson B, Hall BK. 2011. Epigenetics. Linking Genotype and Phenotype in Development and Evolution. Berkeley and Los Angeles: University of California Press
51. Hallgrímsson B, Hall BK. 2011. Epigenetics. Linking Genotype and Phenotype in Development and Evolution. Berkeley and Los Angeles: University of California Press
52. Epigenetic Research. Institute for Medical Research Israel-Canada. http://www.imric.org/research/collaborations/research/epigenetics-research Accessed 16 September 2016
53. Hendrikse JL, Parsons TE, Hallgrímsson B. Evolvability as the proper focus of evolutionary developmental biology. Evol Dev 2007; 9:393-401; PMID:17651363; http://dx.doi.org/10.1111/j.1525-142X.2007.00176.x
54. Hendrikse JL, Parsons TE, Hallgrímsson B. Evolvability as the proper focus of evolutionary developmental biology. Evol Dev 2007; 9:393-401; PMID:17651363; http://dx.doi.org/10.1111/j.1525-142X.2007.00176.x
55. Hallgrímsson B, Hall BK. Epigenetics. Linking Genotype and Phenotype in Development and Evolution. Berkeley and Los Angeles: University of California Press 2011, p. 432
56. Haecker V. Allgemeine Vererbungslehre. Vieweg & Sohn, Braunschweig, 1912, p. 179