100 Years of phenogenetics: Valentin Haecker and his examination of the phenotype

Uwe Hoßfeld · Georgy S. Levit · Elizabeth Watts

Received: 5 July 2018 / Accepted: 3 December 2018 / Published online: 15 December 2018
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Abstract
Following the ‘rediscovery’ of Mendel’s work around 1900 the study of genetics grew rapidly and multiple new inheritance theories quickly emerged such as Hugo de Vries’ “Mutation Theory” (1901) and the “Boveri–Sutton Chromosome Theory” (1902). Mendel’s work also caught the attention of the German geneticist Valentin Haecker, yet he was generally dissatisfied with the simplicity of Mendelian genetics as he believed that inheritance and the expression of various characteristics appeared to be much more complex than the proposed “on–off hypotheses”. Haecker’s primary objection was that Mendelian-based theories still failed to bridge the gap between hereditary units and phenotypic traits. Haecker thus set out to bridge this gap in his research program, which he called Phänogenetik (“phenogenetics”). He outlined his work in a special study “Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik)” in 1918. 2018 thus marks the 100th anniversary of Haecker’s seminal publication, which was devoted to the analysis of the phenotype and highlighted the true complexity of heredity. This article takes a specific look at Haecker and his work, while also illustrating how this often forgotten scientist influenced the field of genetics and other scientists.

Keywords Valentin Haecker · Phenogenetics · Pluripotency · History of genetics · Phenotype · Genotype

Introduction
Valentin Haecker represents a rare species of scientists whose name and person have been almost entirely forgotten but whose ideas and the terms he developed have survived multiple generations and spread throughout the world. 2018 marks the 100th anniversary of the publication of Valentin Haecker’s “Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik)” and simultaneously marks the 110th anniversary of the founding of Molecular Genetics and Genomics (MGAG). When MGAG was founded as Zeitschrift für induktive Abstammungs- und Vererbungslehre (ZIAV) in 1908, it became the first journal dedicated to the field of genetics and has served since that point as a source of information for scientists and medical doctors working in the fields of genetics, genomics, biology, medicine and biotechnology, etc. (Hohmann and Hagemann 2010). To mark these momentous occasions, we have chosen to highlight the work of Valentin Haecker, who served not only as a pioneer in the field of genetics and developmental biology but was also incidentally part of the original editorial board of ZIAV in 1908 together with Carl Correns (Leipzig), Gustav Steinmann (Bonn) and Richard von Wettstein (Vienna).

During his lifetime and also posthumously, Haecker contributed not only the dissemination of information on genetics, publishing more than 30 articles in ZIAV (MGAG) alone, but also developed concepts about the interplay between genotype, phenotype and the environment that still tickle our intellectual curiosity. While modern geneticists have access to cutting-edge technology, Haecker’s ideas on phenogenetics were based almost entirely upon descriptive, morphological methodologies.

His foundational contribution to the field of genetics is seen still today as experts in the field continue to cite his work. For instance, pediatric geneticist John M. Opitz

Communicated by S. Hohmann.

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recently mentioned and celebrated Haecker in his (2017) article “Phenotypes, Pleiotropy, and Phylogeny” in American Journal of Medical Genetics. In this article, Opitz takes a look at the points raised by Gene Fisch’s (2017) and John C. Carey’s (2017) work on phenotype analyses and considers the idea of phenotype analyses from a historical viewpoint. As soon as one begins to talk about phenotype analyses, it is clear that one must mention Haecker as Opitz mentions this may, in fact, be the best translation for Haecker’s “Entwicklungsgeschichtliche Eigenschaftsanalyse” (Phenotype Analysis: translation by Opitz). But Opitz is not the only modern scientist who is still fascinated by Haecker’s work. In fact, if Haecker was alive today, he would enjoy a h-index of 33 as the citations of his work only continue to increase as we can see in the graphic below, which shows the number of times Haecker’s work has been cited per year since 1945 (Fig. 1).

We can see here that Haecker and his work found their way into ever more publications throughout the twentieth century. In fact, Haecker’s work has been cited in over 3800 articles (without self-citation) and was cited 207 times alone in 2017 according to Web of Science (accessed 22 October 2018). Despite the fact that Haecker only published in German and has been dead for over 90 years, he still enjoys higher citation statistics than many modern researches and one could say that the interest in Haecker only continues to grow as our understanding of genetics and the complex relationship between genotype and phenotype increase over time. As Opitz says, “Genotype […] cannot stand on its own as representing the only aspect of genetics worth bothering about. […] Phenotype analysis in medical school and psychology department is better at delimiting what a given condition or character-state is not rather than what our imperfect methods delude us into believing (2017, p. 330).” Although we should point out, that despite Haecker’s critique of the simplicity of Mendel’s work, Mendel’s popularity has also only continued to grow. As a simple comparison, we can see that Mendel’s work has been cited in over 51,000 articles (without self-citation) and was cited 5593 times alone in 2017 according to Web of Science (accessed 22 October 2018).

Genetics in Germany around 1900

The ‘rediscovery’ of Mendel’s laws in 1900 is seen worldwide as a turning point in modern research of heredity and genetics (Simunek et al. 2011a, b; Gayon 2016; Hoßfeld 2017b, c). During this time and later the three Mendelian laws were modified and supplemented to account for more complex patterns of inheritance. The Dutch botanist Hugo de Vries created his “Mutationstheorie” in 1901, Austrian physician Karl Landsteiner (1868–1943) discovered the blood groups, the Danish geneticist Wilhelm Johannsen (1857–1927) first described the cellular location of the “gene” in his Elemente der exakten Erblichkeitslehre (1909) and later coined the terms ‘phenotype’ and ‘genotype’, the German zoologist Theodor Boveri (1862–1915) and the American geneticist Walter Sutton (1877–1916) identified chromosomes as the carriers of genetic material. In Germany there was also a special interest in Mendelism and the study of genetics grew rapidly around this time, as seen through the rapid increase in the publication of related books and journals listed in the following tables:
Books:

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>German title (English translation)</th>
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<tbody>
<tr>
<td>1900/14</td>
<td>Arnold Lang</td>
<td>Die experimentelle Vererbungslehre in der Zoologie seit 1900 (Experimental genetics in zoology since 1900, 1914)</td>
</tr>
<tr>
<td>1905</td>
<td>Heinrich Ernst Ziegler</td>
<td>Die Vererbungslehre in der Biologie (Experimental genetics in biology)</td>
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<tr>
<td>1906/8</td>
<td>Johannes Paulus Lotsy</td>
<td>Vorlesungen über Deszendenztheorie (Lectures in evolutionary theory)</td>
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<tr>
<td>1911</td>
<td>Erwin Baur</td>
<td>Einführung in die experimentelle Vererbungslehre (Introduction into the experimental genetics)</td>
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<tr>
<td>1911</td>
<td>Richard Goldschmidt</td>
<td>Einführung in die Vererbungswissenschaft (Introduction into the general genetics)</td>
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<tr>
<td>1911</td>
<td>Valentin Haecker</td>
<td>Allgemeine Vererbungslehre (General genetics)</td>
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<tr>
<td>1913</td>
<td>Ludwig Plate</td>
<td>Vererbungslehre (Genetics)</td>
</tr>
<tr>
<td>1918</td>
<td>Heinrich Ernst Ziegler</td>
<td>Die Vererbungslehre in der Biologie und in der Soziologie (Genetics in biology and sociology, 1918)</td>
</tr>
<tr>
<td>1922</td>
<td>Ernst Lehmann</td>
<td>Die Theorien der Oenotherenforschung (Theories in oenothera research)</td>
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<tr>
<td>1923</td>
<td>Johannes Meisenheimer</td>
<td>Vererbungslehre (Genetics)</td>
</tr>
<tr>
<td>1923</td>
<td>Günter Just</td>
<td>Praktische Übungen zur Vererbungslehre. Für Studierende, Ärzte und Lehrer (Practical inheritance theory exercises. For students, doctors and teachers)</td>
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<tr>
<td>1927</td>
<td>Günter Just</td>
<td>Die Vererbung (Genetics)</td>
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Journals:

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<th>Year</th>
<th>Name of journal [English translation]</th>
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<tbody>
<tr>
<td>1899</td>
<td>Zeitschrift für Morphologie und Anthropologie [Journal of morphology and anthropology]</td>
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</table>

Valentin Haecker, the zoologist and geneticist from Halle University, was a key figure and networker during this time. He had a broad interest in different fields of biology such as genetics, ornithology, animal physiology, marine biology (Radiolaria), developmental genetics and philosophy and played a key role in the scientific developments in Germany (Haecker 1965; Immelmann 1965a, b; Rensch 1965; Osche 1965; Heberer 1964, 1965; Kosswig 1965). Following Richard Goldschmidt (see for instance his later book *Physiologische Theorie der Vererbung* in 1927—physiological theory of inheritance) Haecker was the second German geneticist to become interested in development. Although Conrad Hal Waddington (1905–1975) failed to cite Haecker’s work or to give him any credit in his 1962 book *Genetics and Development* (1962), he did mention Haecker in his prominent work “The Epigenotype” in 1942. Here Waddington clearly described Haecker’s early contribution to this new field:

“For the purpose of a study of inheritance, the relation between phenotypes and genotypes can be left comparatively uninvestigated; we need merely to assume that changes in the genotype produce correlated changes in the adult phenotype, but the mechanism of this correlation need not concern us. 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 […] to describe what can be seen of the developmental processes. For enquiries of this kind, the word ‘phenogenetics’ as coined by Haecker. 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
Fig. 2  Title page 1908 with Haecker as a member of the editorial board (Library New York Botanical Garden) https://archive.org/details/zeitschriftfri01berl

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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” (Waddington 1942, p. 18).

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” (Waddington 1942, 1975, pp. 218). Forty years later Medawar and Medawar defined the modern usage of “epigenesis” as all processes that are involved in the implementation of genetic instructions within a fertilized egg (Medawar and Medawar 1983).

**Valentin Haecker: life and work**

Ferdinand Carl Valentin Haecker was born on September 15, 1864 in Hungarian Altenburg (today Mosonmagyaróvár, Hungary) as the son of the Professor of Agriculture Christian Ludwig Haecker. He began school in 1870 at the Volksschule in Altenburg and 3 years later his father suddenly died of a stroke. It is known that the young Haecker focused on the natural sciences and had a particular interest in biology early on his childhood. After the death of his father, Haecker’s family moved to Stuttgart in August 1874. He began his school career at a Gymnasium in Stuttgart. As one of the best 12 from 108 applicants he later transferred to two elite schools of the time Maulbronn at the Klosterschule (1879) and 2 years later to Blaubeuren, where he received his Reifeprüfung (school-leaving exam) on August 15, 1883. After graduating from high school, Haecker served 1 year as lieutenant, the so-called “Einjährigen-Jahr”. In the fall of 1884, together with his brother Walter, he graduated and enrolled first at Tübingen convent (Stift), and later at Tübingen University where he studied mathematics and natural sciences. Here, Haecker attended lectures by Theodor Eimer (1843–1898), founder of the orthogenesis theory. He spent his fifth semester in Straßburg and finished his studies in spring 1889 at Tübingen University. After receiving his PhD (Über die Farben der Vogelfedern; On the color of avian feathers) in 1889 with Eimer as his advisor, he spent the next decade in Freiburg working as an assistant to the neo-Darwinian August Weismann (1834–1914) in his institute, then as a Privatdozent after his habilitation, and finally as außerordentlicher Professor (Professor extraordinarius, i.e., a professor without chair-function) starting in 1895. Later Haecker commemorated their time together in Freiburg by dedicating two of his later books to Weismann on his 70th and 80th birthday, Bastardierung und Geschlechtszellenbildung (Bastardization and the Production of Germ Cells) (1904) and Über Gedächtnis, Vererbung und Pluripotenz (On Memory, Inheritance and Pluripotency) (1914). During this time, he also published his first book about Praxis und Theorie der Zellen- und Befruchtungslehre [On the theory of the cell- and fertilization] (1899).

In 1900, when Haecker was 36 years old, he was called to the chair of zoology at the Technische Hochschule Stuttgart as follower of Carl Benjamin Klunzinger (1834–1914), where he taught students of agriculture and veterinary medicine, and became interested in Mendelism. During his time in Stuttgart Haecker evaluated the Radiolaria collection (starting in 1902) from the Valdivia-expedition (1898–1899) with Karl Chun (1852–1914) and he married Johanna Lucia Anna Kühn in 1903 (Haecker 1908, 1909). Together they had two children: a daughter Hertha and a son Rudolf. In 1908 he joined the editorial board of the newly founded journal ZIAV (Hohmann and Hagemann 2010) (Fig. 2). His main research interest in Stuttgart focused on problems with neoteny in axolotls. In 1909, he moved as Ordinarius for zoology at the philosophical faculty to Halle University and was elected member of the Leopoldina academy in 1910. In 1920 he was also a co-founder of the “Deutsche Gesellschaft für Vererbungswissenschaft” [German Society of Heredity] (1920).

During Haecker’s teaching time at the University of Halle, two later architects of the synthetic theory of evolution in Germany, Bernhard Rensch (1900–1990) and Gerhard Heberer (1901–1973), received their Ph.D.’s under his leadership. Rensch published his study on the cause of dwarfism and gigantism in the domestic fowl [Über die Ursachen von Riesen- und Zwergenwuchs beim Haushuhn] in 1922. Heberer followed in 1924 with his study on sperm formation in copepods [Die Spermatogenese der Copeoden]. As a student of Haecker, Rensch was especially well informed regarding the process of speciation and the course of phylogeny (Reif et al. 2000). He quickly recognized the great theoretical importance of this new systematic. His studies contributed to Haecker’s research on the analysis of the development of different characteristics. Haecker, on the other hand, emphasized that Lamarckian explanations had received strong theoretical objections: “Haecker […] also thought that the geographic color differences of birds and mammals – more brownish in Western and more grayish in Eastern Europe – were nongenetic modifications, whereas I [Rensch] was convinced of their genetic nature” (Rensch 1998, p. 294). In general, it can be said that Heberer and Rensch were influenced not only by Haecker’s work but also his personality and mode of thinking (see Heberer’s diaries in Hoßfeld’s possession or Rensch’s autobiography 1979). Heberer had his first contact to the field of genetics through his work.
with Haecker (cytogenetic with cœpods, chromosomal theory of heredity) while Haecker’s philosophy along with Theodor Ziehen influenced Rensch’s later ‘Biophilosophy’. Both Heberer and Rensch were key players in the development of the Modern Synthesis (Levit 2008; Hoßfeld 1997; Reif et al. 2000). The influence that Haecker had on Rensch is further highlighted by abundant citation of Haecker not only in Rensch’s work but also in his autobiography (Rensch 1947, 1968, 1971, 1979).

In 1911, Haecker published his first edition of his Allgemeine Vererbungslehre (3ed ed. 1923 [General Genetics]), in 1918 his major work Phänogenetik [phenogenetics] appeared, together with the philosopher Theodor Ziehen he wrote Zur Vererbung und Entwicklung der musikalischen Begabung (1923) [On the heredity and development of musical talent], and finally he published his analysis on Goethes morphologische Arbeiten und die neuere Forschung (1927) [The morphological works on Goethe and new research]. In 1923 Haecker lectured on human racial and family research. His lectures on agriculture were attended by Richard W. Darré (1895–1953), the advocate of the regeneration of the peasantry (Weindling 1989, p. 330). In 1926 Haecker became the rector of the university and held his inaugural lecture entitled “Environment and Heredity” (Umwelt und Erbgut). Haecker died suddenly of a stroke at the age of 63 in Halle on December 12, 1927 (Freye 1965a, b; Hoßfeld 2017a) shortly after he handed his rector’s position over to Theodor Ziehen (Fig. 3).

In the 1930s, interest in experimental genetics rose in Germany out of interest in understanding the genetics of human pathology. During this time there was a conceptual orientation towards experimental genetics at the Kaiser Wilhelm Institute for Anthropology, Human Heredity, and Eugenics (Kaiser-Wilhelm-Institut für Anthropologie, menschliche Erblehre und Eugenik, KWIA) with a special focus on phenogenetics (Baader et al. 2005). Yet, Haecker’s work did not play a large role here, as Hans-Walter Schmuhl explains, that the only true link between Haecker and the KWIA was a reference by KWIA director Eugen Fischer made to Haecker in 1938, but this reference appears to be made only in reference to the origin of the term ‘phenogenetics’ (Schmuhl 2005). With regard to content, Fischer relied much more on the work of Richard Goldschmidt who published his Physiological Theorie der Vererbung in (1927) just prior to Haecker’s death (ibid.). Our own random sampling of the literature from that period, Menschliche Auslese und Rassenhygiene (Eugenik) [Human Selection and Race Hygiene (Eugenics)] by Erwin Baur, Eugen Fischer and Fritz Lenz (1932) and Menschliche Erblehre und Rassenhygiene (Eugenik) [Human Heredity and Race Hygiene (Eugenics)] by Erwin Baur, Eugen Fischer and Fritz Lenz (1936) showed that Haecker was mentioned three times in Menschliche Erblehre with regard to musical talent and only two times

![Image](Fig. 3 Valentin Haecker (second from left) handing his rector’s office over to Theodor Ziehen in 1927 at the University of Halle (UAHW, Rep. 42, N1338)
On phenogenetics and pluripotency

One of Haecker’s objections to the Mendelian chromosome theory was its failure to bridge the gap between hereditary units and phenotypic traits (Haecker 1915, 1917). His research program, which he called Phänogenetik (“phenogenetics”) was focused precisely on building this bridge between the genotype and the phenotype (see the chapter “Genotype–Phenotype Map” in Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik)). He outlined this program in a special study of 1918 (Fig. 4). In the preface Haecker described a new research field that should explore the appearance of the organism’s “external characteristics in terms of morphogenetics and developmental physiology” (Haecker 1918, p. 4).

According to Haecker, phenogenetics always begins with the so-called “differential diagnostics”, i.e., with histological, morphological and physiological studies of the differences between species or breeds. All his phenogenetic investigations were descriptive, such as colour differences in different breeds of mammals, axolotls, birds and plants (ch. 7–13) as well as the stripe patterns in various species (ch. 14), or the growth of the skin (ch. 16–18), while it is now known that albinism in axolotl is the result of the mutant alleles, Haecker makes no reference to the genetic or genotype basis of these differences. This “phenoanalysis” is followed by a “phenogenetic descriptive” investigation of variations of a certain trait. The traits in question are traced back to a “phenocritical phase” (phenocrisis), the point of bifurcation in which the developmental stage manifests an initial divergence of the trait. However, the timing of this bifurcation can be very different depending on the species and external characteristics as Haecker points out in his book: “[…] among many of the colorful breeds of chickens this point falls during of the transition from down feathers to the first plumage, while in the colorful Axolotls it occurs during the last stages of embryonic development (1918, p. 5).

Phenogenetics focused on divergent development paths, which the general study of genetics (heredity) could not adequately explain, according to Haecker’s point of view. For Haecker, it was imperative that the underlying internal causes, i.e., the actual phenocritical causes of the divergence, be considered and determined. Phenogenetics thus became the mediator between developmental mechanics and physiology (Wilhelm Roux, Hans Driesch, Hans Spemann). Haecker’s analytical approach to his phenogenetic interpretations was primarily a descriptive analysis of the varying phenotypes. This descriptive methodology in seen clearly in his considerations of ectoderm formation, in his interest in color differences among different breeds of mammals, the axolotl, birds and plants as well as in his illustrations of wild animals and skin growth, together with as his studies of skull shapes and face types in humans and domestic mammals.

Through his analyses of variation and developmental history, Haecker recognized that cranial and facial skulls showed a high degree of independence from the animal’s general body size (Hoßfeld et al. 2018). By this point in time, Darwin (1868) had also already made the suggestion that skull variations between domestic rabbits and wild hares was directly caused by changes to the brain and indirectly through their ecosystem (e.g., captivity versus wild). From a developmental perspective, Haecker regarded the skull shape and face forms as well as certain regions of the face to be komplex-verursacht (having complex origins), i.e., that the development took place through the interaction of different developmental processes and under the influence of the neighboring organs. He also recognized allometric principles, according to which the size of the brain (brain cavity) decreased disproportionately slower than the size of the animal and thus he analyzed, for example, how masticatory musculature and neck muscles affected the shape of the skull. Later, Berthold Klatt (1885–1958) also described these allometric relationships in dogs (e.g., Bolognese and St. Bernard), Haecker also discussed the problem of human asymmetry, e.g., handedness, in 1918, which he considered to be hereditary, as well as the phenogenetic problems of limb abnormalities such as polydactyly, syndactyly and brachydactyly in animals and humans (Fig. 4).

In Haecker’s eyes, another task of the field of “phenogenetics” was to understand the phenomenon of pluripotency, especially in terms of development (i.e., the investigation of its role in variability.) As examples, he named variations of radiolarian skeletons, the webbed toes found in certain pigeon populations, as well as the appearance of a white throat patch among polecats, normally a characteristic feature of stone martens, etc. Haecker first used the term Pluripotenz des Artplasmas (“Pluripotency of species-specific plasm”) in his book Über Gedächtnis, Vererbung und Pluripotenz (1914, p. 40) and explained his hypothesis in detail in a later work on Pluripotenzerscheinungen (“The manifestations of pluripotency”) (Haecker 1925). In Über Gedächtnis, Vererbung und Pluripotenz, we see how Haecker integrated ideas from many of his contemporaries and predecessors such as those from Hugo de Vries, Theodor Ziehen, Ernst Haeckel, Charles Darwin, Ludwig Plate, Wilhelm Roux, August Weismann and a number of other scientists—yet he does not reference Driesch, Spemann or Mendel. 1 While

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1 Haecker did spend some time discussing Mendelian genetics in later publications such as the two chapters he devoted to Mendelian rules in his 1921 book “Allgemeine Vererbungslehre” (General Genetics).
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

Fig. 4 Title page of Haecker’s Entwicklungsgeschichtliche Eigenschaftsanalyse (Phänogenetik) from 1918
he often cites de Vries and his Mutation Theory, he omits Roux, Driesch and Spemann and their ideas regarding developmental mechanics and developmental physiology almost entirely. Here we get a clear picture of how Haecker acted as a conduit of information, integrating concepts from zoology, evolution and genetics to form his ideas on pluripotency and then as he built upon his ideas, passed on his mode of thinking to his students Rensch and Heberer, who in turn played a crucial role in the development of the Modern Synthesis (Mayr and Provine 1988; Levit et al. 2008) (Fig. 5).

In general, Haecker’s theory of pluripotency postulated a relatively plastic concept of hereditary material suitable to account for the inheritance of acquired characteristics (Harwood 1993, p. 131). In 1925 he published the most complete definition of the term: “In a narrow (evolutionary) sense, I understand by pluripotency an essential ability of every organism (not only of species and races, but also of any individual germ and any cell at the embryonic stage of any individual) to develop under certain circumstances in directions deviating from the basic type. Therefore, pluripotency is a presence of a greater, although not unlimited number, 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” (1925, pp. 1–2. Haecker’s italics. Our translation). With the term Artplasma (“species-specific plasm”), Haecker describes hereditary material in a very broad and flexible sense, whereas the germ plasm was for him identical with nuclear substance of germ cells and germ line cells. Pluripotency enters the stage when the Artplasma moves into another state of equilibrium. According to Haecker, when germ cells become pluripotent, then it is referred to as “germ plasmatic pluripotency”, while pluripotent phenomena during the ontogenesis of embryonic organs is known as “somatic pluripotency”. Haecker maintained that it was possible for heritable variations of germ cells to be transferred to non-heritable variations of soma (1925, p. 3). In such cases as atavisms and rudiments, pluripotency manifests itself in the ontogenetic development. Soon after this 1925 publication, Haecker’s concept of pluripotency was introduced in English language literature as well. For example, the Austrian geneticist Hans Przibram (1874–1944) published a short paper in *Nature* in 1930 discussing the concept of pluripotency while making a direct reference to Haecker...
and his 1925 publication (Przibram 1930). It is now well established that cellular pluripotency exists in its purest form within the stem cell of the epiblast and that these cells lose their pluripotency as these embryonic cells become specified during development (Hallgrimsson and Hall 2011, Graw 2010). These pluripotent stem cells offer numerous potential applications in the field of medicine as Paul J. Tesar writes, “The discovery of pluripotent stem cells and now the ability to generate them from differentiated cells has had a profound impact on a vast array of scientific disciplines. In addition to their clinical potential as a source of therapeutic cell types, pluripotent stem cells provide scalable access to otherwise experimentally inaccessible development- and disease-associated biology (Tesar 2016, p. 163).” Due to his work analyzing the pluripotent potential of cells, many modern geneticists credit Haecker with helping form the basis of modern stem cell research. In the book Stem Cells & Regenerative Medicine: From Molecular Embryology to Tissue Engineering (2010), Krishnarao and Raghu K. Appasani credit Haecker along with Ernst Haeckel, Theodor Boveri and Edmund Wilson with establishing the foundation of our modern understanding of stem cells. Lucie Laplane also credits Haecker, Boveri, Haeckel and Richard Weissenberg (1882–1974) with developing the idea of a pluripotent stem cell in her (2016) book Cancer Stem Cells. The applications of stem cells range from reversal of baldness to the treatment of Parkinson’s disease, while the general understanding of stem cells has provided a new perspective on cancer research and tissue engineering.

**Conclusion**

Haecker was dissatisfied with the simplicity of Mendelian genetics as inheritance and expression of factors appeared to be much more complex than simply the presence or absence of one particular gene and even went as far to say in his *Entwicklungsgeschichtliche Eigenschaftsanalyse*, “For all of those who have followed the progression of Mendelism from the outset, it must appear, that after a decade and a half of work, Mendel’s research has reached a dead-end as his most important speculative tools, the idea of the absence or presence of particular factors, is increasingly incapable of sufficiently explaining cross-over effects (1918, p. 1)”. What Haecker failed to realize is that Mendel’s inability to explain the true complexity of heredity was not a sign of incompetence but a general characteristic of scientific endeavors. This point was poignantly captured in the obituary written by paleoanthropologist John Hawk honoring the distinguished geneticist Luigi Luca Cavalli-Sforza, who died on 31 August 2018. “More than any other human geneticist, Cavalli-Sforza believed in the potential of genes and culture to trace humanity’s origins. In the course of his work, he pioneered new ideas and models that brought together these two distinct areas of science. Like most scientists, many of his ideas would turn out to be wrong in the details. But his work helped form the foundation of our current knowledge of human genome variation across the world” (emphasis added). The same could be said of Haecker, whose work has become overshadowed by subsequent work in the field of genetics, but his theory of phenogenetics and his later conceptual work on pluripotency contributed to the advancement of our knowledge of genetics. Moreover, his work and his teaching influenced researchers in his field, such as Rensch and Heberer, who in turn affected the manner in which we regard evolutionary theory and understand heredity.

**Compliance with ethical standards**

**Conflict of interest** Uwe Höflfeld, declares that he has no conflict of interest. Georgy S. Levit, declares that he has no conflict of interest. Elizabeth Watts, declares that she has no conflict of interest.

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