MENDELIAN GENETICS AND POSTGENOMICS: THE LEGACY FOR TODAY

GARLAND E. ALLEN

INTRODUCTION

It is with great pleasure that I can pay tribute in this essay to Ernst Mayr on his one hundredth birthday. As one of my two advisors when I was writing my dissertation in the history of sciences in the mid 1960s (the other was Everett Mendelsohn) Ernst was especially interested in the questions of how classical Mendelian genetics had developed in relation to Darwinian theory during the first three decades of the twentieth century. I was working on T.H. Morgan's conversion from skeptic to strong proponent of both Mendelism and the chromosome theory, and Ernst exhorted me to show why Morgan had been "wrong" in his criticisms of Darwin and in his failure to see how genetics could be applied to an understanding of natural selection. Historiographically, however, I had been carefully schooled to not judge earlier scientific endeavors by present-day standards ("presentism" it was called), and I resisted saying Morgan was "wrong." But Ernst's point was well taken in one important regard. It did force me to look in much closer detail at what Morgan actually thought he understood about the "gene" and its relation to the process of evolution, a view that subsequently affected the way in which the Mendelian-chromosome theory was presented to the wider biological community. For example, despite the considerable amount of attention Morgan and his students devoted to chromosomal rearrangements, he never accorded such recombinations much of a role in evolution. Genes and gene mutation were for him the major source of evolutionary innovation. This view had an impact on biologists concerned with evolutionary matters (from field naturalists to taxonomists to paleontologists) and thus shaped debates around the Evolutionary Synthesis of the period 1930-1950.

That was just one of the lessons I learned from Ernst over the years. Thus, I think that it is appropriate in celebrating his centennial to apply that same perspective I developed under his guidance 35 years ago to

Department of Biology, Washington University, St. Louis, MO 63130, USA.
allen@biology2.wusl.edu

another case in the history of genetics, one that goes back to the beginning of the field itself, with the work of Gregor Mendel. In so doing, I have taken advantage of a considerable amount of scholarship about Mendel and his context that has been published in the last quarter-century. In addition, through several conferences and joint publication projects organized by Vitezslav Orel, former director (now emeritus) of the Mendelianum, the Mendel archives of the Moravian Museum in Brno, I have been able to learn first-hand from vigorous discussion with the best scholars of the subject the difficulties that have beset historians trying to understand what Mendel was aiming to do with his decade-long experiments on hybridization. This enterprise has more than historical or antiquarian interest. The way in which we have come to think about the nature of genes and what they do at the present time is very much a product of both how Mendel presented his work originally and how it was taken up and publicized by others after 1900.

Although Gregor Mendel (1822-1884) first presented his work at a meeting of the Brünn (Brno was then part of the Austro-Hungarian empire) Natural History Society in 1865, and published in its *Proceedings* in 1866, it received only a modicum of attention until 1900, when it was more or less "simultaneously" rediscovered by three different investigators: Carl Correns (1864-1933) in Germany; Hugo De Vries (1848-1935) in the Netherlands, and Erich von Tschermak-Szeneygg (1871-1962) in Austria. While all three found Mendel's work suggestive, it is not clear that any of them, other than Correns, really saw the significance of what Mendel had done, and none of the "rediscoverers" became a major promoter of the new genetics [1].

The first major publicist for Mendel's work was William Bateson (1865-1926) in England. Through the Royal Horticultural Society, Bateson had Mendel's paper translated into English for the first time, and wrote a general exposition that laid out the basic principles of what soon came to be known as "Mendelism" [2]. Bateson's work brought Mendel to the attention of numerous workers in England, Scandinavia and the United States, in particular to many of those involved in practical animal and plant breeding [3]. Although there was reluctance among some quarters—especially among academic biologists—to embrace Mendel's work immediately, by the end of the first decade of the twentieth century the theory had gained a considerable following. However, one of the main problems to which critics pointed was that, in the context of the beginning years of the twentieth century, the explanation Mendel offered of his breeding data seemed reminiscent of so many of the speculative, particulate theories of heredity that had abounded in the post-Darwinian era (including Darwin's own "provisional hypothesis of pangenesis," August Weismannn's elaborate theory of "ids, idants and biophors," Ernst Haeckel's imaginary "plastidules," and Hugo de Vries' postulated "pangenes," among many others). As a result, to some at least, Mendel's work seemed like just one more of the sort of abstract proposals they had encountered all too frequently. In point of fact, the paper probably seemed extraordinarily dense, having no illustrations, and loaded with binomial expansions which, while technically not very difficult, were likely to have been a put-off for many biologists who were as a community at the time notoriously math-shy. For whatever reason, for the first decade of its re-emergence into the scientific world, Mendel's contribution remained controversial at best, dismissed by significant sections of the biological community at worst.

What ultimately served to establish Mendelism on more firm ground was its unification with the cytological work on chromosome structure and behavior, carried out on a number of fronts, but most well known through the work of Thomas Hunt Morgan (1866-1945) and his young, enthusiastic team of investigators at Columbia University between 1911 and 1925. The work of the Morgan school was able to demonstrate that the abstract elements or "factors" discussed by early twentieth century Mendelians could be regarded as discrete, material units arranged linearly along the chromosomes, and that observed variations in the patterns of inheritance of traits (independent assortment, linkage, non-disjunction, etc.) could be traced to the mechanics of chromosome behavior during meiosis (gamete formation). Thus, the failure of certain groups of traits to show Mendel's independent assortment, or the occasional and unexpected dissociation of traits that were otherwise inherited together, could all be accounted for by reference to chromosomal behavior. Mendel's "factors" (after 1909 referred to as "genes") thus seemed to be real, material units, not metaphysical postulates. In recognition of this work, in 1933 Morgan was awarded the first Nobel Prize ever given for work in genetics [4].

The common picture of Mendelian theory, therefore, that has emerged from this early work and has been promoted in textbooks ever since, consists of the following claims:

(1) Mendel observed the inheritance patterns of *traits* or *characteristics* in pea plants, (such as height, pod color, or seed shape) each of which showed two alternative forms: Tall/Short, Yellow/Green, Smooth/Wrinkled, respectively;

(2) Mendel referred to these alternate conditions as dominant and recessive, respectively in the pairs listed above;

(3) Mendel hypothesized that each trait was represented in the germ cells of adult plants by two *determinants* (referred to in his paper as "*Anlagen*" or "elements"), one received from each parent; these determi-

nants were symbolized by Mendel with capital letters for the dominant form (*i.e.,* A) and lower case letter for the recessive form (*i.e.,* a);

(4) The determinants could be combined in one of three ways: two dominants (AA), two recessives (aa) or a dominant and a recessive, or *hybrid* (Aa);

(5) Although he knew nothing about the cytology of chromosomes, Mendel hypothesized that in the formation of the pollen or egg cell, the two factors for each trait would separate and go into different gametes; thus a parent that was pure dominant would produce gametes all of which contained the dominant factor (A), and a parent that was pure recessive would produce gametes all of which contained the recessive factor (a); hybrid parents, however, would produce two kinds of gametes: 50 per cent would contain the dominant factor (A) and 50 per cent the recessive factor (a);

(6) At fertilization the double-determinant condition would be restored;

(7) If both parents were hybrids, any of the three possible combinations could occur and would be distributed randomly, according to the laws of probability: 1 AA : 2 Aa : 1 aa; since organisms that are Aa and AA look alike, the ratio based on appearance of the traits (what later came to be called "phenotype," in contrast to the actual combination of determinants, the "genotype") would be 3 : 1;

(8) When two or more characteristics (Aa, Tt) are followed, in a dihybrid cross, the two sets of determinants segregate randomly, so that any combination of A, a, T and t is possible (what came to be known as the principle of random assortment).

(9) Factors produce or somehow *determine* traits, so that after the term "gene" was introduced in 1909, it was common to speak of a "gene for tallness," or a "gene for wrinkled seed," etc.; during the early years of the Mendelian theory, this was referred to as the "unit-character" hypothesis;

(10) Factors are not modified by being combined with their alternate form; thus, the factor, t, for shortness is not affected in any way by being combined with the dominant factor, T, for tallness in the hybrid (this came to be known as the concept of the "purity of the gametes").

This scheme has made for a very heuristic pedagogy, and has been replicated in an almost infinite number of high school and college biology textbooks. Although it has enjoyed a certain intellectual neatness, this formulation has a number of problems that have now begun to surface as molecular genetics has provided a far more sophisticated understanding of gene function than was available in the first half of the twentieth century. The first problem is simply a historical one: It is not at all clear that this neat textbooks scheme is the sort of picture Mendel himself had in mind. The second is that, as an introduction to the study of genetics, it has led to a variety of unfortunate and now long-entrenched misunderstandings of how genes really function, and the relationship between genes and the development of adult traits that has carried over into molecular genetics.

Thus, I would like to go back to the roots of genetics itself to ask: (1) What sort of picture did Mendel himself have of the ultimate uses of his work, in contrast to what the early twentieth century Mendelians put forward in his name? (2) What were Mendel's motivations in carrying out the extensive experiments he conducted on hybridization in the common pea, *Pisum sativum*? (3) How did Mendel's own conception of his work compare (or contrast) to the collection of ideas and methodologies—the paradigm if you will—that later became known as Mendelian genetics? (4) How has Mendel's legacy affected the way we understand genetics today as we stand in the long shadow of DNA? With genetics so much at the center of our present biomedical and biotechnological research, an examination of the history of our concepts in the field can help us better understand what we should and should not expect from current genetics claims. For that enterprise there is no better starting place than Mendel himself.

MENDEL'S BACKGROUND

Gregor Johann Mendel was born on July 22, 1822, in the small rural village of Hyncice, in Moravian Silesia, then part of the Austro-Hungarian Empire. As the only son of a peasant farmer, Mendel was expected to follow in his father's footsteps and take up farming, but early on his interest in natural history, and his studious ways brought him to the attention of the priest, friar Schreiber and the local schoolteacher. Although it was a financial hardship for the family, young Johann was sent off to a larger school in a village some twelve miles from Hyncice. Eventually, he qualified for Gymnasium in the city of Opava (Troppau), where he paid for his own room and board by giving private tutoring lessons to other students. It was a period of extreme privation, but Mendel managed to graduate in 1840 with considerable academic success. One of the chief influences on him at the time was Schreiber's Enlightenment ideals, particularly his emphasis on science as a way of dispelling superstition and ignorance. True to other Enlightenment ideas, friar Schreiber was strongly interested in applying scientific principles to the improvement of humanity—and as such was heavily involved with local agricultural groups and the Pomological Society [5].

Financial problems continued to plague Mendel as he tried to continue his studies at the Philosophy Institute in Olomuc (Olmütz), a two-year preparatory program for entrance to university-level studies in law, theology and medicine. After several periods of illness, brought on it, is thought, by his poverty and overwork, Mendel managed to finish his studies at the Institute and entered Olomuc University. There, according to records, he took a course of lectures in physics, mathematics and logic. Despite some small financial help from his family, money remained such a problem that Mendel was unable to complete his degree. It was at this juncture that he decided to enter the priesthood as a means of earning his keep. He applied for, and was accepted into, the Augustinian monastery of Saint Thomas at Brno in 1843. Although he did not feel a particularly fervent spiritual calling, Mendel realized shortly after joining the monastery that at last he was free from constant financial worries and could pursue his intellectual interests in exchange for attending to pastoral duties.

Mendel's choice was a good one for him at the time. The monastery at Brno was a center of learning in the early and mid-nineteenth century, especially in the natural sciences and agriculture [6]. Indeed, it gained most of its income from extensive landholdings that were given over to a variety of local farmers, so that the practical and economic benefits of promoting new agricultural practices had become among the monastery's top priorities. The Abbott (administrator) at the time Mendel entered Saint Thomas was friar F. Cyril Napp (1792-1867), an enthusiastic naturalist, member of several local agricultural and scientific societies, and author of a number of technical papers, particularly on plant pests. In 1830 he had given over one part of the monastery garden to another monk, Matous Klácel (1808-1882) for experimental cultivation of rare Moravian plants. The monastery also had an extensive library containing a variety of scholarly texts, to which Napp added during his tenure, especially in the natural sciences. Mendel was much influenced by Napp and Klácel. The latter was a Hegelian in philosophy, amateur botanist, known for his broad interests in the natural sciences, and a member of the Brno Agricultural Society. Klácel was a convinced Darwinian from 1860 onward, and indeed it was he who asked Mendel to take over responsibilities for the small experimental garden when he was away promoting a pan-Slavonic congress in Prague during the revolutionary year of 1848. Eventually forced to emigrate (to the United States) in 1869 for his radical, nationalistic views, Klácel was nonetheless a great inspiration to Mendel in turning his interests and attention to the study of natural sciences [7].

Roger Wood and Vitezslav Orel have emphasized the importance of agricultural concerns in Mendel's developing interests in the natural sciences [8]. The amount of experimental breeding, both with plants and animals, in Moravia at the time was extensive. Indeed, the Brünn Natural History Society, before which Mendel read his *Pisum* paper in 1865, was a section of the larger Brünn Agricultural Society (of which friar Schreiber was a corresponding member). The peas with which Mendel worked were derived from major commercial strains, suggesting the close connection between studies on hybridization and agricultural interests. We will return to this point shortly, but for the moment I want to stress two important aspects of Mendel's background up to the time he began his experiments (1856): (1) The atmosphere promoting science in Brno and at the monastery was highly supportive of Mendel's own budding interests in natural science and mathematics; and (2) The emphasis on agriculture, particularly animal and plant husbandry, among local agriculturalists and various members of the monastery staff turned Mendel's interests in a specific direction that ultimately led to his extensive series of breeding experiments.

After being unable to cope with his initial assigned duties as a parish priest (he was upset too easily by ministering to the sick, aged and dying) Mendel's first assigned work as a member of the Augustinian order was as a schoolteacher in the town of Znojmo in southern Moravia, starting in the fall of 1849. Education was being expanded in the Hapsburg Empire as a result of the revolutionary upheavals of 1848, and the Church was being pressured by the government to provide teachers. As part of that expansion, however, teachers were also being required to pass a certification exam. Mendel took the exam for the first time in August, 1850, but failed. He appears to have been seriously affected by what in today's lingo we would call "exam anxiety." Although he was much acclaimed as a teacher and colleague in Znojmo, Mendel was recalled by friar Napp to the monastery, with the idea of continuing his studies in natural science and eventually taking up teaching duties in Brno. Sensing Mendel's gifts as a teacher and his strong intellectual interests in natural science, Napp petitioned the local bishop for permission (and funds) to send Mendel for two years of study (beginning in 1852) in the natural sciences and mathematics at the University of Vienna.

At the University Mendel took courses in physics with Christian Doppler (1803-1853), an eminent experimentalist and discoverer of the "Doppler effect" (the shift in wavelength of light or sound, as the source approaches or recedes from the observer), and plant physiology with Franz Unger (1800-1870), a fervent evolutionist and exponent of the view that new variations arise by special combinations of simple cell elements. At the same time, through Unger, Mendel read some of the most important works on plant hybridization, particularly Friedrich Gärtner's *Versuche und Beobachtungen über die Bastardzeugung im Pflanzenreich* (1849), which described over 10 000 separate experiments with over 700 plant species and their hybrids [9]. There was considerable emphasis in both his physics and physiology courses on experimentation, and hands-on practical work. Mendel also took courses in mathematics and its application to physics with professor A. Ettinghausen (1796-1878), who emphasized the importance in natural science of expressing regularities in nature through mathematics. While in Vienna, Mendel also participated fully in the city's scientific life, attending lectures and, among other activities, becoming a member of the *Zoologisch-botanischer Verein.* In July, 1853, Mendel returned to Brno having completed his course of studies, but without having taken the examinations necessary to qualify as a permanent secondary school teacher. He was soon offered the opportunity to teach in the newly opened *Realschule*, a technically-oriented high school which, along with the Brno Technical School (for post-high-school students) offered a broad course of study aimed at preparing young men to work in the city's growing industrial sector. One further attempt was made to pass the teacher certification exams in May, 1856, but Mendel again was seized with anxiety and broke down during the first written part of the exam and withdrew from the others. Thus, despite his outstanding qualities in the classroom, Mendel remained a "substitute teacher" at the *Realscule* for the next twelve years (until 1868), when he was elected Abbot of the monastery on the death of his old mentor, frair Napp.

MOTIVATION FOR MENDEL'S *PISUM* EXPERIMENTS

It was during his period as a teacher at the *Realschule* that Mendel began his systematic breeding experiments with *Pisum* in the monastery's experimental plot. One of the major reasons that have been put forward for why a clergyman and schoolteacher would have undertaken such an unusual investigation is that he wanted to provide a generalized theory of heredity that would complement Darwin's theory of natural selection (or, as at least one author has also suggested, to counter Darwin's theory by demonstrating the fixity of species limits during hybridization). Darwin's theory had encountered considerable theoretical difficulties because of the prevailing belief by naturalists and breeders (including Darwin himself) in what was known as "blending inheritance," namely, that any trait in the offspring of a cross was a "blend" between the trait observed in the two parents. If parental differences blended in the offspring, it was realized, new variations would be diluted more and more every generation, and would have little chance of being acted upon by natural selection. At attractive as the notion might be, however, it is clear that Darwin's work could not have been Mendel's initial motivation, since he had already begun his experiments in 1856, three years before the publication of *The Origin of Species*.

On the other hand, Mendel was clearly interested in the evolution question. By the time he got around to writing up his *Pisum* results in 1865, he had read the German edition of the *Origin*, and in several places in his paper addresses the question of whether hybridization could lead to the transformation of species. In the section titled "Concluding Remarks" (pp. 102 ff), for example, Mendel distinguishes between two types of hybrids, those that breed true (members of the Columbine, Mallow and rose families, among others) and those that do not (such as his *Pisum* and other legumes). Those hybrids that breed true must be fundamentally different in the composition of their germ cells, Mendel argues, than those, like *Pisum*, that show segregation. The existence of true-breeding hybrids, Mendel claims, is particularly important for the evolution (*Entwicklungsgeschichte*) of plants, since, however they are produced, "constant hybrids acquire the status of new species" [10].

In his own experiments, Mendel had found that if he continually intercrossed only his hybrids for many successive generations, the ratio of original parental types to hybrids continually increased. This was the phenomenon commonly known to breeders as the tendency toward reversion to parental type. It was one of the main obstacles for breeders in establishing true-breeding hybrids. From an evolutionary perspective it was clear to Mendel that plants such as his peas could be transformed into stable hybrids only with great difficulty, if at all. Despite these problems, however, Mendel did not agree with earlier hybridists such as J.G. Kölreuter and K.F. von Gärtner that species could not change beyond their "natural limits." It is clear that in discussing this issue toward the end of his *Pisum* paper, Mendel was relating his findings to the larger question of evolution that was by then such a controversial topic among both naturalists and agriculturalists. Whatever he thought of the details of Darwin's work (and there is little documentation available on this issue) there is certainly no indication anywhere in Mendel's writings that he was hostile to the idea of evolution in general, or to Darwin's specific formulation in particular. But it also seems clear that evolution *per se* was not at the heart of Mendel's work.

If not evolution, what was the initial, and more long-range motivation for Mendel's experiments? And what did his paper say, both to his contemporaries and to those who read him after the "rediscovery" in 1900?

MENDEL'S REAL MOTIVATION: WHAT DOES HIS PAPER TELL US

A revision of our understanding of what Mendel's original paper may have been about began with the work of historian Robert Olby in 1979. Olby was motivated to strip Mendel's reputation of Whiggish interpretations that portrayed his breeding experiments in light of its later twentieth century interpretation instead of in the context of the mid-nineteenth century when the work was carried out. The question Olby asked was: If Mendel were to come back today and read a description of his work in any modern textbook, would he be a "Mendelian?" [11] His conclusion was that Mendel was *not* a Mendelian in any modern senses of that term, and that proponents of Mendelism, from Bateson onward, had read all sorts of ideas into Mendel's work that were, historically, not part of the original formulation. Similar reevaluations were made subsequently by Augustine Brannigan[12], Ono Meijer[13] and Floyd Monaghan and Alain Corcos[14]. The gist of these various claims are:

(1) The motivation for Mendel's work was not to provide a generalized theory of heredity to replace the multitude of individual theories that existed in the mid-nineteenth century, nor to fill in the lack of an explicit theory of heredity in Darwin's work;

(2) Rather, his interest was far more immediate and practical: to establish patterns of hybridization that would have been of interest to agricultural breeders and others in Moravia at the time;

(3) Mendel never stated the two *laws* of heredity usually associated with his theory—*i.e.*, the "law" of segregation (first law) and the law of independent assortment (second law);

(4) Mendel never proposed that there were material particles, "factors" or "*Anlagen*" in the germ cells, or that such particles were necessarily transmitted *via* pollen and egg cells to the offspring; he only suggested that statistically speaking, traits seemed to be inherited in a fashion commensurate with the assumption that their determiners were distributed according to the laws of probability. In other words, Mendel remained far more agnostic about the physical basis of inheritance than later "Mendelians." (Bateson was the exception, however, having a strong aversion to material theories, as exemplified in his long-standing opposition to the Morgan chromosome theory [15].)

Concerning the first two claims, it seems clear that Mendel was primarily interested in the problem of *hybridization* and not heredity in some abstract or theoretical sense. It is much more likely that the direction of Mendel's research was guided by the strong agricultural interests not only among his fellow Augustinians, including friar Napp, but also among local farmers and breeders within the natural history and agricultural society to which Mendel, as we know, belonged. It is also clear that Mendel's interest in mathematics and the physical sciences, his quantitative turn of mind, and his experience in the physical sciences at the University of Vienna, all helped him establish a consistent and rigorous methodology without which his breeding experiments would likely have led him no further than most of his predecessors and contemporaries.

But why would hybridization *per se* be of such great interest in an agricultural context? It was precisely through hybridization that breeders could hope to generate new combinations of characters that they could exploit to form of new breeds. The problem was, as we noted above, that most hybrids do not breed true and have a tendency to revert to the original parental types. What Mendel was able to explain was the conditions under which that happened, and, most important, methods for distinguishing between hybrids and true-breeding forms that might look externally (phenotypically, in our modern terminology) alike. Most important, Mendel's hypothesis of *dominant* and *recessive* characters provided an alternative to the common belief in blending inheritance. When Mendel's hybrids produced one-fourth purely recessive offspring, these were not changed in any way from the original recessive grandparents. Whatever happened physiologically within the germ cells of the hybrids, the characters were not altered (or blended) by residing together. This became as important a principle for breeders as it would become later for Darwinian evolutionists, since it freed both groups from the problem that would otherwise have resulted in the loss of distinct variations through "swamping" (as it was called) in the hybrid.

At the same time, I would argue that it is not possible to be interested in the process of hybridization without simultaneously being drawn into accepting, however, loosely, some concept of *heredity*. Hybridization involves mixing germ lines from two different parents, two different ancestries, and how those germ lines interact (blending, particulate, etc.) by definition forms a theory of heredity. Thus to claim that Mendel was interested only in hybridization, and not in any general principles of heredity, seems to make a needless and indeed a confusing distinction. The two processes are not only not mutually exclusive, they are complementary. The revisionist view has made an important point, however: Mendel's major motivation (and interest) lay in establishing principles of hybridization, not in establishing a generalized theory of heredity as was assumed by his early twentieth century followers.

Another issue raised by Olby, Brannigan, Monaghan and Corcos and others relates to whether Mendel thought his paired characters (tallness and shortness, green and yellow) were represented in the pollen and egg cells by discrete, particulate determiners, what twentieth century Mendelians came to call "genes." Olby *et al.* argue that Mendel nowhere states explicitly that the germ cells contain particles that determine the tallness or the shortness trait, green color or yellow color. Thus, according to this view, Mendel's symbols, T, t, A, a, and the like were merely algebraic notations and were never meant to represent material entities in any biological sense. It is true that Mendel is not explicit on this matter. He talks in his paper about alternate characters (phenotypes such as tall, short) segregating in the germ cell of the hybrid parent, but he does not refer to determiners or particles; moreover, he does not talk about segregation of the two characters in the homozygous forms, and in fact represents homozygotes symbolically with only *one* letter (such as 'A' for the dominant parent or 'a' for the recessive), whereas he always represents the hybrids with *two* letters, as in 'Aa'. Thus, he consistently shows the results of a monohybrid cross (represented in the parents as Aa x Aa) as 'A + 2Aa + a'.

After a careful re-reading of Mendel's paper, I find his position on this question of hereditary particles ambiguous, but not explicitly agnostic. The ambiguity lies in the fact that throughout his paper Mendel consistently talks primarily about the "characters" [using the German word *Charactere*] of the parents or offspring of his crosses, which of course refer to the visible adult traits. His empiricism and training in the physical sciences most probably led him to emphasize what he could *see* in the plants he was breeding and raising. At the same time, at various points toward the end of his paper, Mendel wrote about the implications of his experiments for understanding the composition of the "fertilization cells" (*i.e.*, pollen and egg). Here, he introduces the terms "*Anlage*" and "*Elemente"* in reference to what is transmitted from parent to offspring through fertilization. In introducing the term "*Anlage*" Mendel wrote:

> *Soweit die Erfahrung reicht, finden wir es überall bestätigt, dass constante Nachkommen nur dann gebildet werden können, wenn die Keimzellen und der befruchtende Pollen gelichartig, somit beide mit der* Anlage [emphasis added] *ausgerüstet sind, völlig gleiche Individuen zu beleben, wie das bei der normalen Befruchtung der reinen Arten der Fall ist* [16].

I include it here in German because the passage has been translated in different ways in different versions. For example, in the translation by the Royal Horticultural Society, made at Bateson's instigation in 1902, the passage reads:

> So far as experience goes, we find it in every case confirmed that constant progeny can only be formed when the egg cells and the fertilizing pollen are of like character, so that both are provided with the *material for creating* [emphasis added] quite similar individuals, as is the case with the normal fertilization of pure species [17].

The phrase "material for creating" as a rendering for "*Anlage*" is more or less equivalent to "potential." However, in a different and much later (1966) translation, by Eva R. Sherwood, "*Anlage*" is translated as "factor" [17]. Now, "*Anlage*" is one of those German words that has multiple meanings, which have also changed over time. In the writings of August Weismann later in the century, for example, "*Anlage*" was determined untranslatable into any meaningful English equivalent, and so was simply rendered in the German throughout the various English versions of Weismann's work. In other cases, it was translated more explicitly to mean a potential for something coming into being, but not yet realized, a process of building up or creating in the future (a derivative German term today means to "invest" financially). Embryologists used it well into the twentieth century to refer to tissues predestined to develop (but not yet developed) into a particular part, such as limb-buds (called limb-primordia, or limb-*Anlage*). What is important to recognize is that the term itself had multiple meanings, colorations and associations, and that it did not necessarily denote a discrete, atomistic particle, like the classical "gene" as portrayed in today's textbooks. At the same time it was clearly a "something," a material component of the cell or the embryo in some fashion; it was not, it seems to me, what historian L.A. Callendar has suggested, an abstract "essence" growing out of Mendel's early Catholic training in Aristotelian philosophy [18].

Mendel also uses the term "*Elemente*" in several places in his paper, most notably in the section titled "*Schluss-Bemerkungen*" or "Concluding Remarks" where he suggests the reasons why he may have obtained the various ratios with hybrids. After pointing out that it is now known that in flowering plants [Phanaerograms in the terminology of the day] both pollen and egg cell must unite to form a single cell, which by assimilation [metabolic activity] forms new cells that become an independent organism, Mendel writes: "The development proceeds from a constant law which is grounded in the *material* [emphasis added] composition and arrangement of the elements, which come together in the cell in a viable union" [19]. A little further down in the same paragraph, Mendel goes on to say, "if it happens that a germinal [egg] cell combines with a dissimilar pollen cell, we must assume that between those elements of the two cells, which represent opposite characters, some compromise must take place" [18]. What is clear in these cases (and in a few other sentences in the conclusion) is that Mendel is describing in general terms the union of some sort of cell components that (through metabolism or "*Stoffaufnahme*") interact in such a way as to produce the adult character or trait. Mendel had taken plant physiology at the University of Vienna, where the material union of sperm and egg had been discussed in Unger's lectures. Orel is convinced that by the time he was working on his pea experiments, Mendel had heard explicitly of the work of N. Pringsheim who, in a paper published in 1855 (a year before Mendel began his *Pisum* experiments), reported his observation of fertilization of an egg cell by a motile spermatozooan in the alga *Vaucheria* [20]. Such observations were being discussed among several of Mendel's colleagues at the Brno Institute of Technology, and were considered exciting verification, for the first time clearly observed, of the union of gametes in plant fertilization. That Mendel chose to discuss his hybridization work in terms of the newest findings in cell biology suggests strongly that he was interested in the actual mechanisms occurring during gamete formation among hybrids.

Indeed, it would have been unusual in Mendel's day, and given his own training, not to at least have thought in terms of some sort of discrete hereditary particles being passed from parent to offspring during reproduction. Virtually every theory of heredity proposed during the middle and later years of the nineteenth century was couched in particulate terms, so that it was common among biologists, especially in the German-speaking world, to think in terms of atom-like particles or molecules as agents of hereditary transmission. The problem with most of these theories, as we noted earlier, was that they were completely speculative, and based on a few observations and very little, if any, experimental evidence. Mendel would thus not have been unusual in at least hinting toward such components in the germ cells. Moreover, while couching the hereditary process in particulate terms does not automatically lead to a concept of non-blending inheritance (Darwin, after all, incorporated his postulated "gemmules" into a blending theory) particulate theories clearly open the way.

In trying to understand what Mendel was really thinking with regard to the nature of the hereditary process it is important to remember that he was first and foremost an empiricist, and highly restrained when it came to theorizing about mechanisms behind what he observed. His constant emphasis on the "characters" he was observing (the phenotype) of the parents and offspring in his crosses, his recognition that it was sometimes difficult to determine in what character-class a given individual should be placed, and his meticulous record-keeping, all testify to his strongly empirical and no-nonsense approach to his experiments. At the same time, this is not inconsistent with his also recognizing that something material, which determines a discretely described character, must be transmitted by each gamete during the fertilization process. While his empiricism may have prevented him from engaging in large-scale speculation about invisible units of heredity within germ cells, his strong biological interests and background, his continual reference of the process of hybridization to pollen and egg cell formation, make his work compatible with a particulate approach. This compatibility is exactly what allowed early twentieth century geneticists to interpret the theory in its later, highly atomistic framework.

MENDELISM AND THE "UNIT-CHARACTER" HYPOTHESIS

By the time Mendel's paper was rediscovered in 1900 and had begun to receive attention from biologists and breeders in Western industrialized countries, economic, social and intellectual conditions were significantly different than they were in Central Europe in 1866. The industrial revolution in Europe, and especially by 1900 in the United States, had placed many new demands on agriculture [21]. Not only were there increasing requirements for food to supply the large urban workforces that had developed in industrial areas, but much of that workforce had come from rural areas and thus from the agricultural sector leaving it in short labor-supply. Mechanization of agriculture had proceeded with great rapidity in the latter decades of the nineteenth century, a process that had initiated what has been called the "industrialization of agriculture" [22]. Scientific agriculture based on the organic and physiological chemistry of Justus von Liebig (1803-1873) and his school in Giessen had greatly improved yields by attention to problems of fertilizers, animal and plant nutrition and the like. But by 1900 those inputs had achieved their technical limits (for the time). Improvements in breeding higher-yielding varieties, on the other hand, held out a wholly new potential. As United States Secretary of Agriculture James Wilson noted in 1910:

> Improvements in breeding are unlike those secured by adding new acres of the country, by deeper plowing, by more frequently cultivating the crop, by adding to the soil larger supplies of fertilizers, or by giving a more expensive ration to farm animals. These improvements, though they greatly increase the farmers' profits, are secured at a cost which sometimes equals the value of the added product. But the cost of improvements through breeding usually represents only a small fraction of the added values. The increase of product secured by breeding pays the cost in a short time, and, since there is no further expense, the annual increase afterward is sheer profit. The farmer will be able to retain a part of the larger production in the form of added profit, and part will help reduce the cost of living to those in our cities. Larger production on the farm will also give increased business to the transportation company, the manufacturer, and the merchant, and will provide the nation with a larger product with which to hold our balance of trade [23].

One aspect of agriculture, husbandry, was still in its rudimentary stage of development at the turn of the twentieth century. Most animal and plant breeders operated by various rules of thumb they had developed themselves, in their separate localities, or had learned and modified from others. It was largely a craft, with no general rules that seemed to apply across the boards. The reintroduction of Mendel's work into the scientific world at this point in time provided the hope that at last some general principles of heredity might provide the breeder with methods that could yield more predictable results. Although in reality the application of Mendelian principles to improving animal and plant productivity turned out to be more difficult than it seemed at first, nonetheless in the early decades of the century Wilson's optimism was shared by a wide variety of academic biologists, United States Department of Agriculture officials, and breeders. The economic and social conditions made Mendel's work look *profitable* in 1910 in a way it had not looked in 1866.

But with the nascent science of "Mendelism [24]" how did those academics and breeders who took up the new practice visualize its theoretical structure? How did they come to regard Mendel's "elements" or "*Anlage*"? Some remained as agnostic as Mendel had been about the nature of *what* was actually transmitted from parent to offspring during fertilization. Although Wilhelm Johannsen (1857-1927), the Swedish plant breeder who coined the term "gene," and William Bateson, who coined the term "genetics," both favored a more abstract statistical model of the hereditary unit, others, especially in the United States from 1903 onward, gave Mendel's scheme a more material, atomistic interpretation. The abstract "element" of Mendel's paper had quickly become the discrete "gene" of the rediscovered Mendelism. Textbooks began to present images of Mendelian crosses using Mendel's capital and small letters for dominant and recessive traits, respectively.

Among the generation of biologists between 1900 and 1910 who were beginning to learn about the new genetics, this rendering communicated two important associations. The first was that there was no hard-and-fast distinction yet drawn between the letter/factor and the adult character for which it stood. Thus, geneticists would write about the inheritance of "height" or "wing shape" or "red eyes" as if the trait itself, full-blown, was what was carried in the male or female gamete. As we have seen, in describing his experiments Mendel did not make that conflation, using throughout his paper only the term of the adult character, the descriptor for the actual appearance of the plants themselves. In the early decades of Mendelian theory the identification of the hereditary unit with the adult trait blurred the distinction between the appearance of the organism with its genetic make-up (what would become known after 1911 as the "genotype-phenotype" distinction), and gave the impression that the inherited factor *was* the trait in miniature. It was this conflation that led embryologists, such as the young Thomas Hunt Morgan, to actually reject the Mendelian hypothesis for a period of time [25]. For Morgan and others, the Mendelian "factor" or "gene" smacked too much of the embryologists' old bugbear, preformationism (the idea that the complete adult exists already preformed in the fertilized egg, and that embryonic development involves only an unfolding or growth of the embryo in size). Epigenesis, the alternative view, had replaced preformationism by the end of the eighteenth century, so that Mendel's work initially seemed like an throwback to a long-discarded idea.

The second association that went along with interpreting Mendel's letters as equivalent to adult traits was what came to be known as the "unit character hypothesis." The unit-character hypothesis presupposed that each character we identify is controlled by one Mendelian factor, or gene. Thus, red or white color in morning glories was thought to be controlled by one factor pair, or "allelomorph," as Bateson named them, R and r; height in peas by T and t, and so forth. This association was reinforced by the diagrammatic representation of Mendelian crosses through the "Punnett Square" (figure 1). While such a view seemed to preclude interaction of Mendelian factors among themselves, a variety of gene interactions were beginning to be uncovered by 1915. Even so, such interactions were initially, and continued to be presented in most textbooks as a variant of, and exception to, the unit-character pattern. Thus, the well-worn phrase "X is the gene for ..." became the common way to describe genes throughout almost the whole of the twentieth century.

With the wedding of Mendelian theory to the cytological investigation of chromosomes by Morgan and his group after 1910, the material, discrete and atomistic concept of the gene gained further support. By carefully correlating the inheritance patterns of gene mutations with observable changes in chromosome structure, Morgan and his students were able to show that genes could be clearly regarded as material entities that occupied specific positions, or loci, along the length of the chromosome. By 1915, when the group published the their path-breaking book, *The Mechanism of Mendelian Inheritance* [26] the "beads on a string" model of the chromosome had become an icon (figure 2). Not only did this model promote the idea of genes as atomistic units, it also further supported, indirectly, the unit-character hypothesis. The gene was now viewed not only metaphorically, but literally as an atom, entering now into this, now into that combination, and emerging each time with its own integrity in the same fashion as atoms entered into and emerged from molecular combinations. Indeed, the language of chemistry began to enter genetics explicitly in relation to the discreteness of the Mendelian factor. Harvard geneticist W.E. Castle (1867-1962) wrote early on that "all observed inheritance phenomena can be expressed satisfactorily in terms of genes, which are supposed to be to heredity what atoms are to chemistry, the ultimate, indivisible units, which constitute gametes much as atoms in combination constitute compounds" [27]. (While Castle was making this reference in order to argue that genes were not quite like atoms in that they could be altered by the selection process, the very fact that he mentions the analogy at all indicates something of its prevalence.)

Somewhat earlier his colleague E.M. East had written that "Mendelism is therefore just such a conceptual notation as is used in algebra or in chemistry [28], while British polymath J.B.S. Haldane (1892-1964) as late as the 1930s claimed that"the atomic nature of Mendelian inheritance suggests very strongly that even where variation is apparently continuous

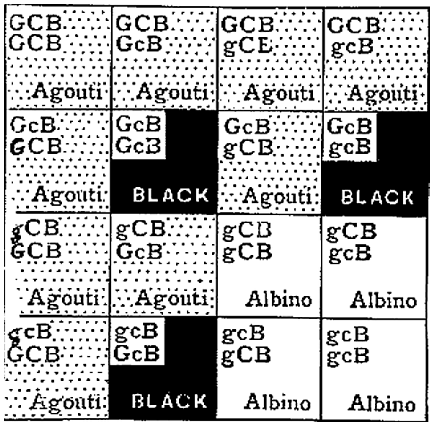

FIGURE 1
Example of a "Punnett Square", one of the means of representing Mendelian crosses designed by Bateson's student R.C. Punnett around 1906. This Punnett Square shows second generation (F_2) results of the mating between agouti (mottled) and albino mice. The use of different colors, textures (as in this case) and even word descriptions, indicates the actual appearance, or phenotype, of the organism. [From Punnett, R. C. (1911), *Mendelism.* New York: The Macmillan Co., p. 52.]

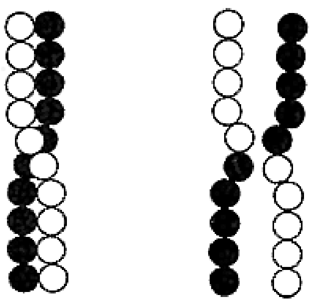

FIGURE 2
The representation of a chromosome as a linear array of discrete Mendelian genes is shown in this 1915 "beads on a string" model from the Morgan group. Although chromosomes were more frequently drawn as solid bars or lines, the clear intent here is to show the discrete quality of the gene line-up and exchange during crossing over. [From Morgan, T. H., Sturtevant, A. H., Muller, H. J. and Bridges, C.B. (1915), *The Mechanism of Mendelian Heredity*. New York: Henry Holt & Co.]

this appearance is deceptive. On any chemical theory of the nature of genes this must be so" [29].

The discreteness of the gene implied the organism constructed as a "mosaic" of adult traits; idea that was given explicit voice by Bateson within the first year of his encounter with Mendel. In 1901 he wrote: "In so far as Mendel's law applies, the conclusion is forced upon us that the living organism is a complex of characters of which some, at least, are dissociable and are capable of being replaced by others. We thus reach the conception of *unit characters*, which may be rearranged in the formation of reproductive cells" [30].

The next year Bateson wrote even more boldly: "The organism is a collection of traits. We can pull out yellowness and plug in greenness, pull out tallness and plug in dwarfness" [31]. This mosaic view of the adult organism parallels the mosaic view of the genome, and thus pictures the organism as an assemblage of interchangeable parts that can be arranged and rearranged by putting together the right combination of genes. Admittedly, not all early Mendelian geneticists took quite this mechanical an approach to the hereditary process, but Bateson was one of the leaders in the field and among its most vocal proponents. His influence was therefore considerable.

As fruitful as the atomistic and mosaic conceptualization of the gene may have been initially (and it did allow biologists to develop a quantitative, experimental and predictable aspect of their science that they could point to as being as rigorous and "hard" a science as anything in chemistry or physics [32]), it created problems almost from the outset. It allowed biologists to put aside questions of gene function, or the relationship between Mendelian genes, embryonic development, and evolution. From 1915 onward, most attention was paid to the mechanics of gene shuffling during transmission of chromosomes from parent to offspring. This trend, which marked the hey-day of classical genetics, led to the extraordinary feat of mapping the chromosomes of several model organisms (fruit fly, maize, mouse). But it also led to several developments that can only be viewed as an unfortunate legacy. The first is that, by perpetuating the unit-character concept of the gene, even with lip-service paid to the idea of gene-gene and gene-environment interactions, the vast majority of the public and many biologists as well, still perpetuated the view that one, or at best a very few, genes determined a trait. Even today we read almost daily in the media the purported discovery of a new gene for this or that trait. So common have become these claims that a recent cartoon showed a scientist rushing into the lab, beaker in hand, announcing excitedly to his colleagues: "Eureka! I've found the gene that makes us think everything is controlled by genes."

Nowhere is the tendency to ascribe specific discrete gene elements to specific traits more common, and perhaps more socially troublesome, than in the area known as human behavior genetics. To date, social and personality traits as complex and varying as schizophrenia, manic depression, alcoholism, criminality, violence, shyness, risk-taking and religiosity, have all been headlined at one time or another as caused by "a gene." Not only do such claims greatly oversimplify the biological process of development, during which genes interact with other genes and the environment, it suggests a far too easy set of potential solutions: drug therapy, gene therapy or sterilization. The latter was implemented in a very real way in both the United States and Germany in the days of the old eugenics movement, when simplistic Mendelian notions allowed the legislation of compulsory sterilization laws for those claimed to have undesirable hereditary conditions [33]. Today, Norplant can replace surgical sterilization, and pharmacogenetics looms on the horizon as not only a way to possibly counteract the effects of defective genes, but also as a major boon for the pharmaceutical industry. Already, an estimated 1.5 million American children have been prescribed with Ritalin (methylphenidate) to control one of the newer, purported genetic diseases, attention deficit hyperactivity disorder [34] (ADHD). Genes are of course critical components in one way or another of all of our traits. But the picture of what genes do and how they function in the development of adult human characters has changed dramatically from the legacy built out of the early interpretations of Mendel's work. With his skepticism about undue speculation regarding the mechanics of the hereditary process, Mendel might indeed have been more in tune with modern genomics than with the Mendelians who crafted the classical concept of the gene in his name.

CONCLUSION

As we stand on the brink of the "post-genomic era," where the fruits of sequencing of the human genome (and other species for comparison) are becoming available to create new understandings of how genes function, and possibly suggest ways to manipulate our genomes in unprecedented ways, it is important to see where we have come from and where we may be going. The discovery that we have only about 30 000-35 000 genes in our entire genome, instead of the 100 000 or more originally predicted, has given molecular geneticists pause to consider how potentially flexible our genetic organization must be. Segments of DNA may function as parts of several genes, or processes such as "alternative splicing" (where messenger-RNA transcribed from one segment of DNA can be cut and spliced in a variety of combinations) can give rise to dozens, even hundreds of different proteins. The complex signaling and control mechanisms by which such rearrangements are guided have yet to be worked out. It is becoming more and more clear that the process of development is now a key to understanding the relationship between genes and traits. One of the legacies of Mendel, as he was interpreted by the classical geneticists, was to divorce genetics from embryology and focus almost exclusively on the mechanism of transmission, chromosome structure and mapping of loci. Happily, that divorce may be in the process of reconciliation as molecular biologists learn more about genetic control mechanisms and environmental triggering processes.

As we look forward, it is clear that one of the most important forefronts of modern genetic research lies in the area of what has been called, variously, "the genetics of development," "developmental genetics," and when combined with evolutionary theory, the "evolution of development" (or "evo-devo" for short). These newly-emerging fields, synthesizing as they do the classical genetics of the first half of the twentieth century with the molecular genetics and evolutionary biology of the second half, promises to bring us a much more complex, though perhaps ultimately more realistic, picture of how the genome functions both in guiding the individual organism from fertilization to adulthood, and how this process as a whole evolves over time.

We are truly standing at a continental divide between an old and a new genetics: a mosaic and mechanical view of the organism and a holistic and integrated perspective that promises to yield exciting results in the years ahead. It behooves us to understand the pathway that has brought us to this historic juncture, not only so that we may take the fullest advantage of our newest research paths, but also that we avoid the disastrous social consequences that can arise from misplaced expectations of what genetics can do. Like all other scientific and technological findings, we must first understand the science itself and its history to recognize both its potential and its limitations.

With that thought, let me return to Ernst Mayr, who has spent such a significant part of his long career helping scientific colleagues and others understand the science of evolutionary biology and its historical development. That has been what has made Ernst's contributions to the history of science so valuable—as a working scientist he has always recognized the importance of knowing the history of the field, how that informs the questions that we ask and the kinds of answers we will accept. Ernst has thus left his mark on not only the field of evolutionary biology but also the history of science. And still going strong at one hundred, he is an inspiration for us all.

NOTES

1 Sturtevant, A.H. (1965), *History of Genetics* New York: Harper & Row; in chapter 21 the author reviews the claims that the three rediscoverers were really independent, while several papers by Alain Corcos and Floyd Monaghan suggest that only Correns had really collected in his own experiments data that was really comparable to that which Mendel had obtained. See, Corcos, A. and Monaghan, F. (1985), "Role of de Vries in the recovery of Mendel's work," *Journal of Heredity* 76: 187-190; (1986), "Tschermmak: a non-discoverer of Mendelism I: An historical note," *Journal of Heredity* 77: 468-469, and (1987), "Tscheremak: a non-discoverer of Mendelism II: A critique," *Journal of Heredity* 78: 2-10. These various positions have been admirably summarized in Bowler, P. (1989), *The Mendelian Revolution. The Emergence of Hereditarian Concepts in Modern Science and Society*. Baltimore: Johns Hopkins University Press, especially chapter 1.

2 Bateson, W. (1902), *Mendel's Principles of Heredity: A Defense*. Cambridge, UK: Cambridge University Press.

3 Letter from William Bateson to his wife, Beatrice, October 3, 1902, quoted in Paul, D. and Kimmelman, B. (1988), "Mendel in America: Theory and practice—1900-1919," in Rainger, R., K. Benson and J. Maienschein (1988), *The American Development of Biology*. Philadelphia: University of Pennsylvania Press, p. 283.

4 Allen, G. E. (1978), *Thomas Hunt Morgan, the Man and his Science*. Princeton, N.J.: Princeton University Press.

5 Orel, V. (1996), *Gregor Mendel, the First Geneticist*. New York: Oxford University Press, pp. 40-41.

6 Orel, V. (1973), "The scientific milieu in Brno during the era of Mendel's research," *Journal of Heredity* 64: 314-318; see also Orel, V., *Gregor Mendel*, cit. n. 5, chapters 2-3.

7 Orel, V. (1972), "Mendel's elder friar and teacher, Matthew Klácel (1808-1882)," *Quarterly Review of Biology* 47: 435-436.

8 Orel, V. and Wood, R. (2000), "Scientific animal breeding in Moravia before and after the rediscovery of Mendel's theory," *Quarterly Review of Biology* 75: 149-157.

9 Gärtner, F. (1849), *Versuche und Beobachten über die Bastarderzeugung im Pflanzenreiche*. K.F. Herring. Mendel's copy of Gärtner's book is housed in the library of the Mendelianum and contains notes in Mendel's hand especially on sections dealing with experiments using the pea, *Pisum sativum*.

10 Mendel, G. (1866), Versuche über Pflanzen-Hybriden. *Verhandlungen des naturforschenden Vereines, Brünn* 4, pp. 67-111, quotation from p. 104. The passage reads: "Für die Entwicklungschichte der Pflanzen ist dieser Umstand von besonderer Wichtigkeit, weil constante Hybriden die Bedeutung neuer Arten erlangen."

11 Olby, R. (1979), "Mendel no Mendelian?", *History of Science* 17: 53-72.

12 Brannigan, A. (1979), "The reification of Mendel," *Social Studies of Science* 9: 423-454.

13 Meijer, O. (1983), "The essence of Mendel's discovery," in Orel, V. and A. Matalova (eds), *Gregor Mendel and the Foundation of Genetics*. The Mendelianum of the Moravian Museum in Brno, pp. 123-178.

14 Monaghan, F. V. and Corcos, A. (1984), "On the origins of the Mendelian laws," *Journal of Heredity* 75: 67-69; and (1984), "The true Mendelian laws," *Ibid*, pp. 321-323.
15 Coleman, W. (1970), "Bateson and chromosomes: Conservative thought in science," *Centaurus* 15: 228-314.
16 Mendel, G. (1960), *Experiments in Plant-hybridisation*. Cambridge, MA: Harvard University Press: 41 pp.: p. 20.
17 Stern, C. and Sherwood, E. R. (1966), *The Origin of Genetics. A Mendel Source Book*. San Francisco: W.H. Freeman Co, p. 24.
18 Callender, L. A. (1988), "Gregor Mendel—an opponent of descent with modification," *History of Science* 26: 41-75.
19 Mendel, G. Versuche, cit. n. 14, p. 105. The original reads: "Diese Entwicklung erfolgt nach einem constanten Gesetze, welches in der materiellen Beschaffenheit und Anordnung der Elemente begründet ist, die in der Zelle zur lebesnfähigen Vereinigung gelangten."
20 Pringsheim, N. (1855), "Über die Befruchtung und Keimung der Algen und das Wesen des Zeugungaktes," *Monatsberichte der Königliche Preussiche Akademie der Wissenschaften, Berlin* 3: 1-33.
21 Allen, G. (2000), "The reception of Mendelism in the United States, 1900-1930," *Comptes Rendu Academie des Sciences, Paris. Sciences de la vie* 323: 1081-1088.
22 On the industrialization of agriculture in twentieth century America, see Shannon, F. A., (1961), *The Farmer's Last Frontier*. New York: Holt, Rinehart and Winston, pp. 362-365, 366-367; and Kloppenberg, J. R. (1988), *First the Seed. The Political Economy of Plant Biotechnology*. New York: Cambridge University Press, especially chapters 2-4.
23 Wilson, J. (1910), "The new magazine has a place," *American Breeders' Magazine* 1: 3-5.
24 Punnett, R. (1911), *Mendelism*. New York: Macmillan.
25 Allen, G. (1978), *Thomas Hunt Morgan, the Man and his Science*. Princeton, N.J.: Princeton University Press.
26 Morgan, T. H., Sturtevant, A. H., Bridges, C. B. and Muller, H. J. (1915), *The Mechanism of Mendelian Inheritance*. New York: Henry Holt & Co.
27 Castle, W. E. (1919), "Piebald rats and the theory of genes," *Proceedings of the National Academy of Sciences* 5: 126-130; quotation on p. 127.
28 East, E. M. (1912), "The Mendelian notation as a description of physiological facts," *American Naturalist* 46: 633-695.
29 Haldane, J. B. S. (1932), *The Causes of Evolution*. New York: Harper and Brothers, p. 57.
30 This quotation comes from Punnett, R. C. (ed.) (1928), *Scientific Papers of William Bateson*. Cambridge, U.K.: Cambridge University Press, Vol. 2, p. 1.
31 Bateson, W. (1902), *Mendel's Principles of Heredity: A Defense*. Cambridge, U.K.: Cambridge University Press. Quoted from Lewontin, R. C. and Levins, R. (1985), *The Dialectical Biologist*. Cambridge, MA: Harvard University press, p. 180.
32 For a more detailed discussion of the mechanistic view of the gene, see Allen, G. E. (2002), "The classical gene: Its nature and its legacy," in Parker, L. S. and R. A. Ankeny (eds.), *Mutating Concepts, Evolving Disciplines: Genetics, Medicine and Society*. Dordrech, Netherlands: Kluwer Academic Publishers, pp. 11-41.
33 Reilly, P. (1992), *The Surgical Solution: A History of Involuntary Sterilization in the United States*. Baltimore: Johns Hopkins University Press; see also, Allen, G. E. (2002), "The ideology of elimination: American and German eugenics,

1900-1945," in Nicosia, F. R. and J. Huener (eds.), *Medicine and Medical Ethics in Nazi Germany: Origins, Practices, Legacies.* New York: Berghahn Books, pp. 13-39.

34 For estimates of the rate of Ritalin prescription in children, see, Safer, D.J., Zito, J.M., Fine, E.M.(1996), "Increased methylphenidate usage for attention deficit disorder the 1996s," *Pediatrics* 98: 1084-1088; and for the claims that it has a genetic basis, see Comings, D. E. (1996), *The Gene Bomb. Does Higher Education and Advanced Technology Accelerate the Selection of Genes for Learning Disorders, ADHD, Addictive and Disruptive Behaviors?* Duarte, California: Hope Press, especially chapter 11.