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REVIEW

From Mendel's discovery on pea to today's plant genetics and breeding

Commemorating the 150th anniversary of the reading of Mendel's discovery

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Abstract

Key message **This work discusses several selected topics of plant genetics and breeding in relation to the 150th anniversary of the seminal work of Gregor Johann Mendel.**

Abstract In 2015, we celebrated the 150th anniversary of the presentation of the seminal work of Gregor Johann Mendel. While Darwin's theory of evolution was based on differential survival and differential reproductive success, Mendel's theory of heredity relies on equality and stability throughout all stages of the life cycle. Darwin's concepts were continuous variation and "soft" heredity; Mendel espoused discontinuous variation and "hard" heredity. Thus, the combination of Mendelian genetics with Darwin's theory of natural selection was the process that resulted in the modern synthesis of evolutionary biology. Although biology, genetics, and genomics have been revolutionized in recent years, modern genetics will forever rely on simple principles founded on pea breeding using seven single gene characters. Purposeful use of mutants to study gene function is one of the essential tools of modern genetics. Today, over 100 plant species genomes have been sequenced. Mapping populations and their use in segregation of molecular markers and marker–trait association to map and isolate genes, were developed on the basis of Mendel's work. Genome-wide or genomic selection is a recent approach for the development of improved breeding lines. The analysis of complex traits has been enhanced by high-throughput phenotyping and developments in statistical and modeling methods for the analysis of phenotypic data. Introgression of novel alleles from landraces and wild relatives widens genetic diversity and improves traits; transgenic methodologies allow for the introduction of novel genes from diverse sources, and gene editing approaches offer possibilities to manipulate gene in a precise manner.

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Reflection on Mendel's work on pea

In 2015, we celebrated 150 years since the presentation (8 February and 8 March 1865) of the seminal work of Gregor Johann Mendel. Mendel's 1865 work (published in Mendel 1866) was at first largely ignored or not understood. As documented by Olby (1979), Mendel's plant hybridization research was cited 11 times over the period of 30 years beginning in 1865, but it was fully rediscovered and its essence understood in 1900, 34 years after its publication (Correns 1900; Tschermak 1900; de Vries 1900). From then on, Mendel's work has been widely discussed and meticulously analyzed (Fisher 1936). Mendel's insights have been thoroughly tested and became the solid basis of the new discipline of genetics (Weldon 1902; Bateson

1902). Several reviews and commentaries have been published related to Mendel's achievements starting from the controversy over his data (Fairbanks and Rytting 2001; Hartl and Orel 1992; Daniel et al. 2007; Franklin et al. 2008; Radick 2015), to references to his personality and work (Zirkle 1951; Gasking 1959; Orel 1984, 1996; Weiling 1991; Sandler 2000; Ellis et al. 2011; Reid and Ross 2011; Klein and Klein 2013; Gliboff 2013). Although biology, genetics and mainly genomics have been revolutionized in recent years, modern genetics will forever rely on principles of heredity founded on pea using seven single gene characters.

Mendel was not the first to choose pea as an experimental model (Smýkal 2014 and references herein); however, he was the first to apply calculus of ratios to a biological situation (Monaghan and Corcos 1990). In fact, it seems that Mendel had the theory in mind (Dunn 1965). He formulated the hypothesis first and then based on the comparison of observed numbers and expected ratios, he tested them with larger sets (Fisher 1936; Klein and Klein 2013). This is the result of Mendel's training as he was not just a botanist and plant breeder, but also well trained in physical sciences such as meteorology (Klein and Klein 2013), where precise records were always essential and used to predict future situations. One of Mendel's innovations was to look at the inheritance of traits as random events and analyze the results based on expectations. This may have been one reason why his paper was ignored. Random events, statistics and probabilities were more common of the language used by nineteenth century physicists and mathematicians than nineteenth century biologists (Sheynin 1980). His genius is that he discusses the laws of combination in relation to the formation of zygotes. Careful in observations, he denoted manifested traits as dominant, while those "hidden" as recessive. This classification and letter code we use still today. Mendel was also very lucky to have chosen unlinked traits/genes (Reid and Ross 2011). The single case in which he might have detected linkage (depending on whether he studied the *v* or *p* gene), and, if he did study *v*, which is linked to *le*, there are indications in a letter to Nägeli (Mendel 1950) that he studied the alleles in repulsion conformation, and thus would not have been likely to detect linkage as readily as had the recessive alleles been in coupling conformation. Mendel has given new meaning to the word of hybrid, as not a simple mix of parents but a contribution of parents to their progeny.

Besides pea, Mendel tested several other plant species, popular among hybridist scientists at that time, namely *Hieracium, Cirsium* and *Geum* (Orel 2003; Nogler 2006). These species reflected a key question asked at that time, i.e., the transmission of traits after species hybridization, to shed light on the origin of species. There was a common belief in the fixity of species. It seems likely that Mendel himself did not ask questions on the origin of species but rather was looking for laws governing the inheritance of particular characters that did not change over time, rejecting the popular theory of blending of characters and species essence. Thus, whereas Darwin held that species varied over time, Mendel believed that species characteristics remained constant (Wynn 2007). At that time, the existence of constant hybrids was of great interest, as these hybrids attain the status of new species (Mendel 1866; Bishop 1986). However, as pea experimental material did not fulfil the species criteria considered necessary by theoretical biologists of the time (Gasking 1959), Mendel tested 26 different genera over the years (Mendel 1870, 1950, letters to Nägeli in Orel 2003). Some of his results agreed with those he obtained with pea, some however, did not, in particular with different colored beans where he found a great range of colors in hybrids as a result of quantitative inheritance and, with *Hieracium*, where hybrids remained constant as a consequence of apomixis. He suggested first that the common bean phenomenon might be explicable if flower colors were determined not by one, but by two or more pairs of factors. Actually, Mendel discussed the matter of quantitative traits especially with respect to the pea attribute tall/dwarf, which actually was "length of stem". Luckily, Mendel stayed with pea, as with *Hieracium* he would not have been able to make any plausible explanation at that time, due to the existence of apomixis, while several traits easily observable in common bean are encoded by quantitative trait loci as we know today.

Until now, we have molecular evidence for four out of seven (possibly eight, which includes purple pods, not used in Mendel's thesis) traits he used (Hellens et al. 2010; Ellis et al. 2011; Reid and Ross 2011; Smýkal 2014). However, for some of the characters (as Mendel called them "elements") we are unsure which loci were responsible. Moreover, there will likely forever remain uncertainty over the mutations he used. One of the most impressive aspects of Mendel's thinking lies in the notation that he developed to represent his data: a capital and a lowercase letter (Aa) for the hybrid genotype actually represented what we now know as the two alleles of one gene. Mendel deliberately chose specific characters. He wanted to demonstrate stasis, formulate a theory, and then extrapolate to all other modes of inheritance. Mendel did not deliberately use plant mutants, although some of the alleles he used in pea are considered as mutants today (Bhattacharyya et al. 1990, Hellens et al. 2010). The purposeful use of mutants to study gene function is one of the essential tools of modern genetics. This is expected to proliferate even more in the near future, as we understand more the process of directed mutagenesis (Osakabe and Osakabe 2015).

Since the nineteenth and twentieth centuries, when traditional plant science was subdivided into discrete, classical

disciplines, including anatomy, morphology, physiology, biochemistry and genetics, our knowledge has expanded greatly. In addition to the emergence of new research fields and disciplines, including genomics and bioinformatics, we are now combining distant disciplines to uncover complex biological situations. Fundamental plant science is increasingly becoming a collaborative domain, with research projects including aspects of physics, mathematics and chemistry. This is largely fueled by the last decade's technical advances, allowing for more discoveries, but also creating new challenges, such as data storage, analysis and predictions. Interdisciplinary collaborations are often the solution to these challenges. This led to the establishment of systems biology, as an integrative approach to understand complex networks that characterize the phenotypes in the cell. When molecular biology emerged, plants were not the organism of choice for experimentation. As a genetic model for plants, pea was gradually superseded by other species, such as *Nicotiana tabacum* and *Antirrhinum majus*, but it is *Arabidopsis thaliana* that became the prominent model and which has a smaller physical size, much smaller genome and a shorter reproductive cycle (Meyerowitz 2001; Somerville and Koornneef 2002; Koornneef and Meinke 2010). The values of mutant analysis and genetic transformation for plant physiology and biochemistry were demonstrated using *A. thaliana*. Ten years after the publication of the *Arabidopsis* genome sequence, it remains the standard reference for plant biology (Koornneef and Meinke 2010). Today, we do not need to rely only on such simplified models, but can also use more complex crop species (such as maize, rice or soybean and common bean in the case of grain legumes), as well as long-lived trees (poplar) to understand different evolutionary and life strategies.

Mendelizing continuous variation: quantitative trait loci

Immediately after the rediscovery of Mendel's laws, biologists addressed the issue of continuous variation. Castle (1903) remarked "Bateson makes the pregnant suggestion that even cases of continuous variation may possibly prove conformable with Mendelian principles" and gave the example of intermediate height of pea from a short × tall cross. East (1916) discussed the "general proof of the cumulation effect of genes" found in maize (Hayes and East 1915) and "most Mendelizing characters have been shown to be due to several traceable factors." East (1916) presented quantitative data analysis on corolla length in *Nicotiana* as evidence, and then summarized the additional evidence of the authors of numerous studies (citing Belling, Castle, Davenport, East, Emerson, Hayes, Heribert-Nilsson, Kajanus, MacDowell, Nilsson-Ehle, Pearl,

Phillips, Punnett, Shull, Tammes and Tschermak) in support of "plural segregating factors." East and others noted the effect of environment on quantitative trait expression and further proposed eight requirements to test the multiple factor hypothesis. Sax (1923) tested the hypothesis on seed size and seed coat color in common bean and used Castle's (1921) data to estimate the number of factors. He stated that "various assumptions necessary in estimating the number of size factors, based on F_2 distribution, make the results obtained of little value", as also pointed out by Shull (1921). Sax proposed an elegant explanation for bean seed size and coloration segregation ratios by linkage, i.e., genetic factors on the same or different linkage groups and significantly suggested that "the size factors in different chromosomes may not be equal in their effect." Indeed, earlier, Shull (1921) discussed that all factors are not necessarily additive, or equal in effect, while some factors act in a negative direction and some in a positive direction. Linked and unlinked were common terms used in the literature since Sturtevant in 1913 (Frost 1921), but Sax (1923) is credited with the first report of quantitative trait linkage using a marker (seed coat pigmentation) to classify chromosomes and detect linkage between major genes and quantitative genes (seed size) in common bean. Detection of genes controlling quantitative traits using segregating marker genes and analyzing quantitative variation took a significant step forward with Thoday's publication in 1961. Thoday challenged the assumption that the determination of quantitative inheritance for a trait is the end point and presented the basic thesis of using markers in segregating populations to detect genes controlling quantitative traits. Already, breeders had found positive morphological marker–quantitative trait associations (Everson and Schaller 1955). Thoday (1961) suggested that with the first demonstrated quantitative variation (biometrical genetics) by Johannsen (in German, 1909) by progeny testing, and with Sax's 1923 experiments, the theoretical groundwork for mapping quantitative trait loci was complete and was an apparent next research objective for quantitative geneticists. Understatedly, he noted the main limitation as being the availability of markers for the detection of the polygenes. The term quantitative trait locus and the abbreviation (QTL) first appeared in the literature in 1975 by Geldermann studying animal genetics, who also noted the paucity of available markers and added the importance of precise phenotypes for QTL detection. The deployment of co-dominant isozyme markers (Rick and Fobes 1975) in the 1980s improved the detection of possible QTL by increasing the coverage of the genome, while avoiding the dominant/recessive effects of morphological markers but with still too few markers to detect epistasis (Tanksley et al. 1982; Stuber et al. 1982; Edwards et al. 1987). The advent of recombinant DNA techniques ushered in true genetic

maps in humans of "DNA marker loci", based initially on restriction fragment length polymorphisms (RFLPs), also as co-dominant markers but much more plentiful than earlier ones (Botstein et al. 1980). Such maps were found to have broad applications in plant and animal improvement programs for marker-assisted introgressions, especially of QTLs (Beckmann and Soller 1983). The next landmark came with the publication of "Mapping Mendelian factors underlying quantitative traits using RFLP linkage maps" with the improvement of QTL detection using interval mapping and LOD score analysis providing the genetic location and phenotypic effect of the QTL (Lander and Botstein 1989), along with the companion publication (Paterson et al. 1988). RFLPs allowed for the scanning of all the chromosomes (70 markers, 14.3 cM average spacing in the case of tomato) and launched waves of QTL mapping in plants and animals for a wide range of phenotypic traits. Advances in DNA sequencing technologies (Sanger and Coulson 1975) and the breakthrough of the polymerase chain reaction (PCR) (Mullis et al. 1986) steadily increased the DNA marker density of maps, allowing for fine mapping QTL, both innovations resulting in Nobel prizes in chemistry. These discoveries allowed for the eventual cloning of the first causative gene underlying a QTL, fruit size in tomato (Frary et al. 2000), completing the assertion of Bateson that a quantitative trait could be converted to single Mendelian factors. The limitations of many linkage-based QTL studies still included the paucity of high-density genetic maps and the limits of biparental or pedigree-based mapping populations, with resolution to large genetic regions rather than gene(s) due to insufficient recombination events. A new technique was proposed for mapping complex trait loci, named association mapping, based on using collections of genotypes to capture historic meiotic events (Risch and Merikangas 1996). However, it took a breakthrough in statistical genetics to reduce the rate of false positives in association mapping studies with Bayesian-based statistics to identify previously cryptic underlying population structure of the assembled genotypes (Pritchard and Rosenberg 1999; Pritchard et al. 2000). Immediately, Thornsberry et al. (2001) applied this approach to flowering time in maize and identified a deletion in the *Dwarf8* gene as the causal allele. Risch and Merikangas (1996) also noted that the limitations for association studies were the paucity of polymorphisms across the human genome. However, this limitation was solved with the advent of sequencing of whole genomes, notably the first plant species *Arabidopsis thaliana* (The Arabidopsis Genome Project 2000). Application of these advances in agricultural crops has been complicated by problems caused by low predictive power in current models and of resource allocation between phenotyping and genotyping (Heslot et al. 2015). New models under development

are expected to improve prediction. Today, over 100 plant species' genomes have been sequenced (Michael and VanBuren 2015), assisted by the implementation of next-generation sequencing (NGS) technologies and reduced costs (Balasubramanian et al. 2004; Bentley et al. 2008). The advent of widespread whole-genome sequencing has opened a new era of Mendelizing QTL, where a paucity of genetic markers is no longer an issue (Hori et al. 2016). However, new challenges are now revealed. In a recent review of maize genetics summarizing progress with identifying candidate genes, it was stated that most quantitative traits are controlled by a large number of small effect genes "locked away in low-recombination regions", presenting challenges in (even) sequenced and highly genotyped association mapping panels (Wallace et al. 2014).

The advent of plant genomics

Beginning in the early twentieth century, advances in microscopy, chromosome banding, DNA labeling, in situ hybridization, flow cytometry, micromanipulation and chromosome-imaging systems transformed classical cytogenetics, paving the way for present-day molecular cytogenetics. Cytogenetics contributed to the early stages of genome mapping projects in diverse organisms, first by mapping specific repetitive DNA, and later by mapping entire genes using fluorescence in situ hybridization (FISH), or by distinguishing between parental genomes in hybrids using genomic in situ hybridization (GISH) (Kato et al. 2005). Further development of cytogenetic approaches has led to chromosome painting in plants (Lysak et al. 2001). Identification of chromosome territories occupied by specific chromosomes within interphase nuclei using in vivo fluorescent labeling systems, in combination with other methods (e.g., fluorescence recovery after photobleaching, FRAP), have increased our understanding of chromatin dynamics. These methods, which allow for the examination of sequence localization in 3D nuclei, will be soon applied to plant genomes, much as analyses of 4D chromosome dynamics in cycling cells were used in mammals (Strickfaden et al. 2011).

Similarly, genetic mapping using molecular methods, either RFLP based or later PCR based, led to the advent of comparative genetics. The RFLP technique was first applied to plants in the mid-1980s with the aim of producing a new generation of markers for breeders. This method resulted in reports of synteny across genomes, for example, between tomato and potato (Bonierbale et al. 1988). It was not clear at that time that intergenomic synteny holds mostly to genes. Alternative marker systems based on PCR have complemented RFLP since the 1990s. The first consensus grass map, which aligned the genomes

of seven grass species, revealed extensive conservation of gene order, despite many differences in organization among the genomes observed (Moore et al. 1995; Gale and Devos 1998). A multi-species approach allowed plant genomics to evolve into a powerful and routine tool, especially when plant genomes first began to be studied within genome sequencing projects. *A. thaliana* was the first completely sequenced plant species. Rice became the second sequenced plant, not only because of its economic importance, but also due to its small genome, reasonable transformation competence and a detailed genetic map. The list of sequenced plant species grew quickly thereafter (Michael and Jackson 2013). Genomes of model species share reasonable genetic synteny with key crop plants, which facilitates the discovery of genes and the association of genes with phenotypes. During the last decade, large genomic centers have generated massive data sets beneficial for plant biologists. The current decade will bring essentially completed sequences for multiple branches of virtually all angiosperm clades that include major crop and botanical models (Paterson et al. 2010). The acceleration of genome projects was made possible by the invention and widespread use of next-generation sequencing. "Progress in science depends on new techniques, new discoveries, and new ideas, probably in that order," said Sydney Brenner in 2002. The first DNA sequencing techniques were developed in the 1970s by Sanger and colleagues (Sanger et al. 1977) and by Maxam and Gilbert (1977). Sanger sequencing (considered first-generation sequencing) became the prevailing DNA sequencing method for the next 30 years and enabled scientists to complete the genomes of *Arabidopsis*, rice and many other plant species. The emergence of NGS in 2005, first developed by 454 Life Sciences (now Roche), entails massive parallel sequencing (based on an older pyrosequencing method, Ronaghi et al. 1996) and was a great leap forward toward faster, high-throughput and cheaper DNA sequencing. NGS techniques now include several different platforms (454, Illumina, SOLiD, Ion Torrent, PacBio and others; for review see van Dijk et al. 2014) and allow scientists to get billions of sequencing reads corresponding to terabases (Tb) per run. The application of NGS in plant science not only made feasible the whole-genome assembly of many species but also facilitated other studies—e.g., gene expression, DNA–protein interactions, the relationship between genomic variation and phenotype—that covered a wide range of related disciplines from molecular biology via developmental biology to agrigenomics (Varshney et al. 2009). The recent advent of a third-generation technology, represented by nanopore sequencing (Oxford Nanopore Technologies), allows for single-molecule sequencing without the need for library preparation or sequencing reagents. Such technology has established single-cell genomics that has recently been utilized in animals, and its application in plants is only a question of time (Thudi et al. 2012).

Genomes: from *C* values to whole-genome structure and evolution

The amount of DNA in plant nuclei was estimated for the first time 66 years ago, when the genetic role of DNA was already known but before the double helix structure of DNA was discovered in 1953. The haploid nuclear complement was defined as the 1C value (Swift 1950). The *C* values estimated in 2802 plant species (representing 1 % of all angiosperm species and about 30 % of angiosperm families) were obtained by 1997, and the *C* values of approximately 1700 other species were estimated by 2003 (Bennet and Leitch 2005). Several methods have been used to measure plant DNA *C* values, including Feulgen microdensitometry, flow cytometry or computer-based image analysis (Greilhuber 2008). Since plant *C* values were first estimated, it has become evident that there is no correlation between the complexity of an organism and the size of its genome. Closely related species often differ significantly in their nuclear content. These enigmatic differences have led to the term "*C* value paradox". Originally, when the mosaic structure of genes was discovered, differences in genome size were attributed to the introns. Later, when genomes were studied in more detail, it became clear that repetitive DNA sequences, in combination with polyploidization, provide the main keys to resolving the "*C* value paradox". Genome sizes vary by >2000-fold among the angiosperms, from fewer than 10^7 base pairs (1C = 0.065 pg–63.4 Mbp) in *Genlisea margaretae*, Lentibulariaceae (Greilhuber et al. 2006), to more than 10^{11} (1C = 152.23 pg–150 Gbp) in *Paris japonica*, Melanthiaceae (Pellicer et al. 2010).

Genomes evolve by duplication of genes, chromosome or whole genomes, by various rearrangements, insertions of organellar, bacterial or viral DNA that are part of horizontal gene transfer (HGT), (micro)satellite expansions, transposable element insertions and other processes. Although the first comparative studies suggested that plants have a "one-way ticket to genomic obesity" (Bennetzen and Kellog 1997), later phylogenetic evidence showed that the processes leading to the elimination of DNA, which often involve repetitive elements, are also present and result in genome downsizing (Petrov 2001; Petrov et al. 2003).

Genome sequencing projects led to the discovery of the genome structure of many plants. A major part of the nuclear genome of most plants is represented by different repetitive DNA elements (Kubis et al. 1998); these elements contribute to the higher evolutionary dynamics of genomes, while genes represent slowly evolving (conservative) genetic units. A high turnover of repetitive DNA (compared

to genes) results in a fast divergence of these genome components and leads, e.g., to an infeasibility of GISH mapping when more distantly related species are studied (Lim et al. 2007; Koukalova et al. 2010), as well as causing problems with chromosome painting in plants (Schubert et al. 2001). Perhaps, the most distinctive feature of angiosperm genomes is the large amount of genome duplication, i.e., polyploidization. It has long been suspected that many angiosperms were paleopolyploids (Stebbins 1966), but recent analyses of genome sequences suggest that virtually all angiosperms are paleopolyploids (Bowers et al. 2003; Paterson et al. 2004). According to a speculative hypothesis (Chapman et al. 2006), genome duplications are not episodic but rather cyclic, providing various fitness advantages that erode over time, which favors new polyploidizations. Higher repetitive DNA turnover, repeated polyploidizations and subsequent gene losses lead to much more rapid structural changes of plant genomes when compared with vertebrates, where gene order conservation is evident even after hundreds of millions of years of divergence (Kejnovsky et al. 2009).

Repetitive DNA: from junk DNA to a major evolutionary force

Repetitive DNA elements can be divided into two major groups, distinguished by their genomic organization: transposable elements (TEs) that are dispersed throughout a genome and satellites arranged in tandem (Schmidt and Heslop-Harrison 1998). Intermediate forms can also exist, e.g., TEs can contribute to the origin and/or amplification of satellite DNA. Satellite DNA, whose name was inspired by the "satellite" band produced during density gradient centrifugation, is subdivided according to monomer length into microsatellites, minisatellites and satellites. Satellites often constitute long arrays in genomes and could be a subject to concerted evolution (Elder and Turner 1995). Copy numbers of individual repetitive DNA motifs can vary from several hundreds to hundreds of thousands, and the tandem arrangement of their multiple copies have not only nongenic sequences, but also ribosomal genes. The balance between homogenization and mutations results in a specific range of satellite variability. Microsatellites go through the phases of birth, expansion and regression (Ellegren 2004; Kelkar et al. 2011). The discovery of transposable elements by Barbara McClintock (1950) represented a major milestone in genetics, but the greatest importance of her discovery was, much as in the case of Mendel, recognized several decades later when McClintock was awarded the Nobel Prize in 1983. The recessive allele locus *rugosus*, the cause of one of the traits (wrinkled seeds) studied by Mendel, is caused by a DNA transposon insertion into a gene encoding a starch-branching enzyme (Bhattacharyya et al. 1990).

Transposable elements are ubiquitous mobile genetic elements spread through genomes either by a copy and paste mechanism via an RNA intermediate, used by retrotransposons, or by a cut and paste mode used by DNA transposons. These two main classes of TEs are further subdivided into several orders and many families and subfamilies (Wicker et al. 2007). TEs can together constitute up to 80 % of an individual genome, and a single TE family may represent up to 38 % of a whole genome (Neumann et al. 2006). The function of repetitive DNA has not been completely elucidated, despite the many debates ongoing since the discovery of repetitive DNA. Repetitive DNA was originally considered to be "junk DNA" (Doolittle and Sapienza 1980; Orgel and Crick 1980), but the last decades have shown that it represents an important evolutionary force and may even function as a driver and facilitator of evolution. Repetitive DNA, especially transposable elements, can affect genome diversity and plasticity, induce epigenetic changes, influence gene expression or build cellular regulatory networks (Kazazian 2004; Oliver and Green 2009; Biémont and Vieira 2006; Feschotte 2008). Differences in repetitive DNA are the major factors responsible for genome size variation, not only between species, but also within a species. Some TEs are used for important cellular functions in a process called domestication or exaptation (Volff 2006; Kokosar and Kordis 2013). For example, an integral part of the immune systems of vertebrates, V(D) J recombination, evolved from *Transib* DNA transposons (Kapitonov and Jurka 2005). Similarly, telomeres of *Drosophila melanogaster* are formed by *HeT-A* and *TART* retrotransposons (Abad et al. 2004; Biessmann et al. 1992), and the centromere-binding protein CENP-B evolved from the transposase of DNA transposons (Kipling and Warburton 1997). Present genomics views genomes as ecosystems of various elements (genes, various repeats) interconnected by a plethora of interactions, from symbiosis via competition to parasitism. The character of these relationships between elements can change over time, and originally parasitic elements can evolve into cellular functions, simply increase individual variability or induce genome reshuffling, thereby increasing the evolutionary potential of a species.

Impact of Mendelian genetics on plant breeding and food security

From the dawn of agriculture until today, farmers have acted as plant breeders, working almost exclusively through mass selection, that is, by ensuring that some individual plants made a proportionately greater genetic contribution to the following generation than did others. Natural outcrossing was frequent enough, even in self-pollinating species, to generate useful genetic recombinants. Early plant

breeders worked without the benefits of progeny testing or replication, both of which can enhance gain from selection, but they had two other important factors working in their favor: time and ecosystems.

In the twentieth century, many plant breeding techniques were developed on the basis of Mendelian principles of inheritance (Kingsbury 2009). These include pedigree, mass selection, and backcrossing approaches. Mutagenesis techniques have allowed for the identification of many useful new variants. In some crops hybrid approaches are practical and allow for the exploitation of heterosis to achieve substantial gains in crop yield (Bernardo, this issue). Interspecific hybridization methods are being used to introgress alleles for important traits such as disease resistance and to broaden genetic diversity in crops.

Rate of gain in plant breeding has also been enhanced in the past century by several improvements in methodology. Contra-season nurseries allow for the production of more than one generation in a year. Well-managed glasshouse and phytotron chambers also allow for off-season advances. Improved small plot machinery has given rise to major increases in the scale of breeding programs. Improved agronomic practices for disease, weed, and insect control have increased productivity in breeding. Improved sample handling techniques such as bar-coding allow for major improvements in the efficiency of plant breeding. Improved experimental designs and statistical packages have improved the efficiency of selection and made best use of limited resources.

Until the nineteenth century, crop improvement and its production were mainly in the hands of farmers and generally based upon the expansion of the cultivated area to produce the required food grains. The understanding of crop improvement science based on Mendel's genetic principles laid a firm foundation to science-based agriculture. Understanding of trait genetics in the light of Mendel's principles of heredity, Norman Borlaug led the development of high-yielding semi-dwarf varieties of rice and wheat, which revolutionized wheat and rice production in Asia in the mid-1960s. This breakthrough came to be known as the Green Revolution and symbolized the process of using agricultural science to develop modern techniques for the benefit of developing countries. More precisely, these varieties transferred many nations such as India, Pakistan, and the Philippines from "mouth-to-ship" situation. Presently, science-based crop improvement, which owes its foundation to Mendelian principles, contributes 2784 million tons (FAO 2015) of cereal grains to the world food basket to nourish the planet.

Methods of crop breeding have undergone major changes, and a range of technologies is improving the rate and success of crop improvement in some breeding programs, but these are yet to be widely adopted. Contributions are being made through new selection strategies that are informed by sophisticated genetics, the use of computers to track and manage field trials, and biometric methods for field trial design and assessment of interactions between genotype, environment, and management. Heterosis (hybrid vigor) for inbreeding species can offer 20–50 % yield increases. Strategies for using heterosis more widely to increase yields in inbreeding crops center on finding ways of reducing the cost and increasing the efficiency of producing hybrid seed (Kingsbury 2009). These include identifying new sources of male sterility for hybrid creation and using transgenic approaches to engineer sterility and restore fertility. Another potential future mechanism for producing hybrid seeds involves the use of apomixis, where plants produce seeds without the need for fertilization.

Mendel's principles in the era of genomics

Present-day genomics research has developed on three milestone discoveries of biology, namely, Mendelian principles of heredity, evolutionary principles of Darwin, and the discovery of the DNA structure. Mapping populations, their use in segregation of molecular markers and marker–trait association to map and isolate genes, were developed on the basis of Mendelism. With the advent of NGS-based technologies and the rapid decline in per sample cost, many sequencing-based approaches have been proposed. SHOREmap (Schneeberger et al. 2009), next-generation mapping (NGM) (Austin et al. 2011), MutMap (Abe et al. 2012), isogenic mapping by sequencing (Hartwig et al. 2012), SNP-ratio mapping (SRM) (Lindner et al. 2012), MutMap+ (Fekih et al. 2013), MutMap-Gap (Takagi et al. 2013), and Seq-BSA (Singh et al. 2015a, b) are some of the important approaches for trait mapping. These approaches are not only fast and reliable, but more cost-effective in comparison to the conventional approach of trait mapping and deployment.

In addition to classical and modern plant breeding, Mendel's work laid the foundation for today's molecular breeding and genetic engineering. Mendel's laws were helpful for selection of stable and promising plants/events based on segregation ratios. Globally, using Mendelian genetics in terms of foreground selection (selection of plants possessing allele(s) of interest in the segregating generation though linked markers), with and without background selection (selection of plants with a higher proportion of the recurrent parent genome using genome-wide markers), many cultivars have been developed using molecular breeding (especially, through marker-assisted backcross breeding) approaches. This approach is useful for precise and rapid

development of improved breeding lines for the target traits such as disease resistance, nutritional quality, drought tolerance and submergence tolerance across different crops.

Although markers can be used at any stage during a typical plant breeding program, marker-assisted selection (MAS) is a great advantage in early generations, because plants with undesirable gene combinations can be eliminated. This allows breeders to focus attention on a lesser number of high-priority lines in subsequent, more expensive, field generations. Although DNA markers were first developed in the 1980s, more user-friendly PCR-based markers such as SSRs were not developed until the mid- to late 1990s, and SNPs in the past decade. The cost of using MAS compared with conventional phenotypic selection may vary considerably.

Genome-wide or genomic selection (GS) is a recent approach for the development of improved breeding lines (Meuwissen et al. 2001). GS also relies on MAS and is under evaluation for the feasibility of incorporating desirable alleles at many loci that have small genetic effects when used individually. In this approach, breeding values can be predicted for individual lines in a "training population" based on phenotyping and whole-genome marker genotyping. These values can then be applied to progeny in a breeding population based on marker data only, without the need for phenotypic evaluation. Successful examples of the application of GS have been reported in several crops (Heffner et al. 2011; Asoro et al. 2011; Lorenz et al. 2012; Crossa et al. 2014; Spindel et al. 2015). Complex trait dissection using high-throughput technologies have recently been developed to determine the phenotypic components of complex traits, for example, robotic greenhouse systems with nondestructive imaging to monitor growth rates. These phenomic techniques yielding precise digital data in combination with the recent throughput and cost-efficiency in genomics techniques offer the prospect of powerful associative analysis being established to link genotype to phenotype. Increasing genetic diversity requires an expansion of the germplasm base in breeding programs, but this is dependent on enhancing techniques for assessing the value and use of individual accessions from germplasm collections. Improvements in phenotyping and genotyping will help remove this limitation by facilitating the identification and characterization of key adaptive QTLs. Introgression of novel alleles from landraces and wild relatives is often slow and tedious, but options are now being developed for accelerating introgression using molecular approaches (Zamir 2001). The wider deployment of genetically modified (GM) approaches will be needed for the introduction of novel genes and alleles from diverse sources, and particularly for traits that are absent in plant genomes (for example, *Bacillus thuringiensis* toxin from soil bacteria), or where there is insufficient variation for practical utility (for example,

vitamin A accumulation in rice endosperm) (Tester and Langridge 2010). The slow advances in GM crops besides political decisions can be attributed to the "inefficiencies of conventional random mutagenesis and transgenesis" (Shukla et al. 2009) and the lack of target genes of importance to crop production hampered by these inefficiencies (Townsend et al. 2009). Early success in more precise gene editing in plants was reported by Shukla et al. (2009) in maize and by Townsend et al. (2009) in tobacco using engineered Zn finger nucleases (ZNFs). The resulting efficiencies demonstrated in engineering herbicide resistance in tobacco and maize represent a huge step forward followed by Li et al. (2012) using transcription activator-like effector nucleases (TALEN)-based gene editing to produce disease resistance in rice. The breakthrough of the decade was publication of gene editing with the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) system for RNA-programmable genome editing (Jinek et al. 2012) followed quickly by multiplexed genome engineering using the CRISPR/Cas system (Cong et al. 2013). The first CRISPR/Cas system gene editing was demonstrated in model plants (*Arabidopsis* and tobacco) by Li et al. (2013). While not a panacea (Fu et al. 2013), this is an important progress in precision gene editing. Details of the three gene editing systems are presented in a review article by Gaj et al. (2013).

Conclusions

Despite tremendous progress made over the past 150 years, genetics will forever rely on basic principles discovered and formulated by G.J. Mendel in 1865 on garden pea. As a genetical model for plants, pea was gradually superseded by *Arabidopsis thaliana.* Today, however, we do not need to rely only on such simplified models, but we can use more complex crop species with often large genomes. Mendel's experiments were based on qualitative traits; however with the use of statistical analysis the issue of continuous variation, quantitative variation, was made accessible. QTL provide another demonstration that quantitative traits are governed by the same principles as single qualitative genes. During the last 150 year period, key discoveries of hereditary principles were made, among others the relationship between genes and proteins, the double helical structure of the DNA molecule and, based on these, currently flourishing disciplines of molecular biology and genomics. Today, over 100 plant species' genomes have been sequenced, assisted by the implementation of NGS technologies. There is an emergence of new research fields and disciplines, including genomics and bioinformatics, and we are now combining distant disciplines to uncover complex biological situations. In addition to classical and modern plant

breeding, Mendel's work laid the foundation for today's molecular breeding and genetic engineering. This is largely fueled by the last decade's technical advances, allowing for more discoveries but also creating new challenges, such as data storage, analysis and prediction. Genetics has had a tremendous impact on agriculture through crop breeding and similarly genomic knowledge is gradually being translated to molecular breeding and genome-wide or genomic selection for the development of improved breeding lines.

Author contribution statement P.S. coordinated the manuscript layout, assembly and wrote the Reflection on Mendel's work on pea; C.C. and C.D. wrote the section on quantitative traits and gene editing; E.K. wrote the section on cytogenetics and repetitive DNA; R.K.V., V.K.S. and T.W. wrote the section on translational genomics and breeding. All authors edited the manuscript and read and approved the article.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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