Food Reviews International

ISSN: 8755-9129 (Print) 1525-6103 (Online) Journal homepage: https://www.tandfonline.com/loi/lfri20

A Review of Genetic Understanding and Amelioration of Edible *Allium* Species

Geetika Malik, Ajmer Singh Dhatt & Ajaz Ahmed Malik

To cite this article: Geetika Malik, Ajmer Singh Dhatt & Ajaz Ahmed Malik (2020): A Review of Genetic Understanding and Amelioration of Edible *Allium* Species, Food Reviews International, DOI: 10.1080/87559129.2019.1709202

To link to this article: https://doi.org/10.1080/87559129.2019.1709202

FOOD REVIEWS INTERNATIONAL
https://doi.org/10.1080/87559129.2019.1709202

Taylor & Francis
Taylor & Francis Group

A Review of Genetic Understanding and Amelioration of Edible *Allium* Species

Geetika Malik[a], Ajmer Singh Dhatt[b], and Ajaz Ahmed Malik[c]

[a]Division of Vegetable Science and Floriculture, ICAR-Central Institute of Temperate Horticulture, Srinagar, J&K, India; [b]Department of Vegetable Science, Punjab Agricultural University, Ludhiana, Punjab, India; [c]Division of Vegetable Science, Sher-e-Kashmir University of Agricultural Sciences and Technology, Shalimar, J&K, India

ABSTRACT

Alliums are widely consumed as food and medicine but modestly understood for their genetic constitution and design. Huge, complex and repetitive genomes, biennial life cycle, strong inbreeding depression and apomixes have thwarted development of optimal genotypes, especially in the third world. However, genetic diversity assessment, marker-assisted breeding, introgression of some vital genes, doubled haploid production, induction of fertility in apomicts, organellar transcriptome sequences, gene annotation and genetic engineering have been achieved to certain extent and continue to develop further. In this review, current achievements in these areas of research for enhancing yield, processing quality, therapeutic value, storage and biotic stress resistance in important edible *Allium* species have been compiled.

KEYWORDS

Edible *Allium* species; molecular markers; genetic map; inheritance; doubled haploid; transcriptome; genome sequencing; genetic transformation; therapeutic; functional food

Introduction

Allium vegetables are various species of genus *Allium* that belongs to family Alliaceae. Also known as bulb crops, they form specialized culinary ingredients owing to their characteristic aroma arising from organic sulfur compounds released from enzymatic breakdown (by allinase and lachrymatory factor synthase) of the flavor precursors (S-alk(en)yl cystein sulfoxide compounds) found in their cells. The flavor precursors are in the form of S-trans-prop-1-enyl cysteine sulfoxide (isoalliin) and S-propyl cysteine sulfoxide (propiin) in onion, S-allyl cysteine sulfoxide (alliin) in garlic and S-methyl cysteine sulfoxide (methiin) in other alliums.[1,2] Sulphur compounds released from their breakdown along with other bioactives like flavonols and other phenols exhibit prophylactic and curative properties against many human ailments like microbial infections, carcinogenesis and degenerative diseases.[3–5] The commercial commodity obtained from *Allium* vegetables is routinely consumed afresh as well as processed in almost all cultures of the world, making alliums have an 'all-rounder' presence in routine human life. Amongst the vast range of *Allium* species found in nature, economically important ones, used mainly in culinary and medicine preparations are briefly described in Tables 1, 2 and 3.[6–8]

Although alliums are valuable horticultural and food commodities yet genetic and genomic knowledge and its application for their genetic improvement is not sufficient enough to impact farmers' field and industry at significant level.[9–11] Especially in the

CONTACT Geetika Malik geetika.pf@gmail.com ICAR-Central Institute of Temperate Horticulture, Srinagar, Jammu & Kashmir 191132, India

Table 1. Most commonly cultivated *Allium* vegetable species.

Common name	Botanical name	Somatic chromosome number	Ploidy
Common onion	*Allium cepa* L.	16	2X
Garlic			
• Hard neck	*A. sativum* var. *ophioscorodon*	16	2X
• Soft neck	*A. sativum* var. *sativum*		
Multiplier onion/ potato onion	*A. cepa* L. Aggregatum group	16	2X

Table 2. Other *Allium* vegetable species of global popularity.

Common name	Botanical name	Somatic chr. Number	Ploidy	Prominent region of cultivation and commerce
Chives	*A. schoenoprasum L.*	16, 24 and 32	2X, 3X and 4X	Europe and North America
Leek	*A. ampeloprasum* ssp. *porrum*	32	4X	Egypt
Shallot	*A. cepa* var. *ascalonicum L.*	16	2X	Middle East
Japanese bunching onion/Welsh onion	*A. fistulosum*	16	2X	Japan, China, USSR, Siberia

Table 3. Some lesser known Alliums highly valued in niche markets.

Vernacular/ common name	Botanical name	Somatic chromosome number	Ploidy	Niche area
Tree onion/ Egyptian walking onion	*A. cepa* var. *viviparum/ proliferum*	16	2X	Egypt
Great headed garlic	*A. ampeloprasum* var. *ampeloprasum*	32, 48 and 64	4X, 6X and 8X	Africa and Saudi Arabia
Kurrat	*A. ampeloprasum* var. *kurrat*	32	4X	Egypt
Pran	*A. cepa* var. *viviparum/ proliferum*	24	3X	Kashmir (India)
Jaynaut	*A. hookeri*	22	3X	North Eastern India
Jambu/Faran	*A. consanguineum* Kunth. syn. *A. stracheyi* Baker.	–	–	Nepal, Northern Uttarakhand (India), Himalayan Pakistan
Jimbur	*A. wallichii* Kunth.	–	–	Sikkim (India)
Dune	*A. humile* Kunth syn *A. govanianum* Wall. ex Baker.	–	–	Northern Uttarakhand (India), Himalayan Pakistan
Bangalore Rose Onion	*A. cepa* L.	16	2X	Bengaluru (India), with Geographical Indication (GI) status
Rakkyo/scallion	*A. chinense*	16, 24, 32	2X, 3X and 4X	North Eastern India, China, Japan
Kashmir garlic/ chives	*A. schoenoprasum* L.	16, 24 and 32	2X, 3X and 4X	Kashmir and Ladakh divisions (India)

developing countries, apart from unscientific cultural practices followed by uninformed and resource poor farmers, major reason for low productivity and quality is large scale cultivation of genetically inferior and heterogeneous populations that are non-uniform and unstable for yield, quality, stress resistance/tolerance, long storability and processing suitability (that is, high dry matter, high pungency, high TSS and light flesh color for powder, chip and flake making).[12] The challenge of improving these traits can effectively be addressed only by their complete genetic understanding, which is critical to effective selections and hybridization programs. However, attaining this understanding is greatly impaired by serious limitations posed by inherent nature of these species. These limitations are briefly discussed ahead.

Inherently complex nature of allium *species*

Workers find alliums particularly difficult crops, both from cultivation and genomic aspects.[10,13] These crops are typically biennial[14], that means, once sown they will grow and produce bulbs the first year, take physiological rest for the next 4–6 months and then re-grow and produce seeds the next year. This lifecycle takes 18–22 months from seed to seed (bulb to bulb). Thus all the breeding and cultural practices will take twice the time taken by majority of other vegetables, which are annual by nature. This delays genetic improvements by lengthening breeding programs. Secondly, many alliums reproduce asexually, that is, there is no naturally occurring variability in desired traits to perform selection in the progeny of a plant/group of plants. On the other hand, *Allium* species that do reproduce sexually are highly open-pollinated, heterozygous, heterogeneous and exhibit strong inbreeding depression when subjected to self-pollination for various breeding aims.[15,16] Inbreeding depression is of very serious concern to onion breeders and has given rise to the concept of 'doubled haploid onion' being undertaken by major research groups worldwide. Thirdly, alliums have very large genomes that are highly repetitious, extremely complex and heterozygous.[10,17–19] They are thus currently placed among those at the end of the line queued up for full genome sequencing. The breeding behavior and genomes of these species are discussed in more detail below.

Breeding behavior of alliums

Both sexual and asexual reproductions are found among *Allium* species.[20,21] Although most are syngamous (sexually reproducing) with high degree of out breeding (which in itself poses unique problems); apomixis (asexual reproduction) in species like garlic, multiplier onion, tree onion, *pran* and many others is a norm.[22] Genetically, these species remain largely the same because on reproduction, they give rise to their clones. Apomixis through cloves, bulb-lets or top-sets restricts segregation and assortment of genes, leaving no avenue for creation of variability from which to make desirable selections. Development of molecular markers for traits of interest is also hampered because genetic association studies rely on genetic variation.[23]

While apomixis restricts usable variation in some *Allium* species, syngamous alliums on the other hand are highly heterozygous and suffer severe inbreeding depression, which limits the possibilities of obtaining vigorous inbreds (repeatedly selfed parents of a potential hybrid).[14,24] The heterogeneous nature of varieties of such species along with high extent of heterozygosity also becomes a stumbling block in achieving genetic uniformity for desired traits especially bulb shape and color. Thus, both kinds of breeding behavior found in *Allium* species create unique problems for breeders, geneticists and biotechnologists.

Giant genomes

Allium genomes are classified as giant genomes and among the largest ones in plant kingdom.[25] Onion has the largest genome among all vegetable crops[26] although not the largest among alliums. Garlic genome is roughly equal to that of onion. Both onion and garlic; the diploid species, possess around 16.7 Gb DNA/1C[17], which is roughly equal to that of hexaploid wheat, 107 times larger than the model plant *Arabidopsis* genome and 34 times larger than that of rice.[27] For this reason, in times

when important commercial crops like tomato[28], potato[29], *Capsicum* spp.[30], watermelon[31], wheat[32] and rice[33] are fully sequenced, onion and other alliums' genomic revelation remains largely elusive. It is extremely challenging to decode and annotate them for use in genetic improvement. Furthermore, these species lack a reference genome due to unavailability of any closely related species with manageable genome.[34] Till 2013 when the first use of SNPs in sequencing onion genome was reported[13] all efforts on genome sequencing of alliums had rested on RFLP, AFLP and SSR markers[35–37] and resulted in very slow advancement.

Breakthroughs in *allium* genetic research and improvement

Despite abovementioned challenges; altered rearing/production technologies, next generation sequencing platforms, enhanced bioinformatics and ever advancing 'omic' technologies and Systems Biology, sophistication of tissue culture protocols, and refinement of transgene construction and delivery methods have made it possible to more effectively streamline *Allium* breeding by modulating plant phenology, decoding large and complex genomes[34,38–41], marker development and SNP discovery[42–59], molecular cataloguing of transcripts and proteins and gene annotation[11,60–70], improved transgenic outcomes, especially, in onion, garlic, Japanese bunching onion and leek[71–85], and gene mapping and genetic map construction.[10,13,56,57,86–103] Through these achievements, exploration and induction of syngamy in garlic[104–108], offseason bulb production, simplification and shortening of breeding programs in onion and Japanese bunching onion through molecular markers[53,55,58,59,86–90,92,93], transcriptional understanding of extra-nuclear male sterility and other organeller genome-based traits, development of doubled haploid lines (to replace low performing inbreds) to evolve high performance hybrids in onion[14], interspecific hybridization to combat notorious pathogens, improved biochemical quality and induced male sterility[109–117], genetic transformations in onion, garlic and leek to down regulate alliinase action[83], induce pathogen resistance[78–80,82], herbicide resistance[81] and male sterility[77] are being gradually met. The mentioned studies and achievements are discussed under pertinent headings.

Molecular markers

Alliums being biennial species take long time for genetic improvement. Molecular markers in such cases are of immense benefit, as they are based on DNA, which remains the same irrespective of growth and developmental stages. DNA markers give the option to select out desirable plants at early stages of development and save breeder's time and other resources. Selections and rejections can be done as soon as the seedling emerges and there is no need to wait for specific developmental stage.

A very important case is of male sterility in onion, which is a pre-requisite to development of F_1 hybrids.[60] F_1 hybrids have the advantage of not only uniformity but the mean values of productivity and quality parameters like dry matter content, pungency, processing value and shelf life are also significantly enhanced over the parental variety/inbred values.[14,118–121] However, it is commercially impractical to emasculate the hundreds of minute flowers of each female parent flower before crossing with male parent manually. Thus, it becomes imperative to develop female parents

Table 4. Markers developed for male sterility (CGMS) in alliums.

Trait/gene	Species	Marker name	Reference
N/S/T-cytoplasm	*Allium cepa* L.	*orfA501*	[122]
		Cob	[29]
		orf725 and *cox1*	[123]
	Allium fistulosum L.	S327and N1412	[125]
		$SCAR_1$	[126]
Ms/ms or *Rf/rf*	*Allium cepa* L.	Isotig 34671_610 Isotig 30856_1351 Isotig 29186_1830	[127]
		DNF 566 and RNS 357	[128]
		Jnurf13	[129]
		Acms 1100	[130]
		Jnurf05, Jnurf17	[131]
		AcSKP1	[132]
Male fertility transcripts	*Allium cepa* L.	Transcript contigs 2,71,665 in number (CUDH2107 transcript catalogue)	[133]

that are male sterile, i.e., lack viable pollens and need not to be emasculated. However, to develop such male sterile lines, flowering stage is awaited for 2 years before selecting plants with natural male sterility. Furthermore, for identifying their maintainers (the plants that maintain the male sterile line generation after generation in the absence of its ability to pollinate itself), another 2 year time is required. Thus determination of sterile cytoplasm and development of its maintainers take at least 4 years time.[122,123] Fortunately, with the advent of molecular markers linked to male sterility in cytoplasm and in nuclear DNA (Table 4), the selection has been preponed to seedling stage, that is, earlier by two years to identify male sterile plants and by 4 years to identify maintainer plants. Also, ambiguity in identifying true male sterile and maintainer plants is reduced to negligible. Although F_1 hybrids in onion have been on the scene since mid 1940s particularly in the USA after famous works of Jones and Clarke in the field of onion male sterility[134], reports of utilization of DNA-based markers in identifying the sources of male sterility and isolation of male sterile and maintainer lines in onion have been observed in recent times.[135–137] Nonetheless, contrary to the results obtained in the cited publications, there have also been reports claiming the inaccuracy of these markers in predicting true genotype.[138,139] This suggests the need for involving larger onion populations from as diverse geographical locations and gene pools as possible so as to ascertain highest linkage disequilibrium (no or least recombination) between trait and marker. Once dependable markers are developed for diverse populations, the tedious work of onion F_1 hybrid development will be greatly simplified and economized. Many countries, despite having agro-climatic richness, are still far behind in productivity and quality. Their onion production can improve significantly only with the widespread availability and cultivation of competent hybrids, the development of which will be highly benefitted with stable and robust male sterility linked molecular markers.

Bulb color is another characteristic that enjoys considerable attention from consumers who want their onion, garlic, leeks or scallions to be of particular color. To meet their demands, the grower, the food processing industry and the chef also look for great variability in these crops. But to breed bulbs of as many colors as the market demands

is a daunting work on part of a plant breeder since bulb color inheritance in bulb crops is complex, as it involves multiple alleles.[140] To have genetically uniform varieties of different colors, a breeder must have large base population(s) to perform selection or hybridization and develop a variety that breeds true for desired bulb color. Molecular markers, especially the codominant type, assist this procedure by alleviating ambiguity since the involvement of multiple alleles limits the certainty of obtaining target color in next generation. Functional markers for different bulb colors in onion have been developed and being used for inheritance studies, for example, marker *DFR-PS* for yellow[53] and GST-1 for white[58] bulbs. These markers are most reliable owing to their origin from the gene of interest itself and involve no recombination.

In addition to these two most extensively studied traits of onion, molecular markers have been developed for other traits also like disease resistance, dry matter and pungency. Few markers for important traits in other species have also been reported and are being used in diversity studies, genetic fingerprinting and development of genetic maps in alliums. These markers have been briefly explained in Table 5.

Table 5. Molecular markers in alliums for various breeding objectives.

Type of marker	Purpose	*Allium* involved	Reference
Microsatellite, EST-SSR, ISSR	Inter-specific taxonomic analysis	*Allium cepa* L., *Allium fistulosum* L, *Allium galanthum, Allium roylei, Allium vavilovii, Allium altaicum*	[137]
	Intra- and interspecific relatedness within subgenus *Rhizirideum*		[138]
	Genetic diversity studies, allele mining, mapping and associative studies	*Allium sativum* L.	[139]
	Diversity analysis, genotype identification, assessment of population structure	*Allium sativum* L.	[86]
	For transfer to other *Allium* species for their genetic analysis	*Allium sativum* L.	[87]
	EST-SSRs for genetic diversity, mapping and association studies	*Allium sativum* L.	[88]
	SSRs and ISSRs for genetic diversity analysis	*Allium sativum* L.	[89]
	EST-SSRs for diversity studies, mapping, association studies and fingerprinting	*Allium sativum* L.	[90]
	Construction of genetic map and phylogenetic relationship studies with other Alliums	*Allium fistulosum* L.	[91]
ILP	To assess genetic separateness among Czechoslovakian garlic varieties	*Allium sativum* L.	[92]
SNP	Genetic variability and diversity studies	*Allium cepa* L.	[93]
Functional (named DFR-PS)	Marker assisted selection (MAS) of yellow bulbs	*Allium cepa* L.	[94]
Functional (MS2 gene based)	MAS of fertility in garlic	*Allium sativum* L.	[95]
CAPS	MAS at *ANS-PS* locus (bulb color)	*Allium cepa* L.	[96]
SNP, RFLP (named ACP052 and API66C-E5, respectively)	MAS for low levels of lachrymatory factor	*Allium cepa* L.	[97]
Not available	Marker assisted back crossing for DM resistance	*Allium roylei* and *Allium cepa* L.	[57]
Functional (named GST-1)	MAS of white bulbs (*C/c* locus)	*Allium cepa* L.	[58]
Not available	MAS of bulb colors	*Allium cepa* L.	[59]

Gene/QTL mapping and genetic map construction

Gene mapping implies placing of expressed DNA pieces (genes) on an organism's genome to explicate its structure and recombination behavior. A genetic map can be based on recombination frequency among genes in which case it is called linkage map or it can be constructed on the basis of physical location of genes on the genome, where it is known as physical map. Significant work has been done during the last one and half decade in the field of genetic map construction using both intra- and inter-specific crosses but in only a few alliums. They give information on the genetic structure, sequence and linkage/recombination about the organism in question. Both help breeders to predict recombination outcome of a breeding strategy, whether it involves hybridization or self-fertilization and a plant biotechnologist is also greatly benefitted with the knowledge of physical location of his/her gene of interest since it helps in isolation of the gene and its transfer to recipient variety/species through genetic transformation. In genus *Allium*, important genes have been mapped to respective locations on chromosomes mainly in onion, Japanese bunching onion and wild species *Allium roylei* Stearn. during the last two decades. These include male sterility (S/T/N cytotype, *Ms/ms* locus)[86–88], fertility restoration (*Rf/rf*)[89], quality characteristics like pungency (sulfur content)[56,93], dry matter content[92], antioxidant/medicinal potential (quercetin levels)[96], bulb pigments (anthocyanins/flavonoids)[91,94], plant physiological disorders[97] and resistance to pathogens.[90] The studies are described in Table 6. These discoveries have now made it possible to develop elite cultivars with specific agronomic or industrial applications (food processing, pharmaceuticals, cosmeceuticals) in shortest possible time through marker assisted breeding and genetic transformation. Enhanced understanding of inheritance mechanism and associations among traits has reduced onion breeders' dependence on phenotypic scoring, which is oftentimes misleading. An example of the merit of gene mapping is association study of low pungency and high solid content in onion with two molecular markers; ATPS and SiR.[93] For many onion breeders, the objective is to develop low pungency cultivar with high soluble solid content since most countries in the West like their onions to be mild but transformable into powder, chips, flakes and rings. This necessitates the onions to have high soluble solid content. However, the objective is difficult to achieve through phenotypic evaluation, as low pungency (mildness) appears to be strongly linked with low soluble solid content.[141] However, with the mapping of ATPS and SiR markers on onion genome, it is now possible to select low pungency genotypes without linkage drag with low soluble solid content in bulbs. This will save resources as well as increase selection efficiency to breed mild onions with high soluble solids suitable for processing industry.

Germplasm and cultivar duplicates are other problems of especially the technologically less advanced countries that lead to continual and inadvertent efforts by multiple agencies on the same germplasm for the same trait. The unfruitful impact of this situation makes itself evident after years and decades when no significant improvement in economic returns is seen at farmers' level. The false impression of diversity/variability that arises due to variations in growing environment causes erroneous phenotyping and can only be avoided by DNA-based genotyping. DNA fingerprinting by using gene and non-gene-based DNA markers like SSR and SNP is an infallible strategy to ascertain diversity among populations and reduce redundant efforts. With the advancing number of genes/markers

Table 6. Mapping of genetic factors responsible for important traits in alliums.

Gene/QTL/Trait	Type of marker	Location	Allium species involved	Methodology	Reference
Downy mildew resistance	Functional (named DMR_1)	Chr. 3	*Allium cepa* L.	cDNA sequencing, indel polymorphism study, primer pair development	[57]
Nuclear male sterility locus (*Ms/ms*)	SSCP and SNE	Chr. 2	*Allium cepa* L.	RFLP and AFLP analysis	[86]
Cytoplasmic male sterility (N/S)	SCAR and RAPD (named SCS13 and $S200_{2400}$)	mtDNA	*Allium fistulosum* L.	–	[87,88]
Male fertility restorer locus (R*f*)	–	Chr. 5F	*Allium fistulosum* L.	Backcrossing and GISH	[89]
Botrytis squamosa resistance (*Bs1*)	SNP	Chr. 6	*Allium roylei*	Transcriptome sequencing followed by QTL mapping	[90]
I (locus for white bulb color)	SSR	21 cM from ACM006	*Allium cepa* L.	–	[91]
B (seed coat color)	SSR	Chr. 1	*Allium cepa* L.		
C (bulb color)	SSR	Chr. 6	*Allium cepa* L.		
Frc (bulb dry matter)	SSR	Chr. 8	*Allium cepa* L.	–	[92]
Low pungency	Functional (named ATPS and SiR)	Chr. 3	*Allium cepa* L.	–	[93]
Structural genes for bulb color	SCAR (named CHS-A, CHS-B, CHI, F3H, DFR, ANS)	Chr. 2A, 4A, 3A, 3A, 7A, 4A	*Allium cepa* L. Aggregatum group	Alien monosomic additions and PCR-based marker analysis	[94]
Lachrymatory Factor Synthase (*LFS*)	SNP and RFLP	Chr. 5	*Allium cepa* L.	Use of A. fistulosum-shallot monosomic addition lines, F2 mapping population from the interspecific cross A. cepa × A. roylei, BAC-FISH study	[56]
Flavonoid 3′ hydroxylase (*F3′H*) for quercitin formation	–	Chr. 7A	*Allium cepa* L.	Direct comparison between chromosome constitution and flavonoid contents of multiple alien addition lines	[95]
Molecular markers (406 no.)	SSR and EST		*Allium cepa* L. and *Allium fistulosum* L.	Bunching onion-shallot monosomic addition lines and allotriploid bunching onion single alien deletion lines	[96]
Bolting	Functional named *ACBlt1*	Chr. 1	*Allium cepa* L.		[97]

being mapped in *Allium* species, establishing genetic separateness will be easier and faster in order streamline onion breeding programs in the developing world by avoiding duplication of efforts and resource expenditure.

Continual mapping of genes, markers and quantitative trait loci on genomes lead to build up of genetic maps. However, contrary to most of the major vegetable and cereal crops, linkage or physical maps of *Allium* species are far from complete and difficult to correlate by virtue of very large and repetitive genomes. The first online resource, wherein, accessing the many partial genetic maps, markers, sequence resources and studies underlying them was made possible was developed under the name AlliumMap-A.[142]

Table 7. Genetic maps constructed in important *Allium* vegetables.

Species	Type of markers used	Number of markers	Genome coverage	Reference
Allium cepa L.	*Ms/ms*, light red bulb color, alliinase, RAPD and RFLP	127	–	[98]
	EST	100	1907 cM (14 linkage groups)	[91]
	EST	11008	–	[99]
	SNP	936	10 linkage groups	[13]
	SNP mining with genotyping-by-sequencing approach		1383 cM in 8 linkage groups	[10]
Allium sativum L.	Alliinase, chitinase, sucrose-1-fructosyltransferase, chalcone synthase, AFLP™	366	Map1: 1166 cM Map2: 862 cM	[100]
Allium sativum L.	SNP, SSR and RAPD	53	415 cM	[101]
Allium fistulosum L.	AFLP™, SSR, CAPS	MP1: 164 MP2: 120	MP1: 947 cM MP2: 775 cM	[102]
Allium fistulosum L.	SSR, InDel, CAPS, dCAPS	254	2069 cM (17 linkage groups)	[103]
Allium fistulosum L.	SSR	228	1261 cM (16 linkage groups)	[96]

Restricted access to the resource is available at http://alliumgenetics.org/. This resource includes information and data on different onion intra-specific mapping populations as well as those raised from *A. fistulosum* L. and *A. roylei* and has been especially built to assist comparative genomic studies in alliums. Lately, an unrestrictedly accessible online resource of onion genomic information has been created under the name 'The Onion Genomic Resource'.[26] It carries information on 20204 ESTs, 20755 Transcriptome Shotgun Assembly (TSA) sequences; EST based 1915 SSRs, 15 SNPs and 13 InDels; TSA based 249987 unigenes, 123282 SSRs, 135424 SNPs and 11891 InDels. Apart from this, the resource also houses information on 8 miRNAs with their targets and 200 validated molecular markers for onion breeding. It can be freely accessed at http://webtom.cabgrid.res.in/ogr/. Similarly, in garlic, the first EST database and mining resource by the title GarlicESTdb has been constructed to help workers discover and annotate crucial genes.[143] The database can be accessed at http://garlicdb.kribb.re.kr. The most commonly employed markers have been simple sequence repeats (SSR), single nucleotide polymorphism markers (SNP), cleaved amplified polymorphic sequences (CAPS), expressed sequence tags (EST) and randomly amplified polymorphic DNA (RAPD). In some cases, especially, onion and garlic, the gene/locus of concerned trait itself has also been mapped on the genome, which is the highest possible level of precision in map construction. These genes are cytoplasmic male sterility, light red bulb color and alliinase activity (determinant of pungency) in onion[98]; and alliinase, chitinase (antipathogen activity), sucrose-1-fructosyltransferase (for fructan biosynthesis that determines soluble solid content) and chalcone synthase (flavonoid synthesis) activities in garlic.[100] In Table 7, these studies have briefly been described.

Genome sequencing

To sequence onion genome a collaborative project was started in the Netherlands between Wageningen University and Research and private seed companies. The workers succeeded in achieving first *de novo* assembly of onion genome, constituting 10.6 Gb DNA with great number of ancient repeats and majority of the eukaryotic core genes.[38] The facility for long read sequencing was proposed to further strengthen the assembly. Onion genome is

being sequenced elsewhere also but full sequencing of this species is still expected to take a long time. Various groups are working on obtaining draft assembly of onion and garlic genomes[34,40] and analyses of their transcriptomes for sulfur metabolism[40] and cold acclimation.[41]

However, there are several reports of organellar genome sequences, partly sequenced genomes and assembled genomes in *Allium* species. In onion, since the very useful trait of male sterility is governed by mitochondrial genome, the first complete sequence of mitochondrial genome harboring male sterility factor (*orf725*, a putative chimeric gene responsible for male sterility) was revealed through next generation sequencing platform Illumina NextSeq500 to understand its nature and structure and confirm open reading frame responsible for male sterility.[39] As an advancement to this work, complete sequence of same mitochondrion but of different accession was reported, which confirmed its three circled structure using pulsed field gel electrophoresis (PFGE) for the first time and obtained transcript data of the genome[60], both of which were lacking in the previous report.

Chloroplast genome sequencing in various edible, underutilized and/or medicinal *Allium* species is being done to divulge phylogenetic relationships within Alliaceae and to develop genomic resource for myriad applications in *Allium* genetics and transgenic studies. Complete chloroplast genomes are being rapidly sequenced using high throughput NGS platforms. Till date, these have been reported for garlic[144], *Allium fistulosum* (Japanese bunching onion)[61], *Allium obliquum* (lop sided onion)[62], *Allium victorialis* (victory onion)[63], *Allium monanthum* (Korean wild chive)[64], *Allium kingdonii*[65], *Allium prattii*[66] and *Allium ovalifolium* var. *leuconeurum*.[67] These discoveries have generally pointed towards close relationship of other *Allium* species with onion and garlic.

Transcriptome analysis and gene annotation

The transcriptome data and gene annotation for better understanding of gene expression with respect to various economically important traits is also adding to the genomic resources in *Allium* species. These databases are mainly being developed for biochemical and health-related traits of onion. There are many biochemical compounds in alliums that exhibit medicinal properties and phytopathological resistance. Steroidal saponins are one such class of secondary metabolites. The transcript analysis of saponin biosynthetic pathway was done in Japanese bunching onion containing 2A chromosome from shallot (*Allium cepa* L. group Aggregatum) and candidate genes *Cytochrome P450, glycosyltransferases* and *beta-glucosidase* were discovered to play role in saponin downstream pathway. The transcript obtained can be applied for molecular marker development to identify species/varieties with therapeutic potential.[68] In another study, a transcriptome for flavonoid (quercitin, anthocyanin and flavones glucosides) biosynthesis pathway was generated in *Allium fistulosum* having shallot chromosome 5A. The findings confirmed the presence of unigene (for flavonoid biosynthesis) on this chromosome and generated gene regulatory information for development of varieties with enhanced disease countering compounds.[69] In fertile garlic, organ specific transcriptome related to flowering, stress response, sulfur metabolism and photosynthesis was catalogued and presented a useful genomic resource for marker development in garlic related to flowering and disease resistance.[70] A first of its kind study of allergen genetics in onion was done using

NGS platform to sequence and annotate 46 putative genes responsible for eliciting allergic reaction in human body for their further use in mapping IgE epitopes and developing genetically modified allergen free onions[11]

The structural and functional annotation of economically significant genes and study of proteins and metabolites transcribed from those genes help understand the expression mechanism of a trait, which ultimately reveals the strategy that can alter this expression. The modulation of expression has been shown to happen through exogenous chemical application (methylation/demethylation/enzyme inhibition)[145,146], chemical/radiation mutation[147,148], environmental modification[149,150] or genetic transformation. In case of alliums, LFS gene has been altered in onion to reduce tear causing compounds, and resistance to some diseases has also been incited (discussed ahead) through genetic transformation. The potential genes in alliums that may be stressed upon for expression modulation by transcriptional, post-transcriptional or post-translational manipulation are resistance to purple blotch and Stemphylium blight in onion, virus complex in garlic in tropics, higher soluble solids in long day cultivars, resistance to bolting and bulb sweetness since these traits most crucially steer the global onion market.

Inheritance studies of major economic traits

Inheritance studies in crop species have been the mainstay of crop breeding. Understanding of the inheritance of desired traits helps breeders decide the most effective strategy of breeding and in designing experiments. Before the advent of molecular understanding of genomes, pleiotropy, linkage drag and epigenetic modification had impacted breeding programs adversely by reducing or altering the effect of selection. But increasing molecular understanding of inheritance is now making plant breeding a more exact and rewarding science. Major historical inheritance studies among alliums have been done most frequently in onion, the most elaborate being inheritance of bulb color[151–154] and male sterility.[155–158] Following the use of traditional methods of heredity studies, molecular markers began to be utilized for linkage studies and thus trace the inheritance of bulb color with respect to these markers. This helped in marker assisted selection for bulb color, which is far more rapid, easy and reliable strategy than selecting the colors on morphological basis, which may later yield generation of segregants. The two major loci *ANS* (*anthocyanin synthase*) and *DFR-A* (*dihydroflavonol-4-reductase-A*) were assumed to be instrumental in onion bulb colors. However, genetic basis of appearance of so many different colors and hues of onion across onion genepools was less understood. With the development of general or trait linked DNA markers, it has now become possible to understand the genetics and inheritance of different colors. DNA polymorphism studies of segregants from a cross between yellow and dark red lines revealed single recessive mutation in *ANS* leading to formation of *P* allele responsible for pink bulb.[159] A similar study involving red and yellow bulb parents and using real time-PCR (RT-PCR) technique to detect DNA sequence changes attributed yellow bulb color to $DFR\text{-}A^{PS}$ and $DFR\text{-}A^{DEL}$ mutants of *DRF-A*.[59] Three other studies that utilized crossing and RT-PCR techniques to delve into the inheritance pattern of bulb color genes and mutations revealed complementary action among *DFR-A* and its mutants ($DFR\text{-}A^{PS}$, $DFR\text{-}A^{PS2}$ and $DFR\text{-}A^{DEL}$), and *ANS* and its mutants (ANS^{PS} and ANS^{S188L}) in different combinations to give rise to variety of bulb colors (yellow, pink, light red, etc.).[160,161]

Apart from this trait, major emphasis has been on factors responsible for bolting (untimely emergence of reproductive organs) because of its negative economic impact on yield, dry matter content and pungency (last two being quality determinants in industrial use of alliums). The inheritance of bolting has been found to be of complex nature by virtue of its control by three locations each being on chromosomes 1, 3 and 6.[162]

Pungency, the most crucial deciding factor of onion quality, has been found to be highly significantly associated with plastidic ferredoxin-sulfite reductase (*SiR*) and plastidic ATP sulfurylase (*ATPS*) genes on chromosome 3.[93] Superdominance and dominance were found to control bulb fresh weight[163] while dry matter content (fructans, fructose, glucose and sucrose) was found to exhibit major action of *Frc* gene.[92] This gene was located on chromosome 8 and found to have strong linkage disequilibrium with SSR marker ACM235.[92]

Bulbing and the flowering characteristics are very crucial in onion since they define yield and seed production potentials, respectively, which are vital from farmers' viewpoint. The problem of bolting (reduces bulb yield and quality) and reduced flowering (due to unfavorable climatic parameters, especially, photoperiod and temperature) is worldwide and thought to be at least partially genetic.[164] Genes thought to influence flowering in plants are commonly known as *Flowering Locus T* (*FT*). To understand the functioning of flowering locus in onion and bulbing behaviors, sequencing of putative RNA from an onion DH line and its BLASTING led to the recovery of six *FT* like transcripts. Sequences corresponding to these transcripts were inserted to *Arabidopsis thaliana* genome to study their behaviour, which finally confirmed the role of *AcFT1, AcFT2* and *AcFT4* flowering loci in onion flowering.[165]

Such understanding of molecular/genetic controls of economically important traits of *Allium* species has significant application in setting up of crossing programs, as the genetic makeup at the loci of interest in the breeding lines involved in the crosses will already be known to the breeder. The clarity of molecular and biochemical processes involved in the expression of target traits can be exploited for altered (up or down regulation) gene expression through genetic transformation, mutations or other means for agricultural and industrial applications. These applications pertain to bulb yield, amount of sulfur compounds, flavonoid and antioxidant levels, bulb dry matter content, total soluble solids, bulb shape, size, bulbing duration and flowering among others.

Interspecific hybridization

Commonly cultivated alliums (onion and garlic) are plagued by notorious diseases and have less refined quality traits compared to other alliums, including less cultivated species and wild relatives. For example, *Allium roylei* Stearn., *Allium fistulosum* L. (Japanese bunching onion) and *Allium galanthum* possess natural resistance to downy mildew (*Peronospora destructor*)[113,166], leaf blight (*Botrytis squamosa*)[167], anthracnose (*Colletotrichum gleosporioides*)[168], Fusarium basal rot[169], pink root (*Phoma terrestris* E.M. Hans)[170] and onion fly (*Hylemyia antiqua* Bouche).[170] *A roylei* and *A schoenoprasum* have been found resistant to purple blotch (*Alternaria porri*) .[171] In addition, *Allium fistulosum* L. has other beneficial traits like cold hardiness and high dry matter content.[170] There are other identified sources of resistance genes also, as

Table 8. Wild relatives identified for resistance/tolerance genes.

Trait	Source relative	Methodology	Reference
Anthracnose (*Colletotrichum gloiosporioides* Penz.)	*Allium galanthum, Allium altaicum, Allium pskemense*	Artificial inoculation, genetic studies of resistance	[168]
Fusarium basal rot (various strains)	*Allium fistulosum* *Allium schoenoprasum* *Allium pskemense* *Allium roylei* *Allium galanthum*	–	[169]
Purple blotch resistance (*Alternaria porri*)	*Allium schoenoprasum* *Allium roylei*	Field and artificial inoculation	[171]

mentioned in Table 8. Such beneficial attributes of these alliums warrant their use in interspecific hybridization with others to enhance their performance. In this direction, introgression breeding *via* interspecific hybridization is being attempted since 1980s and some breakthroughs have been achieved to realize practically applicable results. Some cultivars of Japanese bunching onion, namely, Beltsville Bunching, Delta Giant, Top Onion, Wakegi Onion have been reported to have resulted from interspecific hybridization with common onion.[109] Using reciprocal interspecific hybridization with onion, singe dominant gene (*Pd1*) was found to control downy mildew resistance in *Allium roylei* Stearn.[110–112] Evolution of an all together new crop has also been attempted. An interspecific hybrid between leek (*Allium ampeloprasum*) and garlic gave rise to novel crop, which had volatile components of garlic that are lacking in leek and had intermediate bulb size.[112] In addition to these, during the first one and half decades of 21st century, several introgressions of genes such as disease resistance, polyphenol content and male sterility from mainly *Allium roylei* Stearn. to onion and Japanese bunching onion were done by using alien addition lines and alloplasmy.[113–117] However, all these experiments have been limited to lab and as of yet cannot be extended to commercial fields because of elusive barriers to obtaining fully fertile hybrids. The quest to understand and overcome barriers to obtaining successful inter-specific hybrid in terms of fertility, field survival, and optimal target gene expression and yield potential is underway. The success in these endeavors will undoubtedly be of great significance in the form of reduced expenditure on disease management, quality enhancement and yield realization in addition to saving environment from hazardous pesticides.

Development of doubled haploids in onion

The potential parents of a target F_1 hybrid in any crop are first developed into inbreds before crossing them. This involves their continuous selfing (extreme form of inbreeding). Ideally, inbreds are homozygous at all loci, breed true and don't segregate for any trait. However, it is very difficult to create inbreds in case of outbreeding species like onion because continuous forced selfing in such species produces ill-effects, a phenomenon known as 'inbreeding depression', which involves compromising quality and quantity of bulbs and seeds. Doubled haploids (DH) are, apart from some natural ones, majorly the lab-made variants of plants made *in vitro* to have all the gene loci in homozygous condition. However, in onion, inbreeding depression is very high and parental lines cannot be selfed consecutively for more than 2 or 3 generations.[172] This crop is widely considered to be the top second vegetable crop after carrot to suffer inbreeding depression

that expresses as decline in seed set, seed viability, seed germination percentage, bulb size and quality.[14,15,24] Therefore, *in vitro* method of DH development seems an attractive way out.

This method involves chemical assisted doubling of single set of chromosomes inside the gamete. In almost every crop wherein doubled haploids (DH) have been developed, the source of gamete has been male (i.e. anther or pollen). Unfortunately, in case of onion, use of male gamete has been a major failure. The alternative has been gynogenesis (culture involving female parts of the flower), but that too has proved to be cumbersome with limited success. The most responsive organs have been ovary and flower bud, latter being less laborious.[173] Even after the explant has been excised and established *in vitro*; embryogenesis, plantlet survival and chromosome doubling are hindered because all these events have been attributed to variation in environment, genetic background of the population and even the genotype of plant, which are apparently impossible to control.[174–176] Following a trend of two step culture involving pre- flower bud culture and then ovary/ovule culture for many years, a shift to one step culture occurred in which only flower bud culture is done till embryo is achieved.[177] For the next step of chromosome doubling; colchicine, trifluralin and orizalin were found to have their own drawbacks, so, somatic regeneration of spontaneous DH from flower buds was seen as most promising.[174] Another problem encountered in onion DH plants regenerated from *in vitro* embryos is of hyperhydricity induced by chromosome doubling agents. This was solved by inventing a new tissue culture vessel called Eco2box.[176] Despite a long world-wide history of attempts at producing DHs in onion, report on production of usable DH lines has only been from Cornell University, New York. Here, 20 DH lines in onion were produced and found *at par* with conventionally bred inbred lines of commercial F_1 hybrids of the area. The DH lines have exhibited even greater vegetative vigor than the inbreds and shown exceptional combining ability and yield potential. The hybrids bred from these DH lines were also more uniform in bulb shape. For such benefits, these DHs were released by Cornell onion breeding programs for commercial use as parental lines for breeding F_1s.[14] This is probably the only reported case of successful DH development and release for practical onion breeding programs.

Garlic fertility

It has been reported that genetic variability in garlic may arise from alterations in the number and morphology of somatic cell chromosomes.[178] This is seen as an indication of the possibility of obtaining heritable variability in crops like garlic, multiplier onion and tree/Egyptian onion, which do not set true seed and are thus difficult to propagate. The bulky propagating material, that is, cloves, top-sets and bulb-lets, require large space and storage facilities and thus increased expenses on the part of farmers. They also act as source of viral load and the crop obtained is infected.[179] On the other hand, true seeds are inexpensive to store, do not transmit viruses and hence act as disease free propagation material. Certainly, obtaining sufficient enough seeds in garlic and possibly other apomict alliums is greatly sought after by farmers.

Findings suggest that in antiquity the obligatory apomict garlic of today was fertile and cross pollinated in the wild. In due course of time, it lost its fertility as genetic response to human intervention in the form of age old practice of flower removal or scape knotting to

enlarge bulb size.[180] Furthermore, garlic is assumed to have gradually evolved from sexual to an asexually reproducing species since there is a one way transition of garlic apical meristem from flowering primordia to top set differentiation in bolting types.[178] Considering both these assumptions, possibly, garlic ancestors had been sexually propagating giving rise to great variability we see in garlic round the globe today. Applying this knowledge, many studies took place in Japan, the USA and Israel during last three decades and gave insight into garlic fertility and its restoration and also produced some true seed producing lines with different experiments yielding between hundreds and thousands of true seeds.[104–108,179] With developments in understanding and standardization of procedures to enhance true seed production potential in garlic, considerable improvement in fertility restoration has been achieved. In the last few years, some molecular studies were also done to comprehend the mechanism of sterility/fertility in garlic. Garlic homologues of *AP3* (*APETALA 3), MMD1* (*MALE MEIOCYTE DEATH 1-LIKE), MS2* (*MALE STERILITY 2*) and *GPAT2* (*GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE)* were proposed to control fertility owing to their known roles in flower differentiation, exine formation, tapetum development, male meiosis, pollen development and tapetum viability in other species in addition to their differential expressions in fertile versus sterile garlic accessions.[54] The gene *MS2* was also proposed as a potential marker for fertility in garlic owing to its intense expression in fertile garlic in this study.

Despite six decades of studies and experimentation on garlic fertility restoration, true seed production and its molecular mechanism[181], true seed supply to farmers is non-existent. Cloves are still the only means of propagating this crop with its inherent problems, the most challenging being storage losses and viral diseases especially in tropics. It is necessary to bridge this gap between lab and field so that true seeds replace cloves and commercial propagation of garlic is revolutionized throughout the world. One way can be release of true seed producing lines in public domain by the governments and large scale efforts towards standardization of their production technology in region specific farmer field conditions.

Genetic transformation

Work on genetic transformation of alliums started in 1990s. Initially, *Agrobacterium tumefaciens* and micro-projectile based gene transformations were standardized for onion, garlic and leek[71–77] followed by transformation with specific genes that gave rise to *Bt* onion, *Bt* shallots[78,79] and *Bt* garlic[80] resistant to *Spodoptera exigua* Hübner, herbicide resistant onion[81] and male sterile leek.[77] The transformants also exhibited the transferred trait. In the latest advancement, garlic was transformed with tobacco chitinase and glucanase genes through *Agrobacterium tumefaciens* for conferring resistance to *Sclerotium cepivorum*, the causal organism of white rot. This first of its kind transformation led to retrieval of transformants that exhibited late fungal symptoms., However, complete resistance was not obtained.[115] As the most famous example of genetic transformation among alliums, tear-less onion production through gene silencing (RNAi) technology was achieved by Eady and coworkers.[83] The transgene caused down-regulation of Lachrymatory Factor Synthase gene, which is responsible for synthesis of tear inducing lachrymatory factor when the onion bulb tissue is ruptured. Most recently, with regards to onion genetic transformation, an efficacious means of *in planta* transient

Agrobacterium mediated genetic transformation with a transformation efficiency of 43.87% in onion leaf epidermal cells was suggested to develop transient transgenic plants for protein studies.[84]

The chemical and electroporation methods have not been successful in onion due to non-feasibility of protoplast regeneration.[85] The acceptance of DNA followed by regeneration capacity of transformed cell is the foundation of successful genetic transformation. Unfortunately, in onion, regeneration of transformants has been the major obstacle. However, onion basal plate callus and embryo or seedling derived callus have been found to be most responsive to regeneration of transformants.[85] The important traits that can be transferred to major alliums through genetic transformation include weed control, disease/pest control, bulb color, pungency and flavor, few of which have already been transferred, as noted above.

Functional components of therapeutic application

Genus *Allium* is well known for the functionality of its species in preventing and curing human diseases and disorders. Due to the presence of flavonoids (anthocyanin, flavonols, catechins), carotenoids, tocopherols, saponins and most importantly organic sulfur compounds, these species are proven effective in cardiovascular diseases, neurodegenerative diseases, diabetes, obesity, inflammation, cancer and infections.[182] Even in the absence of scientific knowledge of *Allium* phytochemistry, they were consumed as home remedy and in traditional/alternative medicine systems for various diseases and disorders in ancient times. However, with the advancement in research on isolation, synthesis, *in vitro/in vivo/in silico* analysis and evaluation of *Allium* biomolecules, there is a steady rise in understanding of molecular and genetic mechanisms of their effectiveness in curing.

Quercetin, a flavonol, is the most documented functional compound of alliums, especially onion, with respect to its biochemical, genetic and molecular aspects.[183–185] Its concentration has been found to vary within the onion bulb with outer rings having higher levels.[186] It has been found antioxidant[187–189], anticarcinogenic[190,191], cardiovascular and heart disease preventive[192–195] and anti-obesity.[196,197] Antioxidant activity of quercetin is due to its ability to reduce oxidative stress in cells through modulation of intracellular signals.[198] This happens due to endogenous defense system involving catalase, super oxide dismutase and glutathione.[199,200] A study for elucidation of antioxidant mechanism of quercetin has suggested down regulation of protein kinase (PKC) gene *via* activation of extracellular signal-regulated kinase 1/2 (ERK1/2) as key reason for reduced oxidative stress in the cells.[201] Studies on anti-obesity function of onion extracts have pointed at pancreatic lipase inhibition[202–204], adipogenesis inhibition[196,205], increased energy expenditure[206] mechanisms and expression modulation of inflammatory mediators from adipose cells[197,207,208] through which quercetin along with other flavonoids and sulphur compounds helps relieve obesity. The anticancer effect of quercetin through interaction with neuropilin-1 (NRP-1), a co-receptor that plays role in cancer development, has been demonstrated to contribute significantly better than many other biomolecules from different spice species.[191]

The important preventive and curative compounds of 'organosulfur' category include S-allyl-L-cysteine, S-propyl-L-cysteine, S-ethyl-L-cystein, S-methyl-L-cysteine, dimethyl trisulfide, diallyl sulfide, diallyl trisulfide, and thiosulfenates. Probably the most studied

compound among these has been 'Allicin', a thiosulfenate that is produced by enzymatic breakdown of alliin found in intact cells of *Allium* plants. In addition to rendering flavor, it has been demonstrated to act against various human disorders and illnesses. Interaction of allicin with various cellular processes resulting in human cancers has been shown to inhibit carcinogenesis.[209–212] Inhibitory effect of this compound *via* interaction with molecules vital for molecular pathways leading to various inflammatory diseases has also been documented.[213–215] The attenuating effects of allicin on neural injuries[216] and antimicrobial action[217] have been studied in *in vivo* and *in vitro* conditions. In addition to allicin, similar bioactivities have been observed in other sulfur compounds, for example, S-allyl-L-cysteine. The neuroprotective activity of garlic S-allyl-L-cysteine against endoplasmic reticulum (ER) stress induced neurodegenerative diseases like Alzheimer's, Parkinson's and Huntington's has been attributed to its suppressing effect on caplain, a Ca^{+2} dependent cysteine protease enzyme *via* binding to its Ca^{+2} interaction sites.[218] However, the same activity by S-ethyl-L-cysteine, S-methyl-L-cystein and S-propyl-L-cysteine was found to be independent of caplain inhibition and stronger than that of S-allyl-L-cysteine.[219] Diallyl sulfide, another S-compound has been well studied in garlic for bioactivity against periodontitis. It has been found to have inhibitory effect on mRNA expressions of IL-1B, IL-6 and TNF-α genes, protein expression of IL-1B and TNF-α genes and nuclear translocation of NF-κB gene in human gingivalis fibroblasts (HGFs) that elicit this disease on stimulation by lipopolysaccharides released by pathogen *Porphyromones gingivalis*.[220] Thiosulfenates found in garlic and onion are also well known to have antidiabetic effects.[221] Their activity against accumulation of excess sugar in blood was found to be through their antioxidant action, which prevents oxidative damage to pancreatic β-cells responsible for insulin secretion and also through inhibition of α-glucosidase enzyme responsible for hydrolyzing polysaccharides into absorbable monosaccharides causative of sugar elevation in blood.[222] Organosulfur compounds of *Allium* species have also shown bioactivity against obesity and are preferred over conventional drugs with side effects.[223–225]

Although research on their functionality and modes of action is considerable, progress in genetic enhancement of *Allium* species, most importantly onion and garlic, for quantitative and functional enrichment of these bioactives seems juvenile. Allinase, the enzyme responsible for synthesis of allicin, has been most widely studied compared with all therapeutically relevant entities found in *Allium* species. Pioneering studies on alliinase involved analysis of encoding gene(s) to understand evolutionary history and phylogenetic relationships among *Allium* species with respect to this enzyme. cDNA constructed from garlic alliinase was found to have high degree of similarity among different species and a family of closely related genes was thought to encode alliinases across this genus.[226] Within a species, cDNA cloning revealed low homology between root alliinase and bulb alliinase of the same plant. This DNA sequence divergence suggested their encoding from two different genes.[227] In yet another study, alliinase cDNA sequence from onion roots was found to have different per cent homologies with known root and bulb alliinases. This cloned sequence also showed similarity with the same region in dicot plants with respect to G + C content.[228] Later, alliinases began to be analyzed in other species. Their per cent homologies with onion and garlic alliinases shed more light on its evolution and expression. Alliinase specific primers were used to isolate two new versions and their homologs of alliinase from *Allium obliquum, Allium senescens* ssp. *montanum, Allium fistulosum* and

Allium schoenoprasum. Sequencing revealed high variability among species where similarity ranged from 55.5% to 77.5%.[229] At species level, dissimilarities among garlic genotypes from five different countries were divulged at intron level facilitating development of alliinase specific molecular marker.[230] Variant alliinase amplicons from four different cultivars of garlic exhibited not only sequence diversity in introns but provided for the development of ILP (intron length polymorphism) marker for use in garlic breeding. Multicopies of alliinase gene confirmed that enzyme is encoded by a gene family. In line with previous findings, exons were found highly conserved.[231]

Among flavonoids, quercetin has traditionally enjoyed greatest attention. Genetically, quercetin is responsive to improvement through breeding, as it shows variability among onion populations[183,184] but is largely independent of growing locations.[232] High level of heritability and response to selection was observed for quercetin expressed as total flavonols, thus suggesting selection as method of breeding to increase quercetin contents in onion. Also genetic control of total flavonols was suggested to be multigenic.[233]

Understanding of these functional components from molecular, genetic and biochemical perspectives needs to be strengthened so as to optimize their therapeutic efficacy alongside providing nourishment. Despite their established reputation as 'natural healing and restorative foods', there is great need to more strongly engage them in developing a new generation of medicine system that would involve plant based pharmaceuticals with no side-effects and toxicity. The findings of above mentioned and many more studies to come; especially on quercetin and alliinase will have significant industrial applications in developing such a system.

Conclusion

Many cosmopolitan as well as niche *Allium* species are cultivated worldwide along with maintenance rearing of wild and non-commercial species like *Allium roylei* Stearn., *Allium galanthum, Allium pskemense* and *Allium altaicum*. These species vary in their ploidy from diploid to octoploid and more. Almost all species are identified for their therapeutic potential apart from the food and condiment uses of many of them, most notably common onion, potato onion, garlic, chives, leek, shallot and scallions. The genetic understanding of these species/crops has till date been mostly elusive due to various intrinsic reasons. However, efforts through genomic and phenotypic studies have accelerated their breeding and genetic improvement, for example, identification of male sterility in onion by Jones and Clark in 1942 that led to discovery and development of male sterile lines in US way back in 1940s. The trend of hybrid development took up pace in the developed world; however, in developing countries, endeavors on identifying male sterility harboring populations and subsequently isolation of CMS lines rose very recently, congruently with the development of molecular markers for male sterility. Today, these markers are capable of determining both mitochondrial and nuclear factors responsible for male sterility in onion. Markers for bulb color are the next fastest evolving aspect of onion marker development studies. Mapping of some important genes has been done with the help of monosomic addition lines and molecular markers, which have paved path for targeted selections and partial linkage maps have been obtained mostly in onion. Genome sequencing in *Allium* species is extremely challenging and till date onion and garlic genomes have only been partially sequenced using NGS platforms. Complete organellar

genomes have been sequenced in many of these species to reveal male sterility related ORFs and phylogenetic relationship amongst them. Transcriptomic studies have been mostly done for therapeutic compounds in onion and flowering in garlic. The inheritance studies of major traits like bulb color in onion had been done for many decades but with advent of molecular markers and linkage maps, the knowledge was further enriched and breeding for these traits made easier. Cross species hybridization was made possible to transfer resistance genes from wild species through conventional back crossing as well as marker assisted back crossing. In order to circumvent the use of inbreds in developing F_1 hybrids because of inbreeding depression, doubled haploids were attempted in onion and success was recorded by few workers in developing DHs for experimental and even commercial use. Contrary to traditionally established apomictic nature of garlic, syngamous garlic accessions were collected as well as induced to flower and set seed under controlled conditions. The success led to other achievements like creation of variability and development of genetic maps in garlic, which was earlier thought to be unattainable. The particle bombardment and *Agrobacterium tumefaciens* mediated genetic engineering in onion, garlic and leek has been done to introduce, among other traits, biotic resistance and low lachrymatory factor, thus, evolving transgenic alliums, most notably 'Tearless Onion'. Therapeutic components in *Allium* species have been studied *in vivo* to understand their molecular modes of action against many human diseases, their homology across species and generation of resources for use in breeding. The most important of these being flavonoids like quercetin and organosulfur compounds like allicin and other thiosulfinates.

References

[1] Jones, M.-G.; Hughes, J.; Tregova, A.; Milne, J.; Tomsett, A.-B.; Collin, H.-A. Biosynthesis of the Flavour Precursors of Onion and Garlic. *J. Exp. Bot.* **2004**, *55*(404), 1903–1918. DOI: 10.1093/jxb/erh138.

[2] Randle, W. M.; Lancaster, J. E. Sulphur Compounds in Alliums in Relation to Flavor Quality. In *Allium Crop Science: Recent Advances*; Rabinowitch, H.-D., Currah, L., Eds.; CABI publishing, 2002; pp 330. DOI: 10.1079/9780851995106.0329.

[3] Liguori, L.; Califano, R.; Albanese, D.; Raimo, F.; Crescitelli, A.; Matteo, M.-D. Chemical Composition and Antioxidant Properties of Five White Onion (*Allium cepa* L.) *Landraces*. *J. Food Qual.* **2017**, *2017*, Article ID 6873651, 9. DOI: 10.1155/2017/6873651.

[4] Nicastro, H.-L.; Ross, S.-A.; Milner, J.-A. Garlic and Onions: Their Cancer Prevention Properties. *Cancer Prev. Res. (Phila.)*. **2015**, *8*(3), 181–189. DOI: 10.1158/1940-6207,CAPR-14-0172.

[5] Bisen, P.-S.; Emerald, M. Nutritional and Therapeutic Potential of Garlic and Onion (*Allium* sp.). *Curr. Nutr. Food Sci.* **2016**, *12*, 190. DOI: 10.2174/1573401312666160608121954.

[6] Gohil, R.-N.; Koul, A.-K. Cytology of the Tetraploid *Allium chinense* G. Don. *Caryologia*. **1981**, *34*(1), 73–81. DOI: 10.1080/00087114.1981.10796874.

[7] Kiełkowska, A. Meiotic Irregularities in Interspecific Crosses within Edible Alliums. In *Meiosis-Molecular Mechanisms and Cytogenetic Diversity*; Swan, A., Ed.; IntechOpen, 2012. https://www.intechopen.com/books/meiosis-molecular-mechanisms-and-cytogenetic-diversity/meiotic-irregularities-in-the-interspecific-crosses-within-edible-alliums (accessed Aug 09, 2018).

[8] Shah, N.-C. Status of Cultivated & Wild *Allium* Species in India: A Review. *Scitech. J.* **2014**, *1* (9), 28–36.

[9] Meena, L.-K.; Bairwa, S.-L.; Kumari, M.; Wadhwani, M.-K. Performance of Onion in Bihar - an Economic Analysis. *Econ. Aff.* **2016**, *61*(2), 299–304. DOI: 10.5958/0976-4666.2016.00038.3.
[10] Jo, J.; Purushotham, P.-M.; Han, K.; Lee, H.-R.; Nah, G.; Kang, B.-C. Development of a Genetic Map for Onion (*Allium cepa* L.) Using Reference-Free Genotyping-by-Sequencing and SNP Assays. *Front. Plant Sci.* **2017**, *8*, 1606. DOI: 10.3389/fpls.2017.01606.
[11] Rajkumar, H.; Ramagoni, R.-K.; Anchoju, V.-C.; Vankudavath, R.-N.; Syed, A.-U.-Z. De Novo Transcriptome Analysis of *Allium cepa* L. (Onion) Bulb to Identify Allergens and Epitopes. *PLoSONE*. **2015**, *10*(8), e0135387. DOI: 10.1371/journal.pone.0135387.
[12] Lawande, K.-E.; Khar, A.; Mahajan, V.; Srinivas, P.-S.; Sankar, V.; Singh, R.-P. Onion and Garlic Research in India. *J. Hort. Sci.* **2009**, *4*(2), 91–119.
[13] Duangjit, J.; Bohanec, B.; Chan, A.-P.; Town, C.-D.; Havey, M.-J. Transcriptome Sequencing to Produce SNP-based Genetic Maps of Onion. *Theor. Appl. Genet.* **2013**, *126*, 2093–2101. DOI: 10.1007/s00122-013-2121-x.
[14] Hyde, P.-T.; Earle, E.-D.; Mutschler, M.-A. Doubled Haploid Onion (*Allium cepa* L.) Lines and Their Impact on Hybrid Performance. *Hort. Sci.* **2012**, *47*(12), 1690–1695. DOI: 10.21273/HORTSCI.47.12.1690.
[15] Khan, S.-A.; Amjad, M.; Khan, -A.-A. The Extent of Inbreeding Depression in Seven Cultivars of Onion (*Allium cepa* L.). *Int. J. Agr. Biol.* **2001**, *3*(4), 498–500.
[16] Khodadadi, M.; Hassanpanah, D. Iranian Onion (*Allium cepa* L.) Cultivars Responses to Inbreeding Depression. *World Appl. Sci. J.* **2010**, *11*(4), 426–428.
[17] Peška, V.; Mandáková, T.; Ihradská, V.; Fajkus, J. Comparative Dissection of Three Giant Genomes: *Allium cepa, Allium sativum*, and *Allium ursinum*. *Int. J. Mol. Sci.* **2019**, *20*(3), 733. DOI: 10.3390/ijms20030733.
[18] Chinnappareddy, L.-R.-D.; Khandagale, K.; Chennareddy, A.; Ramappa, V.-G. Molecular Markers in the Improvement of *Allium*. *Crop. Czech J. Genet. Plant Breed.* **2013**, *49*(4), 131–139. DOI: 10.17221/111/2013-CJGPB.
[19] Cardi, T.; D'Agostino, N.; Tripodi, P. Genetic Transformation and Genomic Resources for Next-Generation Precise Genome Engineering in Vegetable Crops. *Front. Plant Sci.* **2017**, *8*, 241. DOI: 10.3389/fpls.2017.00241.
[20] Karpavičienė, B. Causes of Variation in Sexual and Asexual Reproduction in Diploid and Triploid Populations of *Allium scorodoprasum*. *Plant Syst. Evol.* **2017**, *303*, 105. DOI: 10.1007/s00606-016-1355-x.
[21] Mathew, D.; Forer, Y.; Rabinowitch, H. D.; Kamenetsky, R. Effect of Long Photoperiod on the Reproductive and Bulbing Processes in Garlic (*Allium sativum* L.). *Genotypes. Environ. Experi. Bot.* **2011**, *71*, 166–173. DOI: 10.1016/j.envexpbot.2010.11.008.
[22] Brat, V. Genetic Systems in *Allium* III. Meiosis and Breeding Systems. *Heredity*. **1965**, *20*, 325–339. DOI: 10.1038/hdy.1965.47.
[23] Du, Q.; Lu, W.; Quan, M.; Xiao, L.; Song, F.; Li, P.; Zhou, D.; Xie, J.; Wang, L.; Zhang, D. Genome-Wide Association Studies to Improve Wood Properties: Challenges and Prospects. *Front. Plant Sci.* **2018**, *9*, 1912. DOI: 10.3389/fpls.2018.01912.
[24] Villanueva-Mosqueda, E.; Havey, M.-J. Genetic Analyses of Seed Yield in Onion. *J. Am. Soc. Hortic. Sci.* **2001**, *126*(5), 575–578. DOI: 10.21273/JASHS.126.5.575.
[25] Jaume Pellicer, J.; Kelly, L.-J.; Leitch, I.-J.; Zomlefer, W.-J.; Fay, M.-F. A Universe of Dwarfs and Giants: Genome Size and Chromosome Evolution in the Monocot Family Melanthiaceae. *New Phytol.* **2014**, *20*, 1484–1497. DOI: 10.1111/nph.12617.
[26] Shukla, S.; Iquebal, M.-A.; Jaiswal, S.; Angadi, U.-B.; Fatma, S.; Kumar, N.; Jasrotia, R.-S.; Fatima, Y.; Rai, A.; Kumar, D. The Onion Genomic Resource: A Genomics and Bioinformatics Driven Resource for Onion Breeding. *Plant Genet.* **2016**, *8*, 9–15. DOI: 10.1016/j.plgene.2016.09.003.
[27] Arumuganathan, K.; Earle, E.-D. Nuclear DNA Content of Some Important Plant Species. *Plant Mol. Biol. Rep.* **1991**, *9*, 208–218. DOI: 10.1007/BF02672069.
[28] Sato, S.; Tabata, S.; Hirakawa, H.; Asamizu, E.; Shirasawa, K.; Isobe, S.; Kaneko, T.; Nakamura, Y.; Shibata, D.; Aoki, K.; et al. The Tomato Genome Sequence Provides Insights into Fleshy Fruit Evolution. *Nature*. **2012**, *485*, 635–641.

[29] Xu, X.; Pan, S.; Cheng, S.; Zhang, B.; Mu, D.; Ni, P.; Zhang, G.; Yang, S.; Li, R.; Wang, J.; et al. Genome Sequence and Analysis of the Tuber Crop Potato. *Nature*. **2011**, *475*, 189–195.
[30] Qin, C.; Yu, C.; Shen, Y.; Fang, X.; Chen, L.; Min, J.; Cheng, J.; Zhao, S.; Xu, M.; Luo, Y.; et al. Whole-genome Sequencing of Cultivated and Wild Peppers Provides Insights into Capsicum Domestication and Specialization. *PNAS*. **2014**, *111*(14), 5135–5140.
[31] Guo, S.; Zhang, J.; Sun, H.; Salse, J.; Lucas, W.-J.; Zhang, H.; Zheng, Y.; Mao, L.; Ren, Y.; Wang, Z.; et al. The Draft Genome of Watermelon (*Citrullus lanatus*) and Resequencing of 20 Diverse Accessions. *Nature Genet*. **2013**, *45*, 51–58. DOI: 10.1038/ng.2470.
[32] Appels, R.; Eversole, K.; Feuillet, C.; Keller, B.; Rogers, J.; Stein, N.; Pozniak, C.-J.; Stein, N.; Choulet, F.; Distelfeld, A.; et al. Shifting the Limits in Wheat Research and Breeding Using a Fully Annotated Reference Genome. *Science*. **2018**, *361*(6403). DOI: 10.1126/science.aar7191.
[33] Yu, J.; Hu, S.; Wang, J.; Wong, G.-K.-S.; Li, S.; Liu, B.; Deng, Y.; Dai, L.; Zhou, Y.; Zhang, X.; et al. A Draft Sequence of the Rice Genome (*Oryza sativa* L. ssp. *indica*). *Science*. **2002**, *296* (5565), 79–92.
[34] Canal, D.; Fernandes, M.; Enrique, P.-H.; Santos, -D.-D.; Cruz, T.-I.-D.; Ferreira, M.-F.-D.-S.; Ferreira, A. De Novo Assembly of Onion (*Allium cepa* L.). Presented at XXII Encontro Latino Americano de Iniciação Científica, 2018, XVIII Encontro Latino Americano de Pós-Graduação e, VIII Encontro de Iniciação à Docência -Universidade do Vale do Paraíba, Brazil, Oct 25–26, **2018**.
[35] McCallum, J.; Leite, D.; Pither-Joyce, M.; Havey, M.-J. Expressed Sequence Markers for Genetic Analysis of Bulb Onion (*Allium cepa*). *Theor. Appl. Genet*. **2001**, *103*, 979–991. DOI: 10.1007/s001220100630.
[36] Ohara, T.; Song, Y.-S.; Tsukazak, H.; Wako, T.; Nunome, T.; Kojima, A. Genetic Mapping of AFLP Markers in Japanese Bunching Onion *(Allium fistulosum)*. *Euphytica*. **2005**, *144*, 255–263. DOI: 10.1007/s10681-005-6768-5.
[37] Baldwin, S.; Pither-Joyce, M.; Wright, K.; Chen, L.; McCallum, J. Development of Robust Genomic Simple Sequence Repeat Markers for Estimation of Genetic Diversity within and among Bulb Onion (*Allium cepa* L.) Population. *Mol. Breed*. **2012**, *30*, 1401–1411. DOI: 10.1007/s11032-012-9727-6.
[38] Finkers, R.; Van Workum, W.; Van Kaauwen, M.-P.-W.; Huits, H.; Jungerius, A.; Vosman, B. J.; Scholten, O. E. SEQUON – Sequencing the Onion Genome Source. Proceedings of the Plant & Animal Genome XXIII – PAG, San Diego, CA **2015**.
[39] Kim, B.; Kim, K.; Yang, T. J.; Kim, S. Completion of the Mitochondrial Genome Sequence of Onion (*Allium cepa* L.) Containing the CMS-S Male Sterile Cytoplasm and Identification of an Independent Event of the CCMF $_{N}$ Gene Split. *Curr. Genet*. **2016**, *62*(4), 873–885. DOI: 10.1007/s00294-016-0595-1.
[40] Sun, X.; Zhou, S.; Meng, F.; Liu, S. De Novo Assembly and Characterization of the Garlic (*Allium sativum*) Bud Transcriptome by Illumina Sequencing. *Plant Cell Rep*. **2012**, *31*(10), 1823–1828. DOI: 10.1007/s00299-012-1295-z.
[41] Han, J.; Thamilarasan, S. K.; Natarajan, S.; Park, J.-I.; Chung, M.-Y.; Nou, I.-S. De Novo Assembly and Transcriptome Analysis of Bulb Onion (*Allium cepa* L.) During Cold Acclimation Using Contrasting Genotypes. *PLoS ONE*. **2016**, *11*(9), e0161987. DOI: 10.1371/journal.pone.0161987.
[42] Araki, N.; Masuzaki, S.-I.; Tsukazaki, H.; Yaguchi, S.; Wako, T.; Tashiro, Y.; Yamauchi, N.; Shigyo, M. Development of Microsatellite Markers in Cultivated and Wild Species of Sections Cepa and Phyllodolon in *Allium*. *Euphytica*. **2010**, *173*, 321–328. DOI: 10.1007/s10681-009-0087-1.
[43] Fischer, D.; Bachmann, K. Onion Microsatellites for Germplasm Analysis and Their Use in Assessing Intra- and Interspecific Relatedness within the Subgenus Rhizirideum. *Theor. Appl. Genet*. **2000**, *101*, 153–164. DOI: 10.1007/s001220051464.
[44] Cunha, C.-P.; Hoogerheide, E.-S.-S.; Zucchi, M.-I.; Monteiro, M.; Pinheiro, J.-B. New Microsatellite Markers for Garlic, *Allium sativum* (Alliaceae). *Am. J. Bot*. **2012**, e17– e19. DOI: 10.3732/ajb.1100278.

[45] Ma, K.-H.; Kwag, J.-G.; Zhao, W.; Dixit, A.; Lee, G.-A.; Kim, -H.-H.; Chung, I.-M.; Kim, N.-S.; Lee, J.-S.; Ji, -J.-J.; et al. Isolation and Characteristics of Eight Novel Polymorphic Microsatellite Loci from the Genome of Garlic (*Allium sativum* L.). *Sci. Hortic.* **2009**, *122*, 355–361. DOI: 10.1016/j.scienta.2009.06.010.

[46] Lee, G.-A.; Kwon, S. J.; Park, Y.-J.; Lee, M.-C.; Kim, -H.-H.; Lee, J.-S.; Lee, S.-Y.; Gwag, J.-G.; Kim, C.-K.; Ma, K.-H. Cross-Amplification of SSR Markers Developed from *Allium sativum* to Other *Allium* Species. *Sci. Hortic.* **2011**, *128*(4), 401–407. DOI: 10.1016/j.scienta.2011.02.014.

[47] Ipek, M.; Sahin, N.; Ipek, A.; Cansev, A.; Simon, P.-W. Development and Validation of New SSR Markers from Expressed Regions in the Garlic Genome. *Sci. Agr.* **2015**, *72*(1), 41–46. DOI: 10.1590/0103-9016-2014-0138.

[48] Chen, S.; Chen, W.; Shen, X.; Yang, Y.; Qi, F.; Liu, Y.; Meng, H. Analysis of Genetic Diversity of Garlic (*Allium sativa* L.) by Simple Sequence Repeats and Inter Simple Sequence Repeat Analysis and Agromorphological Traits. *Biochem. Syst. Ecol.* **2004**, *55*, 260–267. DOI: 10.1016/j.bse.2014.03.021.

[49] Liu, T.; Zeng, L.; Zhu, S.; Chen, X.; Tang, Q.; Mei, S.; Tang, S. Large-Scale Development of Expressed Sequence Tag-derived Simple Sequence Repeat Markers by Deep Transcriptome Sequencing in Garlic (*Allium sativum* L.). *Mol. Breeding.* **2015**, *35*, 204. DOI: 10.1007/s11032-015-0399-x.

[50] Yang, L.; Wen, C.; Zhao, H.; Liu, Q.; Yang, J.; Liu, L.; Wang, Y. Development of Polymorphic Genic SSR Markers by Transcriptome Sequencing in the Welsh Onion (*Allium fistulosum* L.). *Appl. Sci.* **2015**, *5*, 1050–1063. DOI: 10.3390/app5041050.

[51] Ovesná, J.; Leišová-Svobodová, L.; Kučera, L. Microsatellite Analysis Indicates the Specific Genetic Basis of Czech Bolting Garlic. *Czech. J. Genet. Plant Breed.* **2014**, *50*, 226–234. DOI: 10.17221/CJGPB.

[52] McCallum, J.; Thomson, S.; Pither-Joyce, M.; Kenel, F.; Clarke, A.; Havey, M.-J. Genetic Diversity Analysis and Single-nucleotide Polymorphism Marker Development in Cultivated Bulb Onion Based on Expressed Sequence Tag–Simple Sequence Repeat Markers. *J. Am. Soc. Hortic. Sci.* **2008**, *133*(6), 810–818. DOI: 10.21273/JASHS.133.6.810.

[53] Park, J.; Cho, D.-Y.; Moon, J.-S.; Yoon, M.-K.; Kim, S. Development of Functional Markers for Detection of Inactive DFR-A Alleles Responsible for Failure of Anthocyanin Production in Onions (*Allium cepa* L.). *Korean J. Hortic. Sci.* **2013**, *31*(1), 72–79.

[54] Shemesh-Mayer, E.; Ben-Michael, T.; Rotem, N.; Rabinowitch, H.-D.; Doron-Faigenboim, A.; Kosmala, A.; Perlikowski, D.; Sherman, A.; Amenetsky, R. Garlic (*Allium sativum* L.) Fertility: Transcriptome and Proteome Analyses Provide Insight into Flower and Pollen Development. *Front. Plant Sci.* **2015**, *6*, 271. DOI: 10.3389/fpls.2015.00271.

[55] Kim, E.-Y.; Kim, C.-W.; Kim, S. Identification of Two Novel Mutant ANS Alleles Responsible for Inactivation of Anthocyanidin Synthase and Failure of Anthocyanin Production in Onion (*Allium cepa* L.). *Euphytica*. **2016**, *212*(3), 427–437. DOI: 10.1007/s10681-016-1774-3.

[56] Masamura, N.; McCallum, J.; Kenel, F.; Pither-Joyce, M.; Khrustaleva, L.; Suzuki, G.; Mukai, Y.; Yamauchi, N.; Shigyo, M. Genome Organization of Gene Encoding Lachrymatory Factor Synthase in *Allium cepa*. *Acta Hortic.* **2012**, *969*, 73–80. DOI: 10.17660/Acta_Hortic.2012.969.6.

[57] Kim, S.; Kim, C.-W.; Choi, M.-S.; Kim, S. Development of a Simple PCR Marker Tagging the *Allium roylei* Fragment Harboring Resistance to Downy Mildew (*Peronospora destructor*) in Onion (*Allium cepa* L.). *Euphytica*. **2016**, *208*(3), 561–569. DOI: 10.1007/s10681-015-1601-2.

[58] Baek, G.; Kim, C.-W.; Kim, S. Development of a Molecular Marker Tightly Linked to the C Locus Conferring a White Bulb Color in Onion (*Allium cepa* L.) Using Bulked Segregant Analysis and RNA-Seq. *Mol. Breed.* **2017**, *37*, 94. DOI: 10.1007/s11032-017-0697-6.

[59] Kim, S.; Baek, D.; Cho, D.-Y.; Lee, E.-T.; Yoon, M.-K. Identification of Two Novel Inactive DFR-A Alleles Responsible for Failure to Produce Anthocyanin and Development of a Simple PCR-Based Molecular Marker for Bulb Color Selection in Onion (*Allium cepa* L.). *Theor. Appl. Genet.* **2009**, *118*(7), 1391–1399. DOI: 10.1007/s00122-009-0989-2.

[60] Tsujimura, M.; Kaneko, T.; Sakamoto, T.; Kimura, S.; Shigyo, M.; Yamagishi, H. Toru Terachi Multichromosomal Structure of the Onion Mitochondrial Genome and a Transcript Analysis. *Mitochondrion*. **2019**, *46*, 179–186. DOI: 10.1016/j.mito.2018.05.001.
[61] Yusupov, Z.; Deng, T.; Liu, L.; Lin, N.; Tojibaev, K.; Sun, H. The Complete Chloroplast Genome of *Allium fistulosum*. *Mitochondr. DNA B*. **2019**, *4*(1), 489–490. DOI: 10.1080/23802359.2018.1545532.
[62] Filyushin, M. A.; Beletsky, A.-V.; Mazur., A.-M.; Kochieva, E.-Z. Characterization of the Complete Plastid Genome of Lop-sided Onion *Allium obliquum* L. (Amaryllidaceae). *Mitochondr. DNA B*. **2018**, *3*(1), 393–394. DOI: 10.1080/23802359.2018.1456369.
[63] Lee, J.; Chon, J.-Y.; Lim, J.-S.; Kim, E.-K.; Nah, G. Characterization of Complete Chloroplast Genome of *Allium victorialis* and its Application for Barcode Markers. *Plant Breed Biotech*. **2017**, *5*(3), 221–227. DOI: 10.9787/PBB.2017.5.3.221.
[64] Xie, D.-F.; Jin, F.-Y.; Xin, Y.; Li, H.; Xie, F.-M.; He, X.-J. The Complete Chloroplast Genome of a Wild Onion Species *Allium monanthum* (Alliaceae). *Mitochondr. DNA B*. **2019**, *4*(1), 854–855. DOI: 10.1080/23802359.2019.1572462.
[65] Yang, X.; Xie, D.-F.; Zhou, S.-D.; He, X.-J. Characterization of the Complete Chloroplast Genome of *Allium kingdonii*. *Mitochondr. DNA B*. **2019**, *4*(1), 868–869. DOI: 10.1080/23802359.2019.1573118.
[66] Jin, F.-Y.; Xie, D.-F.; Zhou, S.-D.; He, X.-J. Characterization of the Complete Chloroplast Genome of *Allium prattii*. *Mitochondr. DNA B*. **2018**, *3*(1), 153–154. DOI: 10.1080/23802359.2018.1436994.
[67] Sun, K.; He, J.; Xiang, Q.; Wang, X.; Guan, W.-B.; Zhao, L. The Complete Chloroplast Genome of *Allium ovalifolium* var. *leuconeurum*, an Endemic Plant in Southwest China. *Mitochondr. DNA B*. **2019**, *4*(1), 16811682. DOI: 10.1080/23802359.2019.1602009.
[68] Abdelrahman, M.; El-Sayed, M.; Sato, S.; Hirakawa, H.; Ito, S.-I.; Tanaka, K.; Mine, Y.; Sugiyama, N.; Suzuki, Y.; Yamauchi, N.; et al. RNA Sequencing-based Transcriptome and Biochemical Analyses of Steroidal Saponin Pathway in a Complete Set of Allium fistulosum—A. cepa Monosomic Addition Lines. *PLoS ONE*. 2017, *12*(8), e0181784.
[69] Mostafa, A.-R.; Sho, H.; Yuji, S.; Hirai, Y.-M.; Sato, S.; Hirakawa, H.; Mine, Y.; Tanaka, K.; Shigyo, M. Widely Targeted Metabolome and Transcriptome Landscapes of *Allium fistulosum–A. cepa* Chromosome Addition Lines Revealed a Flavonoid Hot Spot on Chromosome 5A. *Sci. Rep*. **2019**, *9*, 3541. DOI: 10.1038/s41598-019-39856-1.
[70] Rina, K.; Adi, F.; Einat, S.-M.; Michael, T.-B.; Gershberg, C.; Kimhi, S.; Esquira, I.; Shalom, S.-R.; Eshe, D.; Rabinowitch, H.-D.; et al. Integrated Transcriptome Catalogue and Organ-Specific Profiling of Gene Expression in Fertile Garlic (*Allium sativum* L.). *BMC Genom*. **2015**, *16*, 12. DOI: 10.1186/s12864-015-1212-2.
[71] Eady, C.; Weld, R.; Lister, C. Agrobacterium Tumefaciens Mediated Transformation and Regeneration of Onion (*Allium cepa* L.). *Plant Cell Rep*. **2000**, *19*, 376–381. DOI: 10.1007/s002990050743.
[72] Wu, Z.; Sheng, W.; Wu, Z.; Li, S.; Fen, Y.; Sheng, Z.; Xue, W.; Bao, X. Genetic Transformation of OSISAP1 Gene to Onion (*Allium cepa* L.) Mediated by a Microprojectile Bombardment. *J. Plant Physiol. Mol. Biol*. **2007**, *33*(3), 188–196.
[73] Kondo, T.; Hasegawa, H.; Suzuki, M. Transformation and Regeneration of Garlic (*Allium sativum* L.) by *Agrobacterium*-mediated Gene Transfer. *Plant Cell Rep*. **2000**, *19*, 989–993. DOI: 10.1007/s002990000222.
[74] Sawahel, W.-A. Stable Genetic Transformation of Garlic Plants Using Particle Bombardment. *Cell. Mol. Biol. Lett*. **2002**, *7*(1), 49–59.
[75] Robledo-Paz, A.; Cabrera-Ponce, J.-L.; Villalobos-Arambula, V.-M.; Herrara-Estrella, L.; Jofre-Garfias, A.-E. Genetic Transformation of Garlic by Particle Bombardment. *Hort. Sci*. **2004**, *39*(6), 1208–1211. DOI: 10.21273/HORTSCI.39.6.1208.
[76] Eady, C.; Davis, S.; Catanach, A.; Kenel, F.; Hunger, S. Agrobacterium Tumefaciens -mediated Transformation of Leek (*Allium porrum*) and Garlic (*Allium sativum*). *Plant Cell Rep*. **2005**, *24*, 209–215. DOI: 10.1007/s00299-005-0926-z.

[77] Wang, H. Genetic Engineering Male Sterility in Leek (*Allium porrum* L.). Ph. D. Thesis, Universiteit Gent, Belgium, **1996**.
[78] Zheng, S.-J. Towards Onion and Shallots (*Allium cepa* L.) Resistant to Beet Armyworm (*Spodoptera exigua* Hübner) by Transgenesis and Conventional Breeding. http://library.wur.nl/WebQuery/wurpubs/fulltext/199612 (accessed July 22, 2019).
[79] Zheng, S. J.; Henken, B.; De Maagd, R. A.; Purwito, A.; Krens, F. A.; Kik, C. Two Different *Bacillus thuringiensis* Toxin Genes Confer Resistance to Beet Armyworm (*Spodoptera exigua* Hübner) in Transgenic Bt-shallots (*Allium cepa* L.). *Transgenic Res.* **2005**, *14*, 261–272. DOI: 10.1007/s11248-005-0109-2.
[80] Zheng, S.-J.; Henken, B.; Ahn, Y.-K.; Krens, F.-A.; Kik, C. The Development of a Reproducible *Agrobacterium tumefaciens* Transformation System for Garlic (*Allium sativum* L.) and the Production of Transgenic Garlic Resistant to Beet Armyworm (*Spodoptera exigua* Hübner). *Mol. Breeding.* **2004**, *14*, 293–307. DOI: 10.1023/B:MOLB.0000047775.83715.b5.
[81] Eady, -C.-C.; Davis, S.; Farrant, J.; Reader, J.; Kenel, F. *Agrobacterium tumefaciens*-mediated Transformation and Regeneration of Herbicide Resistant Onion (*Allium cepa*) Plants. *Ann. Appl. Biol.* **2003**, *142*, 213–217. DOI: 10.1111/j.1744-7348.2003.tb00243.x.
[82] Lagunes-Fortiz, E.; Robledo-Paz, A.; Gutiérrez-Espinosa, M.-A.; Mascorro-Gallardo, J.-O.; Espitia-Rangel, E. Genetic Transformation of Garlic (*Allium sativum* L.) With Tobacco Chitinase and Glucanase Genes for Tolerance to the Fungus *Sclerotium Cepivorum*. *Afr. J. Biotechnol.* **2013**, *12*(22), 3482–3492.
[83] Eady, -C.-C.; Kamoi, T.; Kato, M.; Porter, N.-G.; Davis, S.; Shaw, M.; Kamoi, A.; Imai, S. Silencing Onion Lachrymatory Factor Synthase Causes a Significant Change in the Sulfur Secondary Metabolite Profile. *Plant Physiol.* **2008**, *147*(4), 2096–2106. DOI: 10.1104/pp.108.123273.
[84] Xu, K.; Huang, X.; Wu, M.; Wang, Y.; Chang, Y.; Liu, K.; Zhang, J.; Zhang, Y.; Zhang, F.; Yi, L.; et al. A Rapid, Highly Efficient and Economical Method of *Agrobacterium*-mediated in Planta Transient Transformation in Living Onion Epidermis. *PLoS One*. **2014**, *9*(1), e83556. DOI: 10.1371/journal.pone.0083556.
[85] Eady, -C.-C. Towards the Transformation of Onions (*Allium cepa*). *New Zeal. J. Crop. Hort.* **1995**, *23*(3), 239–250. DOI: 10.1080/01140671.1995.9513895.
[86] Gokce, A.-F.; McCallum, J.; Sato, Y.; Havey, M.-J. Molecular Tagging of the *Ms* Locus in Onion. *J. Am. Soc. Hortic. Sci.* **2002**, *127*(4), 576–582. DOI: 10.21273/JASHS.127.4.576.
[87] Gai, S.-P.; Meng, X.-D. Study on Conversion of RAPD Markers Linked to Cytoplasmic Male Sterile Loci to SCAR Markers in Welsh Onion (*Allium fistulosum* L.). *J. Laiyang Agric. Coll.* **2004**, *21*, 189–192. "(article in Chinese with an abstract in English)".
[88] Gai, S.-P.; Meng, X.-D. Development and Identification of RAPD Markers Linked to Cytoplasmic Male Sterility in Welsh Onion (*Allium fistulosum* L.). *J. Agric. Biotechnol.* **2002**, *10*, 94–97. "(article in Chinese with an abstract in English)".
[89] Yamashita, K.; Takatori, Y.; Tashiro, Y. Chromosomal Location Of A Pollen Fertility-restoring Gene, *Rf*, for CMS in Japanese Bunching Onion (*Allium fistulosum* L.) Possessing the Cytoplasm of *A. galanthum* Kar. et Kir. Revealed by Genomic *in Situ* Hybridization. *Theor. Appl. Genet.* **2005**, *111*(1), 15–22. DOI: 10.1007/s00122-005-1941-8.
[90] Scholten, O.-E.; van Kaauwen, M.-P.-W.; Shahin, A.; Hendrick, P.-M.; Keizer, L.-C.-P.; Burger, K.; Van Heusden, A.-W.; Van Der Linden, C.-G.; Vosman, B. SNP-markers in *Allium* Species to Facilitate Introgression Breeding in Onion. *BMC Plant Biol.* **2016**, *16*, 187. DOI: 10.1186/s12870-016-0879-0.
[91] Martin, W.-J.; McCallum, J.; Shigyo, M.; Jakse, J.; Kuhl, J.-C.; Yamane, N.; Pither-Joyce, M.; Gokce, A.-F.; Sink, K.-C.; Town, C.-D.; et al. Genetic Mapping of Expressed Sequences in Onion and in Silico Comparisons with Rice Show Scant Colinearity. *Mol. Genet. Genomics.* **2005**, *274*(3), 197–204.
[92] McCallum, J.; Clarke, A.; Pither-Joyce, M.; Shaw, M.; Butler, R.; Brash, D.; Scheffer, J.; Sims, I.; Heusden, S.-V.; Shigyo, M.; et al. Genetic Mapping of a Major Gene Affecting Onion Bulb Fructan Content. *Theor. Appl. Genet.* **2006**, *112*(5), 958–967.

[93] McCallum, J.; Pither-Joyce, M.; Shaw, M.; Kenel, F.; Davis, S.; Butler, R.; ScheVer, J.; Jakse, J.; Havey, M.-J. Genetic Mapping of Sulfur Assimilation Genes Reveals a QTL for Onion Bulb Pungency. *Theor. Appl. Genet.* **2007**, *114*, 815–822. DOI: 10.1007/s00122-006-0479-8.
[94] Masuzaki, S.; Shigyo, M.; Yamauchi, N. Complete Assignment of Structural Genes Involved in Flavonoid Biosynthesis Influencing Bulb Color to Individual Chromosomes of the Shallot (*Allium cepa* L.). *Genes Genet. Sys.* **2006**, *81*(4), 255–263. DOI: 10.1266/ggs.81.255.
[95] Masuzaki, S.; Shigyo, M.; Yamauchi, N. Direct Comparison between Genomic Constitution and Flavonoid Contents in *Allium* Multiple Alien Addition Lines Reveals Chromosomal Locations of Genes Related to Biosynthesis from Dihydrokaempferol to Quercetin Glucosides in Scaly Leaf of Shallot (*Allium cepa* L.). *Theor. Appl. Genet.* **2006**, *112*(4), 607–617. DOI: 10.1007/s00122-005-0157-2.
[96] Tsukazaki, H.; Yamashita, K.; Yaguchi, S.; Yamashita, K.; Hagihara, T.; Shigyo, M.; Kojima, A.; Wako, T. Direct Determination of the Chromosomal Location of Bunching Onion and Bulb Onion Markers Using Bunching Onion-shallot MonosomicAdditions and Allotriploid-Bunching Onion Single Alien Deletions. *Theor. Appl. Genet.* **2011**, *22*(3), 501–510. DOI: 10.1007/s00122-010-1464-9.
[97] McCallum, J.; Baldwin, S.; Thomson, S.; Pither-Joyce, M.; Kenel, F.; Lee, R.; Khosa, J.-S.; Macknight, R. Molecular Genetics Analysis of Onion (*Allium cepa* L.) Adaptive Physiology of Bulb. *Acta Hortic.* **2016**, *1110*, 71–76. DOI: 10.17660/ActaHortic.2016.1110.11.
[98] King, J.; Bradeen, J.-M.; Bark, O.; McCallum, J.-A.; Havey, M.-J. A Low-density Genetic Map of Onion Reveals A Role for Tandem Duplication in the Evolution of an Extremely Large Diploid Genome. *Theor. Appl. Genet.* **1998**, *96*(1), 52–62. DOI: 10.1007/s001220050708.
[99] Kuhl, J.-C.; Cheung, F.; Yuan, Q.; Martin, W.; Zewdie, Y.; McCallum, J.; Catanach, A.; Rutherford, O.; Sink, K.-C.; Jenderek, M.; et al. A Unique Set of 11,008 Onion Expressed Sequence Tags Reveals Expressed Sequence and Genomic Differences between the Monocot Orders Asparagales and Poales. *Plant Cell.* **2004**, *16*(1), 114–125.
[100] Ipek, M.; Ipek, A.; Almquist, S.-G.; Simon, P.-W. Demonstration of Linkage and Development of the First Low-density Genetic Map of Garlic, Based on AFLP Markers. *Theor. Appl. Genet.* **2005**, *110*(2), 228–236. DOI: 10.1007/s00122-004-1815-5.
[101] Zewdie, Y.; Havey, M.-J.; Prince, J.-P.; Jenderek, -M.-M. The First Genetic Linkages among Expressed Regions of the Garlic Genome. *J. Am. Soc. Hortic. Sci.* **2005**, *130*(4), 569–574. DOI: 10.21273/JASHS.130.4.569.
[102] Ohara, T.; Song, Y.-S.; Tsukazaki, H.; Wako, T.; Nunome, T.; Kojima, A. Genetic Mapping of AFLP Markers in Japanese Bunching Onion (*Allium fistulosum*). *Euphytica*. **2005**, *144*(3), 3255–3263. DOI: 10.1007/s10681-005-6768-5.
[103] Tsukazaki, H.; Yamashita, K.; Yaguchi, S.; Masuzaki, S.; Fukuoka, H.; Yonemaru, J.; Kanamori, H.; Kono, I.; Hang, -T.-T.; Shigyo, M.; et al. Construction of SSR-Based Chromosome Map in Bunching Onion (*Allium fistulosum*). *Theor. Appl. Genet.* **2008**, *117*(8), 1213–1223.
[104] Konvicka, O. Generative Reproduktion Von Knoblauch (*Allium sativum*). *Allium Newslett.* **1984**, *1*, 28–37.
[105] Pooler, M.-R.; Simon, P.-W. True Seed Production in Garlic. *Sex. Plant Reprod.* **1994**, *7*(5), 282–286. DOI: 10.1007/BF00227710.
[106] Inaba, A.; Ujiie, T.; Etoh, T. Seed Productivity and Germinability of Garlic. *Breed. Sci.* **1995**, *45*(suppl. 2), 310.
[107] Jenderek, -M.-M. Generative Reproduction of Garlic (*Allium sativum* L). *Sesja Naukowa*. **1998**, *57*, 141–145. (In Polish).
[108] Kamenetsky, R.; Shafir, I.-L.; Baizerman, M.; Khassanov, F.; Kik, C.; Rabinowitch, H.-D. Garlic (*Allium sativum* L.) and its Wild Relatives from Central Asia: Evaluation for Fertility Potential. *Acta Hortic.* **2004**, *637*, 83–91. DOI: 10.17660/ActaHortic.2004.637.9.
[109] Chuda, A.; Adamus, A. Hybridization and Molecular Characterization of F_1 *Allium cepa* × *Allium roylei* Plants. *Acta. Biol. Cracov. Bot.* **2012**, *54*(2), 25–31.

[110] Kofoet, A.; Kik, C.; Wietsma, W.-A.; De Vries, J.-N. Inheritance of Resistance to Downy Mildew (*Peronospora destructor* [Berk.] Casp.) From *Allium roylei* Stearn. In the Backcross *Allium cepa* L. × (*A. roylei* × *A. cepa*). *Plant Breed.* **1990**, *105*, 144–149. DOI: 10.1111/j.1439-0523.1990.tb00467.x.

[111] Kofoet, A.; Zinkernagel, V. Resistance to Downy Mildew (*Peronospora destructor* (Berk.) Casp.) In *Allium* Species. *J. Plant Dis. Protect.* **1990**, *97*(1), 13–23.

[112] Yanagino, T.; Sugawara, T.; Watanabe, M.; Takahata, Y. Production and Characterization of an Inter-specific Hybrid between Leek and Garlic. *Theor. Appl. Genet.* **2009**, *107*, 1–5. DOI: 10.1007/s00122-003-1232-1.

[113] Scholten, O.-E.; Van Heusden, A.-W.; Khrustaleva, L.-I.; Burger-Meijer, K.; Mank, R.-A.; Antonise, R.-G.-C.; Harrewijn, J.-L.; Van Haecke, W.; Oost, E.-H.; Peters, R.-J.; et al. The Long and Winding Road Leading to the Successful Introgression of Downy Mildew Resistance into Onion. *Euphytica*. **2007**, *156*(3), 345–353.

[114] Vu, H.-Q.; Yoshimatsu, Y.; Khrustaleva, L.-I.; Yamauchi, N.; Shigyo, M. Alien Genes Introgression and Development of Alien Monosomic Addition Lines from a Threatened Species, *Allium roylei* Stearn, to *Allium cepa* L. *Theor. Appl. Genet.* **2012**, *124*(7), 1241–1257. DOI: 10.1007/s00122-011-1783-5.

[115] Yaguchi, S.; Yamauchi, N.; Shigyo, M. Single Alien Chromosome Additions from Shallot (*Allium cepa* L. Aggregatum Group) Increase Endogenous Polyphenol Contents in Japanese Bunching Onion. *J. Japanese Soc. Hortic. Sci.* **2009**, *78*(4), 431–435. DOI: 10.2503/jjshs1.78.431.

[116] Vu, H. Q.; Iwata, M.; Yamauchi, N.; Shigyo, M. Production of Novel Alloplasmic Male Sterile Lines in *Allium cepa* Harbouring the Cytoplasm from *Allium roylei*. *Plant Breed.* **2011**, *130*(5), 601. DOI: 10.1111/j.1439-0523.2011.01855.x.

[117] Yamashita, K.; Arita, H.; Tashiro, Y. Cytoplasm of a Wild Species, *Allium galanthum* Kar et Kir., is Useful for Developing the Male Sterile Line of *A. fistulosum* L. *J. Japanese Soc. Hortic. Sci.* **1999**, *68*(4), 788–797. DOI: 10.2503/jjshs.68.788.

[118] Arold, G. Summer Onion F_1 Hybrid Cultivars Tested in Lower Bavaria. *Gemuse-Munchen.* **1998**, *34*(8), 456–459.

[119] El-Sayed, A.-M.; Atia, -A.-A.-M.; El-Haq, S.-H.-G.; Azab, A.-M.; Mohamed, H.-Y. Studies on Heterosis, Gene Action and Combining Ability of Some Traits in Onion (*Allium cepa* L.). *Egyp. J. Hort.* **1999**, *26*(1), 85–95.

[120] Sato, Y.; Nagai, M.; Ito, K.; Tanaka, M.; Yoshikawa, H.; Uragami, A.; Muro, T. A New Onion Hybrid Variety. *Toyohira Res. Bullet.* **1999**, *168*, 47–57.

[121] Gowda, V.-R.; Rao, E.-S.; Pathak, C.-S.; Singh, T.-H. Development and Commercialization of F_1Hybrids in Short Day Onion-Indian Perspective. Proceedings of International Conference on Vegetables, Bangalore, India, Nov 11–14, **2002**.

[122] Engelke, T.; Terefe, D.; Tatlioglu, T. A PCR-based Marker System Monitoring CMS-(S), CMS-(T) and (N)-cytoplasm in the Onion (*Allium cepa* L.). *Theor. Appl. Genet.* **2003**, *107*, 162–167. DOI: 10.1007/s00122-003-1230-3.

[123] Kim, S.; Lee, E.-T.; Cho, D.-Y.; Han, T.; Bang, H.; Patil, B.-S.; Ahn, Y.-K.; Yoon, M.-K. Identification of a Novel Chimeric Gene, Orf725, and its Use in Development of a Molecular Marker for Distinguishing among Three Cytoplasm Types in Onion (*Allium cepa* L.). *Theor. Appl. Genet.* **2009**, *118*, 433–441. DOI: 10.1007/s00122-008-0909-x.

[124] Sato, Y. PCR Amplification of CMS-specific Mitochondrial Nucleotide Sequences to Identify Cytoplasmic Genotypes of Onion (*Allium cepa* L.) Sequences. *Theor. Appl. Genet.* **1998**, *96*, 367–370. DOI: 10.1007/s001220050750.

[125] Gao, L.-M.; Chen, Y.-Q.; Huo, Y.-M.; Dong, F.; Yang, -Y.-Y.; Kong, S.-P.; Chen, W.; Wu, X. Development of SCAR Markers to Distinguish Male-sterile and Normal Cytoplasm in Bunching Onion (*Allium fistulosum* L.). *J. Hortic. Sci. Biotech.* **2015**, *90*(1), 57–62. DOI: 10.1080/14620316.2015.11513153.

[126] Wang, C.; Li, H.-Y.; Zhang, L.-Y.; Pei, Y.-X.; Wang, Y.-Q. Identification of an AFLP Marker and Conversion to a SCAR Marker to Identify Cytoplasmic Male-sterile or Normal

Cytoplasm in Welsh Onion (*Allium fistulosum* L.). *J. Hortic. Sci. Biotech.* **2013**, *88*(4), 409–414. DOI: 10.1080/14620316.2013.11512984.

[127] Havey, M.-J. Single Nucleotide Polymorphisms in Linkage Disequilibrium with the Male-Fertility Restoration (*Ms*) Locus in Open-Pollinated and Inbred Populations of Onion. *J. Am. Soc. Hortic. Sci.* **2013**, *138*(4), 306–309. DOI: 10.21273/JASHS.138.4.306.

[128] Yang, -Y.-Y.; Meng, Y.; Miao, H.-J.; Liu, B.-J.; Kong, S.-P.; Gao, L.-M.; Liu, C.; Wang, Z.-B.; Tahara, Y.; Kitano, H.; et al. Identification of Two SCAR Markers Co-Segregated with the Dominant *Ms* and Recessive *Ms* Alleles in Onion (*Allium cepa* L.). *Euphytica*. **2013**, *190*(2), 267–277.

[129] Kim, S.; Kim, S. Application of the Molecular Marker in Linkage Disequilibrium with *Ms*, a Restorer-of-Fertility Locus for Improvement of Onion Breeding Efficiency. *Korean J. Hortic. Sci.* **2015**, *33*, 550–558.

[130] Bang, H.; Kim, S.; Park, S.-O.; Yoo, K.-S.; Patil, B.-S. Development of a Codominant CAPS Marker Linked to the *Ms* Locus Controlling Fertility Restoration in Onion (*Allium cepa* L.). *Sci. Hortic.* **2013**, *153*(4), 42–49. DOI: 10.1016/j.scienta.2013.01.020.

[131] Park, J.; Bang, H.; Cho, D.-Y.; Yoon, M.-K.; Patil, B.-S.; Kim, S. Construction of High-Resolution Linkage Map of the *Ms* Locus, a Restorer-of-Fertility Gene in Onion (*Allium cepa* L.). *Euphytica*. **2013**, *192*(2), 267–278. DOI: 10.1007/s10681-012-0851-5.

[132] Huo, Y.-M.; Liu, B.-J.; Yang, -Y.-Y.; Miao, J.; Gao, L.-M.; Kong, S.-P.; Wang, Z.-B.; Kitano, H.; Wu, X. ACSKP1, a Multiplex PCR Based Co-dominant Marker in Complete Linkage Disequilibrium with the Male Fertility Restoration (*Ms*) Locus and its Application in Open Pollinated Populations of Onion. *Euphytica*. **2015**, *204*(3), 711–722. DOI: 10.1007/s10681-015-1374-7.

[133] Khosa, J.-S.; Lee, R.; Bräuning, S.; Lord, J.; Pither-Joyce, M.; McCallum, J.; Macknight, R.-C. Doubled Haploid 'CUDH2107' as a Reference for Bulb Onion (*Allium cepa* L.) Research: Development of a Transcriptome Catalogue and Identification of Transcripts Associated with Male Fertility. *PLoS One*. **2016**, *11*(11), e0166568. DOI: 10.1371/journal.pone.0166568.

[134] Jones, H.-A.; Clarke, A.-E. Inheritance of Male Sterility in the Onion and the Production of Hybrid Seed. *Proc. Am. Soc. Hortic. Sci.* **1943**, *43*, 189–194.

[135] Santos, C.-A. F.; Leite, D.-L.; Oliveira, V.-R.; Rodrigues, M.-A. Marker-assisted Selection of Maintainer Lines within an Onion Tropical Population. *Sci. Agr.* **2010**, *67*(2), 223–227. DOI: 10.1590/S0103-90162010000200015.

[136] Sheemar, G.; Dhatt, A.-S. PCR-based Rapid Identification of Indian Onion Populations Possessing S-cytoplasm for Isolation of CMS Lines. *Res. Crop.* **2015**, *16*(1), 133–138. DOI: 10.5958/2348-7542.2015.00019.4.

[137] Malik, G.; Dhatt, A.-S.; Malik, -A.-A. Isolation of Male Sterile and Maintainer Lines from North Indian Onion (*Allium cepa* L.) Populations with the Aid of PCR Based Molecular Marker. *Vegetos*. **2017**, *2*(30). DOI: 10.4172/2229-4473.1000249.

[138] Khar, A.; Saini, N. Limitations of PCR-based Molecular Markers to Identify Male-sterile and Maintainer Plants from Indian Onion (*Allium cepa* L.) Populations. *Plant Breed.* **2016**, *135*(4), 519–524. DOI: 10.1111/pbr.12373.

[139] Ferriera, -R.-R.; Santos, C.-A.-F. Partial Success of Marker-assisted Selection of 'A' and 'B' Onion Lines in Brazilian Germplasm. *Sci. Hort.* **2018**, *242*, 110–115. DOI: 10.1016/j.scienta.2018.08.002.

[140] El-Shafie, M.; Davis, G. Inheritance of Bulb Color in the Onion (*Allium cepa* L.). *Hilgardia*. **1967**, *38*(17), 607–622. DOI: 10.3733/hilg.v38n17p607.

[141] Galmarini, C.-R.; Goldman, I.-L.; Havey, M.-J. Quantitative Trait Loci Controlling Solid Content, Pungency and Antiplatelet Activity of Onion (*Allium cepa* L.). Plant & Animal Genome VIII Conference, Town & Country Hotel, San Diego, CA, **2000**.

[142] McCallum, J.; Baldwin, S.; Shigyo, M.; Deng, Y.; Van Heusden, S.; Pither-Joyce, M.; Kenel, F. AlliumMap-A Comparative Genomics Resource for Cultivated *Allium* Vegetables. *BMC Genom.* **2012**, *13*, 168. DOI: 10.1186/1471-2164-13-168.

[143] Kim, D.-W.; Jung, T.-S.; Nam, S.-H.; Kwon, H.-R.; Kim, A.; Chae, S.-H.; Choi, S.-H.; Kim, D.-W.; Kim, R.-N.; Park, S.-H. GarlicESTdb: An Online Database and Mining Tool for Garlic EST Sequences. *BMC. Plant Biol.* **2009**, *9*, 61. DOI: 10.1186/1471-2229-9-6.
[144] Filyushin, M.-A.; Beletsky, A.-V.; Mazur, A.-M.; Kochieva, E.-Z. The Complete Plastid Genome Sequence of Garlic (*Allium sativum* L.). *Mitochondr. DNA B.* **2016**, *1*, 831–832. DOI: 10.1080/23802359.2016.1247669+.
[145] Schröder, W.; Bernhardt, J.; Marincola, G.; Klein-Hitpass, L.; Herbig, A.; Krupp, G.; Nieselt, K.; Wolz, C. Altering Gene Expression by Aminocoumarins: The Role of DNA Supercoiling in *Staphylococcus aureus*. *BMC Genom.* **2014**, *15*, 291. DOI: 10.1186/1471-2164-15-291.
[146] Ruan, D.; Zhu, Y.-W.; Fouad, A.-M.; Yan, S.-J.; Chen, W.; Zhang, Y.-N.; Xia, W.-G.; Wang, S.; Jiang, S.-Q.; Yang, L.; et al. Dietary Curcumin Enhances Intestinal Antioxidant Capacity in Ducklings via Altering Gene Expression of Antioxidant and Key Detoxification Enzymes. *Poult. Sci.* **2019**. DOI: 10.3382/ps/pez058.
[147] Till, B.-J.; Reynolds, S.-H.; Weil, C.; Springer, N.; Burtner, C.; Young, K.; Enns, L.-C.; Odden, A.-R.; Greene, E.-A.; Comai, L.; et al. Discovery of Induced Point Mutations in Maize Genes by TILLING. *BMC Plant Biol.* **2004**, *12*. DOI: 10.1186/1471-2229-4-12.
[148] Beyaz, R.; Yildiz, M. The Use of Gamma Irradiation in Plant Mutation Breeding. In *Plant Engineering*; Intech, 2017; 33–46. https://www.intechopen.com/books/Pant-Engineering/the-use-of-Gamma-Irradiation-in-Plant-Mutation-Breeding
[149] Ida, L.; Ola, A.; Tiffany, L.; Dunbar, E.-A.; Matthew, A.-E.; Allan, G.-R. Changes in External pH Rapidly Alter Plant Gene Expression and Modulate Auxin and Elicitor Responses. *Plant Cell Environ.* **2010**, *33*, 1513–1528. DOI: 10.1111/j.1365-3040.2010.02161.x.
[150] Chinnusamy, V.; Zhu, J.; Zhu, J.-K. Cold Stress Regulation of Gene Expression in Plants. *Trends Plant Sci.* **2007**, *12*(10), 444–451. DOI: 10.1016/j.tplants.2007.07.002.
[151] Tschermak, E. Über Den Gegenwartigen Stand Der Gemiisenzuchtung. *Z. Zucht.* **1916**, *4*, 65–104.
[152] Meunissier, A. Expkriences Gknktiques Faitesii Verri2re. *Bull. Soc. Acclim. Fr.* **1918**, *65*, 81–90.
[153] Rieman, G.-H. Genetic Factors for Pigmentation in the Onion and Their Relation to Disease. *J. Agric. Res.* **1931**, *42*, 251–278.
[154] Clarke, A.-E.; Jones, H.-A.; Little, T.-M. Inheritance of Bulb Color in the Onion. *Genetics*. **1944**, *29*(6), 569–575.
[155] Jones, H.-A.; Clarke, A.-E. Inheritance of Male Sterility in the Onion and the Production of Hybrid Seed. *Proc. Am. Soc. Hortic. Sci.* **1943**, *43*, 189–194.
[156] Berninger, E. Contribution a L"etude De La Sterilite-Male De L"Oignon (*Allium cepa* L.). *Ann. Amelior. Plantes*. **1965**, *15*, 183–199.
[157] Schweisguth, B. Etude D'un Nouveau Type De Sterilite Male Chez L'Oignon, *Allium cepa* L. *Ann. Amelior. Plantes*. **1973**, *23*, 221–233. (Article in French).
[158] Moue, T.; Uehara, T. Inheritance of Cytoplasmic Male Sterility in *Allium fistulosum* L. (Welsh Onion). *Engei. Gakkai. Zasshi.* **1984**, *53*(4), 432–437. DOI: 10.2503/jjshs.53.432.
[159] Kim, S.; Binzel, M.-L.; Yoo, K.-S.; Park, S.; Pike, L.-M. Pink (P), A New Locus Responsible for A Pink Trait in Onions (*Allium cepa*) Resulting from Natural Mutations of Anthocyanidin Synthase. *Mol. Genet. Genom.* **2004**, *272*(1), 18–27. DOI: 10.1007/s00438-004-1041-5.
[160] Kim, B.; Cho, Y.; Kim, S. Identification of a Novel DFR-A Mutant Allele Determining the Bulb Color Difference between Red and Yellow Onions (*Allium cepa* L.). *Plant Breed Biotech.* **2017**, *5*(1), 45–53. DOI: 10.9787/PBB.2017.5.1.45.
[161] Khar, A.; Jakse, J.; Havey, M.-J. Segregations for Onion Bulb Colors Reveal that Red is Controlled by at Least Three Loci. *J. Am. Soc. Hortic. Sci.* **2008**, *133*(1), 42–47. DOI: 10.21273/JASHS.133.1.42.
[162] Baldwin, S.; Revanna, R.; Pither-Joyce, M.; Shaw, M.; Wright, K.; Thomson, S.; Moya, L.; Lee, R.; Macknight, R.; McCallum, J. Genetic Analyses of Bolting in Bulb Onion (*Allium cepa* L.). *Theor. Appl. Genet.* **2013**, *127*(3), 535–547. DOI: 10.1007/s00122-013-2232-4.

[163] Pavlović, N.; Cvikić, D.; Zdravković, J.; Đorđević, R.; Zdravković, M.; Varga, J.-G.; Moravčević, Đ. Bulb Fresh Weight Mode of Inheritance in Onion (*Allium cepa* L.). *Ratarstvo I Povrtarstvo*. **2015**, *52*(1), 24–28. DOI: 10.5937/ratpov52-7723.
[164] Khokhar, K.-M. Flowering and Seed Development in Onion— A Review. *Open Access Lib. J.* **2014**, *1*, e104.
[165] Lee, R.; Baldwin, S.; Kenel, F.; McCallum, J.; Macknight, R. Flowering Locus T Genes Control Onion Bulb Formation and Flowering. *Nat. Commun.* **2013**, *4*, 2884. DOI: 10.1038/ncomms3884.
[166] Khrustaleva, L.; Mardini, M.; Kudryavtseva, N.; Alizhanova, R.; Romanov, D.; Sokolov, P.; Monakhos, G. The Power of Genomic in Situ Hybridization (GISH) in Interspecific Breeding of Bulb Onion (*Allium cepa* L.) Resistant to Downy Mildew (*Peronospora destructor* [Berk.] Casp.). *Plants*. **2019**, *8*, 36. DOI: 10.3390/plants8020036.
[167] De Vries, J.-N.; Wietsma, W.-A.; De Vries, T. Introgression of Leaf Blight Resistance from *Allium Roylei* Stearn. Into Onion (*A cepa* L.). *Euphytica*. **1992**, *62*, 127. DOI: 10.1007/BF00037938.
[168] Galván, G.-A.; Wietsma, W.; Putrasemedja, S.-A.-H.; Permadi, C.-K. Screening for Resistance to Anthracnose (*Colletotrichum gloeosporioides* Penz.) In *Allium Cepa* and its Wild Relatives. *Euphytica*. **1997**, *95*, 173. DOI: 10.1023/A:1002914225154.
[169] Galván, G.-A.; Koning-Boucoiran, C.-F.-S.; Koopman, W.-J.-M.; Burger-Meijer, K.; González, P.-H.; Waalwijk, C.; Kik, C.; Olga, E.-S. Genetic Variation among *Fusarium* Isolates from Onion, and Resistance to Fusarium Basal Rot in Related *Allium* Species. *Eur. J. Plant Pathol.* **2008**, *121*, 499. DOI: 10.1007/s10658-008-9270-9.
[170] Khrustaleva, L.; Kik, C. Cytogenetical Studies in the Bridge Cross *Allium cepa* × (*A. fistulosum*×*A. roylei*). *Theor. Appl. Genet.* **1998**, *96*, 8. DOI: 10.1007/s001220050702.
[171] Nanda, S.; Chand, S.-K.; Mandal, T.-P.; Joshi, R.-K. Identification of Novel Source of Resistance and Differential Response of *Allium* Genotypes to Purple Blotch Pathogen, *Alternaria porri* (Ellis) Ciferri. *Plant Pathol. J.* **2016**, *32*(6), 519–527. DOI: 10.5423/PPJ.OA.02.2016.0034.
[172] Dhatt, A. S.; Thakur, P. Production of Doubled Haploids in Onion: A Review. *J. Hortl. Sci.* **2014**, *9*(2), 107–112.
[173] Bohanec, B.; Jakše, M. Variations in Gynogenic Response among Long-day Onion (*Allium cepa* L.) Accessions. *Plant Cell Rep.* **1999**, *18*, 737–742. DOI: 10.1007/s002990050652.
[174] Jakše, M.; Hirschegger, P.; Bohanec, B.; Havey, M.-J. Evaluation of Gynogenic Responsiveness and Pollen Viability of Selfed Doubled Haploid Onion Lines and Chromosome Doubling via Somatic Regeneration. *J. Am. Soc. Hortic. Sci.* **2010**, *135*, 67–73. DOI: 10.21273/JASHS.135.1.67.
[175] Chen, J.-F.; Cui, L.; Malik, -A.-A.; Mbira, K.-G. In Vitro Haploid and Dihaploid Production via Unfertilized Ovule Culture. *Plant Cell Tiss. Org.* **2011**, *104*, 311–319. DOI: 10.1007/s11240-010-9874-6.
[176] Fayos, O.; Vallés, M.-P.; Garcés-Claver, A.; Mallor, C.; Castillo, A.-M. Doubled Haploid Production from Spanish Onion (*Allium cepa* L.) Germplasm: Embryogenesis Induction, Plant Regeneration and Chromosome Doubling. *Front. Plant Sci.* **2015**, *6*, 384. DOI: 10.3389/fpls.2015.00384.
[177] Jakše, M.; Bohanec, B. Haploid Induction in Onion via Gynogenesis. In *Doubled Haploid Production in Crop*; Maluszynski, M., Kasha, K.-J., Forster, B.-P., Szarejko, I.-E., Eds.; Kluwer Academic Publishers: Dordrecht, 2003; pp 281–285.
[178] Konvička, O.; Levan, A. Chromosome Studies in *Allium sativum*. *Hereditas*. **1972**, *72*, 129–148. DOI: 10.1111/j.1601-5223.1972.tb01035.x.
[179] Dhall, R.-K. True Seed Production of Garlic (*Allium sativum* L.) In Sub-Tropical Plains of India. *Veg. Sci.* **2015**, *42*(1), 44–48.
[180] Kamenetsky, R. https://www.garlicfarm.ca/article-garlic-seeds.htm (accessed Jun 20, 2019).
[181] Jenderek, -M.-M.; Hannan, R.-M. Variation in Reproductive Characteristics and Seed Production in the USDA Garlic Germplasm Collection. *HortScience*. **2004**, *39*(3), 485–488. DOI: 10.21273/HORTSCI.39.3.485.

[182] Zeng, Y.; Li, Y.; Yang, J.; Pu, X.; Du, J.; Yang, X.; Yang, T.; Yang, S. Therapeutic Role of Functional Components in Alliums for Preventive Chronic Disease in Human Being. *Evidence-Based Comp. Alt. Med.* **2017**, *2017*, Article ID 9402849, 13.

[183] Patil, B. S.; Pike, L. M.; Yoo, K. S. Variation in the Quercetin Content in Different Colored Onions (*Allium cepa* L.). *J. Amer. Soc. Hort. Sci*. **1995**, *120*, 909–913. DOI: 10.21273/JASHS.120.6.909.

[184] Bajaj, K. L.; Kaur, G.; Chadha, M. L. Varietal Variations in Some Important Chemical Constituents of Onion (*Allium cepa* L.). *Crop Sci.* **1990**, *30*, 391–395.

[185] Leighton, T.; Glinther, C.; Fluss, L.; Harte, W. K.; Cansado, J.; Notario, V. Molecular Characterization of Quercetin and Quercetin Glycosides in *Allium* Vegetables: Their Effects on Cell Transformation. In *Phenolic Compounds in Food and Their Effects on Health Ed.*; Huang, M.T., Lee, C.Y., Ho, C.T., Eds.; American Chemical Society, ACS Publications. 1992; pp 221–238.

[186] Patil, B. S.; Pike, L. M. Distribution of Quercetin Content in Different Rings of Various Colored Onion (*Allium cepa* L.) Cultivars. *J. Amer. Soc. Hort. Sci.* **1995**, *70*, 643–650.

[187] Selvakumar, K.; Prabha, R. L.; Saranya, K.; Bavithra, S.; Krishnamoorthy, G.; Arunakaran, J. Polychlorinated Biphenyls Impair Blood-brain Barrier Integrity via Disruption of Tight Junction Proteins in Cerebrum, Cerebellum and Hippocampus of Female Wistar Rats: Neuropotential Role of Quercetin. *Human Experi. Toxicol.* **2013**, *32*(7), 706–720. DOI: 10.1177/0960327112464798.

[188] Costa, L. G.; Garrick, J. M.; Roque, P. J.; Pellacani, C. Mechanisms of Neuroprotection by Quercetin: Counteracting Oxidative Stress and More. *Oxid. Med. Cel. Long.* **2016**, *2016*, Article ID 2986796, 10.

[189] Lin, S.-Y.; Wang, -Y.-Y.; Chen, W.-Y.; Chuang, Y.-H.; Pan, P. H.; Chen, C.-J. Beneficial Effect of Quercetin on Cholestatic Liver Injury. *J. Nutr. Biochem.* **2014**, *25*(11), 1183–1195. DOI: 10.1016/j.jnutbio.2014.06.003.

[190] Sak, K. Site-specific Anticancer Effects of Dietary Flavonoid Quercetin. *Nutr. Cancer*. **2014**, *66* (2), 177–193. DOI: 10.1080/01635581.2014.864418.

[191] Yasmin, M.; Ali, T.; Haque, S.; Hossain, M. Interaction of Quercetin of Onion with Axon Guidance Protein Receptor, NRP-1 Plays Important Role in Cancer Treatment: An *in Silico* Approach. *Interdiscip. Sci. Comp. Life Sci.* **2015**, *9(2)*, 184–191.

[192] Jaiswal, N.; Rizvi, S. I. Onion Extract (*Allium cepa* L.), Quercetin and Catechin Up-Regulate Paraoxonase 1 Activity with Concomitant Protection against Low-Density Lipoprotein Oxidation in Male Wistar Rats Subjected to Oxidative Stress. *J. Sci. Food Agric.* **2014**, *94* (13), 2752–2757. DOI: 10.1002/jsfa.2014.94.issue-13.

[193] Lu, T.-M.; Chiu, H.-F.; Shen, Y.-C.; Chung, -C.-C.; Venkatakrishnan, K.; Wang, C.-K. Hypocholesterolemic Efficacy of Quercetin Rich Onion Juice in Healthy Mild Hypercholesterolemic Adults: A Pilot Study. *Plant Food. Human Nutr.* **2015**, *70*(4), 395–400. DOI: 10.1007/s11130-015-0507-4.

[194] Majewska-Wierzbicka, M.; Czeczot, H. Flavonoids in the Prevention and Treatment of Cardiovascular Diseases. *Polski Merkuriusz Lekarski*. **2012**, *32*(187), 50–54.

[195] Park, S.; Kim, M.-Y.; Lee, D. H.; Lee, S.-H.; Baik, E.-J.; Moon, C.-H.; Park, S.-W.; Ko, E.-Y.; Oh, S.-R.; Jung, Y.-S. Methanolic Extract of Onion (*Allium cepa*) Attenuates Ischemia/Hypoxia-Induced Apoptosis in Cardiomyocytes via Antioxidant Effect,". *Eur. J. Nutr.* **2009**, *48*(4), 235–242.

[196] Bae, C.-R.; Park, Y.-K.; Cha, Y.-S. Quercetin-rich Onion Peel Extract Suppresses Adipogenesis by Down-Regulating Adipogenic Transcription Factors and Gene Expression in 3T3-L1 Adipocytes. *J. Sci. Food Agric.* **2014**, *94*(13), 2655–2660. DOI: 10.1002/jsfa.2014.94.issue-13.

[197] Kim, O. Y.; Lee, S. M.; Do, H.; Moon, J.; Lee, K. H.; Cha, Y. J.; Shin, M. J. Influence of Quercetin-rich Onion Peel Extracts on Adipokine Expression in the Visceral Adipose Tissue of Rats. *Phytother. Res.* **2012**, *26*, 432–437. DOI: 10.1002/ptr.3570.

[198] Dai, X.; Ding, Y.; Zhang, Z.; Cai, X.; Li, Y. Quercetin and Quercitrin Protect against Cytokine-Induced Injuries in Rinm5f β-Cells via the Mitochondrial Pathway and NF-κB Signaling. *Internat. J. Mol. Med.* **2013**, *31*(1), 265–271. DOI: 10.3892/ijmm.2012.1177.

[199] Bas, H.; Kalender, S.; Pandir, D. *In Vitro* Effects of Quercetin on Oxidative Stress Mediated in Human Erythrocytes by Benzoic Acid and Citric Acid. *Folia Biol.* **2014**, *62*(1), 57–64. DOI: 10.3409/fb62_1.59.
[200] Alam, M. M.; Meerza, D.; Naseem, I. Protective Effect of Quercetin on Hyperglycemia, Oxidative Stress and DNA Damage in Alloxan Induced Type 2 Diabetic Mice. *Life Sci.* **2014**, *109*(1), 8–14. DOI: 10.1016/j.lfs.2014.06.005.
[201] Lee, B. K.; Jung, Y.-S. *Allium Cepa* Extract and Quercetin Protect Neuronal Cells from Oxidative Stress via PKC- Inactivation/ERK1/2 Activation. *Oxid. Med. Cell. Longev.* **2016**, *2016*, Article ID 2495624, 9.
[202] Trisat, K.; Wong-on, M.; Lapphanichayakool, P.; Tiyaboonchai, W.; Limpeanchob, N. Vegetable Juices and Fibers Reduce Lipid Digestion or Absorption by Inhibiting Pancreatic Lipase, Cholesterol Solubility and Bile Acid Binding. *Int. J. Veg. Sci.* **2017**, *23*, 260–269. DOI: 10.1080/19315260.2016.1258604.
[203] Slanc, P.; Doljak, B.; Kreft, S.; Lunder, M.; Janeš, D.; Štrukelj, B. Screening of Selected Food and Medicinal Plant Extracts for Pancreatic Lipase Inhibition. *Phytother. Res.* **2009**, *23*, 874–877. DOI: 10.1002/ptr.2718.
[204] Kim, H. Y. Effects of Onion (*Allium cepa*) Skin Extract on Pancreatic Lipase and Body Weight-Related Parameters. *Food Sci. Biotechnol.* **2007**, *16*, 434–438.
[205] Moon, J.; Do, H. J.; Kim, O. Y.; Shin, M. J. Antiobesity Effects of Quercetin-Rich Onion Peel Extract on the Differentiation of 3T3-L1 Preadipocytes and the Adipogenesis in High Fat-Fed Rats. *Food Chem. Toxicol.* **2013**, *58*, 347–354. DOI: 10.1016/j.fct.2013.05.006.
[206] Lee, S. G.; Parks, J. S.; Kang, H. W. Quercetin, a Functional Compound of Onion Peel, Remodels White Adipocytes to Brown-like Adipocytes. *J. Nutr. Biochem.* **2017**, *42*, 62–71. DOI: 10.1016/j.jnutbio.2016.12.018.
[207] Lata, S.; Saxena, K. K.; Bhasin, V.; Saxena, R. S.; Kumar, A.; Srivastava, V. K. Beneficial Effects of *Allium sativum, Allium cepa* and *Commiphora mukul* on Experimental Hyperlipidaemia and Atherosclerosis–A Comparative Evaluation. *J. Postgrad. Med.* **1991**, *37*, 132–135.
[208] Lee, K. H.; Kim, Y.; Park, E.; Hwang, H. J. Effect of Onion Powder Supplementation on Lipid Metabolism in High Fat-Cholesterol Fed SD Rats. *J. Food Sci. Nutr.* **2008**, *13*, 71–76.
[209] Wang, X. K.; Wang, X.; Huang, J. Effects of Allicin on Experimental Colorectal Cancer in Rats and its Mechanism. *Prod. Res. Dev.* **2016**, *28*, 943–948. DOI: 10.1080/00207549008942765.
[210] Hu, H. J.; Pan, Y. Q.; Fan, X. J.; Hu, X. M.; Zou, W. W.; Lin, X. L. Allicin Inhibits H2O2-induced Senescence in Human Umbilical Vein Endothelial Cells through Activation of SIRT1. *Chinese J. Biochem. Mol. Biol.* **2016**, *32*(5), 536–543.
[211] Chhabria, S. V.; Akbarsha, M. A.; Li, A. P.; Kharkar, P. S.; Desai, K. B. In Situ Allicin Generation Using Targeted Alliinase Delivery for Inhibition of MIA PaCa-2 Cells via Epigenetic Changes, Oxidative Stress and Cyclin-dependent Kinase Inhibitor (CDKI) Expression. *Apoptosis*. **2015**, *20*(10), 1388–1409. DOI: 10.1007/s10495-015-1159-4.
[212] Zhang, X.; Zhu, Y.; Duan, W.; Feng, C.; He, X. Allicin Induces Apoptosis of the MGC-803 Human Gastric Carcinoma Cell Line through the P38 Mitogen-activated Protein Kinase/caspase-3 Signaling Pathway. *Mol. Med. Rep.* **2015**, *11*(4), 2755–2760. DOI: 10.3892/mmr.2014.3109.
[213] Wan, Q.; Yang, Y. P.; Liu, Z. Y. Allicin Prevents EA. Hy926 Endothelial Cell Injury Induced by PM2.5 Via Inhibiting ERK1/2 Pathway. *Chinese Pharmac. Bulletin*. **2016**, *32*(5), 692–696.
[214] Panyod, S.; Wu, W.-K.; Ho, C.-T.; Lu, K.-H.; Liu, C.-T.; Chu, Y.-L.; Lai, Y.-S.; Chen, W.-C.; Lin, Y.-E; Lin, S.-H.; et al. Diet Supplementation with Allicin Protects against Alcoholic Fatty Liver Disease in Mice by Improving Anti-inflammation and Antioxidative Functions. *J. Agric. Food Chem.* **2016**, *64*(38), 7104–7113.
[215] El-Sheakh, A. R.; Ghoneim, H. A.; Suddek, G. M.; Ammar, E. S. Attenuation of Oxidative Stress, Inflammation, and Endothelial Dysfunction in Hypercholesterolemic Rabbits by Allicin. *Canad. J. Physiol. Pharmaco.* **2015**, *94*(2), 216–224. DOI: 10.1139/cjpp-2015-0267.
[216] Lin, -J.-J.; Chang, T.; Cai, W.-K.; Zhang, Z.; Yang, Y.-X.; Sun, C.; Li, Z.-Y.; Li, W.-X. Post-injury Administration of Allicin Attenuates Ischemic Brain Injury through Sphingosine

Kinase 2: *In Vivo* and *in Vitro* Studies. *Neurochem. Internat.* **2015**, *89*, 92–100. DOI: 10.1016/j.neuint.2015.07.022.
[217] Wallock-Richards, D.; Doherty, C. J.; Doherty, L.; Clarke D.-J.; Place, M.; Govan, J.-R.; Campopiano, D.-J. Garlic Revisited: Antimicrobial Activity of Allicin-containing Garlic Extracts against *Burkholderia Cepacia* Complex. *PLoS ONE*. **2014**, *9*(12), Article ID e112726. DOI: 10.1371/journal.pone.0112726.
[218] Imai, T.; Kosuge, Y.; Endo-Umeda, K.; Miyagishi, H.; Ishige, K.; Makishima, M.; Ito, Y. Protective Effect of S-allyl-l-cysteine against Endoplasmic Reticulum Stress-Induced Neuronal Death is Mediated by Inhibition of Calpain. *Amino Acids*. **2014**, *46*(2), 385–393.
[219] Imai, T.; Kosuge, Y.; Saito, H.; Uchiyama, T.; Wada, T.; Shimba, S.; Ishige, K.; Miyairi, S.; Makishima, M.; Ito, Y. Neuroprotective Effect of S-Allyl-L-Cysteine Derivatives against Endoplasmic Reticulum Stress-Induced Cytotoxicity is Independent of Calpain Inhibition. *J. Pharmacol. Sci.* **2016**, *130*, 185e188. DOI: 10.1016/j.jphs.2016.03.004.
[220] Fu, E.; Tsai, M.-C.; Chin, Y.-T.; Tu, H.-P.; Fu, M.-M.; Chiang, C.-Y.; Chiu, H.-C. The Effects of Diallyl Sulfide upon *Porphyromonas Gingivalis* Lipopolysaccharide Stimulated Proinflammatory Cytokine Expressions and Nuclear Factor Kappa B Activation in Human Gingival Fibroblasts. *J. Periodont. Res.* **2015**, *50*(3), 380–388.
[221] Ahmad, M. S.; Ahmed, N. Antiglycation Properties of Aged Garlic Extract: Possible Role in Prevention of Diabetic Complications. *J. Nutr.* **2006**, *136*(3), 796S–799S. DOI: 10.1093/jn/136.3.796S.
[222] Al-Malki, A. L. Inhibition of α-glucosidase by Thiosulfinate as a Target for Glucose Modulation in Diabetic Rats. *Evid-Based Comp. Alt. Med.* **2016**, *2016*, Article ID 7687915, 5.
[223] Kang, J. G.; Park, C. Y. Anti-obesity Drugs: A Review about Their Effects and Safety. *Diabetes Metab. J.* **2012**, *36*, 13–25. DOI: 10.4093/dmj.2012.36.1.13.
[224] Padwal, R. S.; Majumdar, S. R. Drug Treatments for Obesity: Orlistat, Sibutramine and Rimonabant. *Lancet*. **2007**, *369*, 71–77. DOI: 10.1016/S0140-6736(07)60033-6.
[225] Krentz, A. J.; Fujioka, K.; Hompesch, M. Evolution of Pharmacological Obesity Treatments: Focus on Adverse Side-Effect Profiles. *Diabetes Obes. Metab. J.* **2016**, *8*, 558–570. DOI: 10.1111/dom.12657.
[226] Van Damme, E. J.; Smeets, K.; Torrekens, S.; Van Leuven, F.; Peumans, W. J. Isolation and Characterization of Alliinase cDNA Clones from Garlic (*Allium sativum* L.) and Related Species. *Eur. J. Biochem.* **1992**, *209*, 751–757. DOI: 10.1111/j.1432-1033.1992.tb17344.x.
[227] Rabinkov, A.; Zhu, X. Z.; Grafi, G.; Galili, G.; Mirelman, D. Alliin Lyase (Alliinase) from Garlic (*Allium Sativum*). Biochemical Characterization and cDNA Cloning. *Appl. Biochem. Biotech.* **1994**, *48*(3), 149–171. DOI: 10.1007/BF02788739.
[228] Do, G. S.; Suzuki, G.; Mukai, Y. Genomic Organization of a Novel Root Alliinase Gene, ALL1, in Onion. *Gene*. **2004**, *325*, 7–24. DOI: 10.1016/j.gene.2003.09.033.
[229] Drugă, B.; Şuteu, D.; Rosca-Casian, O.; Pârvu, M.; Sragos, N. Two Novel Alliin Lyase (Alliinase) Genes from Twisted-Leaf Garlic (*Allium obliquum*) and Mountain Garlic (*Allium senescens* var. *montanum*). *Not. Bot. Hort. Agrobot. Cluj.* **2011**, *39*(2), 293–298. DOI: 10.15835/nbha3926355.
[230] Endo, A.; Imai, Y.; Nakamura, M.; Yanagisawa, E.; Taguchi, T.; Torii, K.; Okumura, H.; Ichinose, K. Distinct Intraspecific Variations of Garlic (*Allium sativum* L.) Revealed by the Exon-Intron Sequences of the Alliinase Gene. *J. Nat. Med.* **2014**, *68*(2), 442–447.
[231] Ovesná, J.; Mitrová, K. Kučera, L. Garlic (*A. sativum* L.) Alliinase Gene Family Polymorphism Reflects Bolting Types and Cysteine Sulphoxides Content. *BMC Genet.* **2015**, *16*, 53. DOI: 10.1186/s12863-015-0214-z.
[232] Lombard, K.; Geoffriau, E.; Peffly, E. B. Flavonol Quantification in Onion by Spectrophotometric and High Performance Liquid Chromatography Analysis. *HortSci.* **2002**, *37*(4), 682–685. DOI: 10.21273/HORTSCI.37.4.682.
[233] Smith, C.; Lombard, K. A.; Peffley, E. B.; Liu, W. Genetic Analysis of Quercetin in Onion (*Allium Cepa* L.) 'lady Raider'. *Texas J. Agric. Nat. Res.* **2003**, *16*, 24–28.