



Comprehensive matrices for regulatory approvals and genetic characterization of genetically modified organisms



Narmeen Mallah ^{a, b}, Marc Obeid ^b, Gretta Abou Sleymane ^{b, *}

^a Department of Preventive Medicine, Faculty of Medicine, University of Santiago de Compostela, Santiago de Compostela, Spain

^b Lebanese Reference Laboratory for GMOs Analysis, Department of Laboratory Science and Technology, Faculty of Health Sciences, American University of Science and Technology, Beirut, Lebanon

ARTICLE INFO

Article history:

Received 23 December 2016

Received in revised form

15 March 2017

Accepted 19 March 2017

Available online 22 April 2017

Keywords:

GMOs

DNA

Matrix

Database

Regulations

ABSTRACT

The production of new types of genetically modified organisms (GMOs) and the use of products containing or derived from these materials are expanding globally. This poses a challenge in providing cost-effective comprehensive analyses. In this line, the state of art testing approaches rely on a matrix representing the GM events with their corresponding GM markers - DNA elements used in plants' transformation. Accordingly, this study aimed first at constructing an updated and comprehensive matrix of genetic characterization of GM events based on an extensive review of the relevant databases. Inclusive lists of 356 GM markers and 508 events in 29 plant species were compiled and organized into a matrix. The frequency of occurrence of these elements was then determined. Moreover, for the first time, a matrix representing the regulatory status of every compiled GM event was established. Remarkably, numerous inconsistencies were detected among the databases at the levels of nomenclature, events' registry, molecular characterization and regulatory approvals. Both matrices represent a useful tool for comprehensive and cost-effective analyses. The genetic matrix permits designing the most straightforward testing strategy that provides the maximum information about GMOs in a sample in the minimum number of experimental steps. Moreover, the novel regulatory matrix, allows further decreasing the number of required event-specific identification tests by giving higher probabilities to those authorized in the samples' country of origin. Finally, the genetics and regulatory matrices represent the building-block for establishing an inclusive automated database for GMOs which is instrumental for testing laboratories worldwide.

© 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Genetically Modified Organisms (GMOs) are those whose genetic material has been altered in order to possess novel traits. Genetic modifications are carried out by the insertion of genetic construct(s), which when integrated into the plant's genome constitute(s) a GM event (DG Health and Food Safety, 2017; Gabrielle & James, 1999; Kate, Lina, David, Nicky, & Kerry, 2003; WHO, 2017). GMOs containing more than one GM event combined via conventional crossing of previously existing GMOs are called stacked GM events (Alexander & Emilio, 2009). The production of GMOs is in continuous progression since the mid-nineties. Statistics have shown more than a 100 fold increase from 1996 till 2013, where the global acreage exceeded 175 million hectares (Clive, 2014). In order

to protect the consumer's rights and ensure food and environmental safety, 63 countries around the world have laid down their country-specific regulatory policies to control GMOs authorizations and labeling (Clive, 2014).

The implementation of GMOs regulations requires the availability of analytical methods to detect the presence of GMOs and further identify and quantify the potential GM event(s) in a positively screened sample. The routinely applied testing methods are based on DNA amplification by the polymerase chain reaction (PCR) method (Alexandra et al., 2015, pp. 119–131; Kate et al., 2003; Wentao & Ying, 2015, pp. 343–351).

However, owing to the huge expansion in GMOs production along with a significant increase in the number and genetic diversification of the produced GM events, affordable testing strategies in terms of time and cost have become a requirement. In this context, the testing approaches that are widely adopted nowadays rely on a GMOs matrix, a table representing the list of GM events with their corresponding transgenic elements (Holst-Jensen et al.,

* Corresponding author.

E-mail address: gretta.abousleymane@gmail.com (G. Abou Sleymane).

2012; Querci, Van den Bulcke, Žel, Van den Eede, & Broll, 2010). The number of GM events and targets included in the matrix are flexible, and can be increased or decreased according to the available information and specific needs (Holst-Jensen et al., 2012). The first GMOs screening matrix was established in 2010 and it included 81 GM events and five PCR targets (Waiblinger, Lutz, Mankertz, Engelbert, & Pietsch, 2010). Further efforts were made to establish larger databases for GMOs screening such as the GMO finder and GMO seek which include 324 and 328 GM events, respectively (Gerdes, Busch, & Pecoraro, 2012; Morisset et al., 2014). Such genetic matrices are crucial to significantly minimize the number of required analytical steps for GMOs analysis.

Previously published matrices were based on a genetic representation of the collected GM events with their corresponding genetic elements. Therefore, we intended in the current paper to extensively review the main related GMOs databases in order to provide an updated genetic matrix. Moreover, as the available matrices are exclusive to genetic characterization of GMOs, we established for the first time, an additional comprehensive matrix for the regulatory approvals of all GM events.

The reviewed databases are the Gene and Living Modified Organisms (LMO) registries of the Biosafety Clearing House (BCH Gene Registry, 2016; BCH LMO Registry, 2016), the GM Crop Database of the Center for Environmental Risk Assessment (CERA GM Crop Database, 2016) and the GM Approval Database of the International Services for the Acquisition of Agri-Biotech Applications (ISAAA GM Approval Database, 2016). These databases were selected based on their extensive use in the field of GMOs analyses.

The novel matrix representing the regulatory status of each GM event triggers additional decrease in the number of required GMOs tests, whereby analytical priorities will be given to the GM events that are authorized in the sample's country of origin. The matrix is therefore of special importance in countries that have not developed yet their GMOs regulations. This is the case of most of the Middle East and North Africa (MENA) countries where the absence of regulations has allowed introducing GMOs into the MENA markets (Abdel Mawgood, Gassem, Alsadon, Alghamdi, & Al Doss, 2010; Al Hmoud, Al Rousan, Hayek, & Ibrahim, 2010; Al Rousan, Al Hmoud, Hayek, & Ibrahim, 2010; Bakr & Ayinde, 2013; El Sanhoty et al., 2002; Herzallah, 2012; Oraby, Hassan, & Abou Mossallam, 2005; Premanandh, Maruthamuthu, Sabbagh, & Al Muhairi, 2012; Sakr, Mallah, Chalak, & Abou-Sleymane, 2014). Yet, GMOs analysis is still requested in those countries by local seeds, food or feed stakeholders who intend to voluntarily label their products with information about GMOs for marketing purposes. It is also requested by some local manufacturers who export their products to countries with implemented GMOs regulations.

Therefore, the two matrices provided in this paper represent an informative, cost and time efficient tool for GMOs analyses. They also serve as a sweeping source of information on GM events genetic characterizations and regulations, and are the basis for establishing comprehensive and automated databases for GMOs.

2. Materials and methods

2.1. Establishing the genetic matrix

Data about the registered GM plant species were retrieved from the three databases: Living Modified Organisms (LMO) registry of the Biosafety Clearing House (BCH), GM Crop Database of the Center for Environmental Risk Assessment (CERA) and GM Approval Database of the International Services for the Acquisition of Agri-Biotech Applications (ISAAA) (BCH LMO Registry, 2016; CERA GM Crop Database, 2016; ISAAA GM Approval Database, 2016) and then cross-compared in order to establish a

comprehensive list. The recorded GM events in each species were then compiled from the three databases, compared for consistency, and then an inclusive list was established. Further, the genetic elements associated with each GM event were collected and a complete list of DNA sequences of the inserted genetic constructs used in plants' transformation was established. The elements of few events that are not fully genetically characterized in these databases were retrieved from Biosafety Scanner (Biosafety Scanner, 2016). Subsequently, a comprehensive matrix representing all plant species with their respective GM events and DNA elements was established, and the frequency of occurrence of each of these DNA elements in GM events was calculated.

2.2. Establishing the regulatory matrix

A second new matrix representing the regulatory approvals of each included GM event was constructed by collecting the information from BCH-LMO Registry (BCH LMO Registry, 2016), CERA-GM Crop Database (CERA GM Crop Database, 2016) and ISAAA-GM Approval Database (ISAAA GM Approval Database, 2016), comparing them for uniformity, and organizing them in an inclusive table. The three databases provide summary of authorizing countries and approved type of use of each GM event. The webpage last update for each authorization retrieved from these databases is included in the matrix to facilitate future updating. Moreover, authorizations from the database "Biostradestatus", an external database provided in the BCH, have been included when they were not reported in the BCH itself.

The compiled data for both matrices of genetic characterizations and regulations were double checked to diminish the rate of error. They were last updated in June 2016.

3. Results

3.1. Compiling lists of GM events

A list of 507 GM events from 29 plant species (Table S1) was compiled from the main GMOs databases (BCH-LMO registry, CERA-GM Crop Database and ISAAA-GM Approval Database). All these databases list the worldwide authorized GM events/species. Eight of the 29 compiled plant species are not registered in GM Crop Database of CERA (*Phaseolus vulgaris*, *Solanum melongena*, *Eucalyptus* sp., *Petunia hybrid*, *Prunus domestica*, *Populus* sp., *Saccharum* sp. and *Capsicum annuum*), and two plant species are not recorded in the LMO registry of BCH (*Saccharum* sp. and *Capsicum annuum*).

Among the 507 unique GM events, 220, 391 and 425 were found to be registered in the CERA-GM Crop Database, ISAAA-GM Approval Database and BCH-LMO registry, respectively. 210 of the collected GM events are commonly registered in the three databases, 100 events are registered in BCH and ISAAA only, eight GM events are registered in CERA and ISAAA only, a GM event is registered in BCH and CERA only, 114 GM events are recorded in BCH only, 73 GM events are listed in ISAAA only, and one event is registered in CERA only (Fig. 1). The GM events that are authorized in EU or have an application being submitted were also retrieved from GMO Compass (GMO-Compass, 2015) and checked if they are included in the other three databases. All of them were found to be registered, except for the maize event NK604 × T25 which has a submitted application according to GMO Compass and which was not found registered in any of the databases, raising the number of compiled GM events from 507 to 508.

Since all products containing or consisting of GMOs are required to be labeled by the unique identifier assigned to each GM event (EC 65/2004) (OECD, 2006), the unique identifiers of all compiled GM

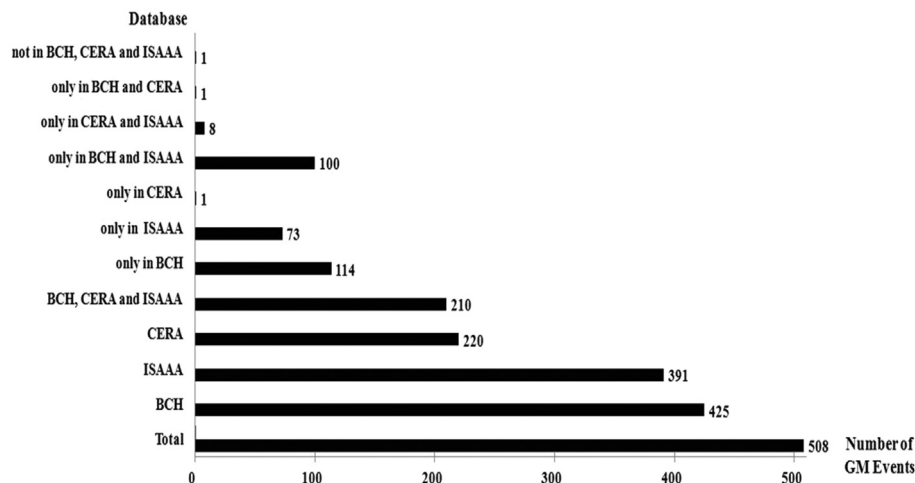


Fig. 1. Comparison of the number of registered GM events among the main three GMO databases: BCH, CERA and ISAAA. The chart shows that the highest number of GM events is registered in BCH, followed by ISAAA and CERA. It also illustrates inconsistent registration of GM events among the databases.

events were also checked for consistency between the databases. Inconsistencies were detected for some events. For instance, CZW3 (squash) and 23-18-17 (canola) which have the identification codes SEM-ØCZW3-2 and CGN-89111-8 respectively are not designated by their corresponding codes in all the databases. The carnation GM event 11363 (1363A) is designated by FLO-11363-2 in BCH and by FLO-11363-1 in ISAAA; however it is not nominated by a unique identifier in CERA. The unique identifier of the maize GM event MON-89Ø34-3 × DAS-Ø15Ø7-1 × MON-88Ø17-3 × DAS-59122-7 × DAS-4Ø278-9 corresponds to an event named MON89034 × TC1507 × MON88017 × DAS59122 × DAS40278 in BCH and ISAAA; however it also belongs to an additional event named MON89034 × TC1507 × MON88017 × DAS40278 in ISAAA. The papaya events 55-1 and 63-1 have the same unique identifier in CERA (CUH-CP551-8), whereas the event 63-1 is designated by CUH-CP631-7 in BCH and ISAAA. Both canola GM events HCN10 and HCN92 are designated by Topas 19/2 in ISAAA whereas only HCN92 is designated by Topas 19/2 in BCH. The maize GM events 676, 678 and 680 are not designated by a unique identifier in CERA; however they are designated by the following respective codes in BCH and ISAAA PH-ØØØ676-7, PH-ØØØ678-9, PH-ØØØ68Ø-2. For some stacked GM events, the order of listing of individual events in the stacked event's name and/or code is changed which renders the search for the same event difficult between the different databases. For instance, the three names 281-24-236 × 3006-210-23 × MON1445, DAS-21Ø23-5 × DAS-24236-5 × MON-Ø1445-2, 3006-210-23 × 281-24-236 × MON1445 correspond to the same event in BCH, CERA and ISAAA, respectively. All remaining discrepancies are represented in Table S2.

3.2. Establishing the GMOs regulatory matrix

Information about the regulatory approvals of the compiled GM events was collected from the databases BCH, CERA and ISAAA, and then compared. Inconsistencies were detected among the registered data at the level of authorizing countries, type of approved utilization(s) and date of the related regulatory approvals among the databases. An illustrative example is represented in Table S3.

We then constructed the first matrix that provides a comprehensive representation of the regulatory approvals collected from the three databases (Table S4). In the table, each event is represented with the countries that have legalized its use, along with the type and date of authorization. The authorizations with no

specified date in the corresponding database are denoted by an asterisk (*). In addition, further notes have been added for GMOs authorizations of some events as indicated in the databases. These notes include the authorizations expiry date and conditions related to the approved use.

3.3. Compiling a comprehensive list of DNA elements used in plants' transformation

The selection of the DNA sequences to be used for GMOs screening is based on the frequency of occurrence of each of these elements and its degree of information. Accordingly, we compiled the registered DNA sequences from the three databases BCH – Gene and LMO Registries, CERA – GM Crop Database and ISAAA – GM Approval Database, and constituted a comprehensive list of 356 sequences. The collected elements include 82 promoters, 55 terminators, 164 genes, 55 other DNA sequences (one enhancer, one integration site, 13 introns, three plasmid vectors, 16 leaders, one recombination site, 18 transit signals and two double stranded RNAs) (Fig. 2). Each retrieved DNA element is represented with its type, name, alternative name, abbreviation, alternative abbreviation and donor organisms in tables S5 – S8.

3.4. Characterizing GM events and establishing an updated frequency of DNA elements

Genetic information about each GM event was mainly collected from BCH-LMO Registry, CERA-GMO Crop Database and ISAAA-GM Approval Database. All data collected from these databases were compared and discrepancies were detected in around 70 GM events. For instance, the sugar beet GM event SY-GTSB77-8 has p-e35S according to BCH, and p-35S according to CERA. The tobacco GM event Vector 21–41 has p-nos according to BCH but not according to CERA. The canola events MON-89249-2 and MON-ØØØ73-7 have T-rbcS-E9 according to BCH but not according to CERA. The maize GM events PH-ØØØ676-7, PH-ØØØ678-9 and PH-ØØØ68Ø-2 have T-35S according to BCH not CERA. The canola event ACS-BNØØ7-1 contains pat gene according to BCH and CERA whereas it includes bar gene according to ISAAA. The maize GM event MON-ØØ81Ø-6 is shown to contain cp4 epsps, nptII and goxv247 genes in ISAAA whereas, according to BCH, and CERA these genes are not present in this event.

The events that are only registered in ISAAA were fully

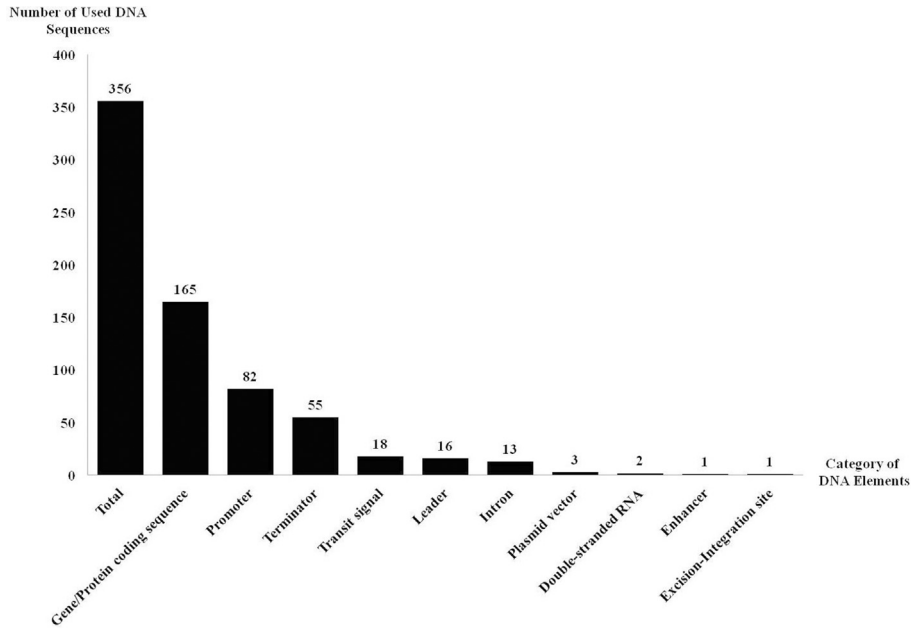


Fig. 2. Representation of the compiled DNA elements. The chart illustrates the different categories of the 356 compiled DNA elements that are used in plants' transformation, as well as the number of DNA elements per each category.

characterized by referring to Biosafety Scanner database, because ISAAA provides only a list of included transgene(s). However, not all of these events are available in the Biosafety Scanner and consequently 54 GM events out of 508, couldn't be completely characterized.

Subsequent to the genetic characterization of all GM events, the frequency of occurrence of each DNA sequence in GM events was calculated (Tables S9–S12 and Figs. 3–6).

3.5. Constructing the genetics GMOs matrix

The compiled complete lists of 29 GM species and 508 events were represented in a table that constitutes a comprehensive GMOs

matrix (Table S13). In the matrix, the species are listed in alphabetical order. They are also indicated by their scientific name in the adjacent column. Then, the GM events of each plant species are represented by their names and codes in the following two columns, respectively. The genetic elements/DNA sequences are listed in the top row by categories. The same order of listing the DNA elements was adopted in all tables. DNA sequences present in a specific GM event are denoted by "1" with a cell filled in green, while those that are not present are designated by "0" with a cell filled in red, whereas those which are inconsistent among the databases are represented by "0/1" with a cell filled in yellow. However, the DNA elements for which there is no information about their presence/absence in the corresponding database are denoted

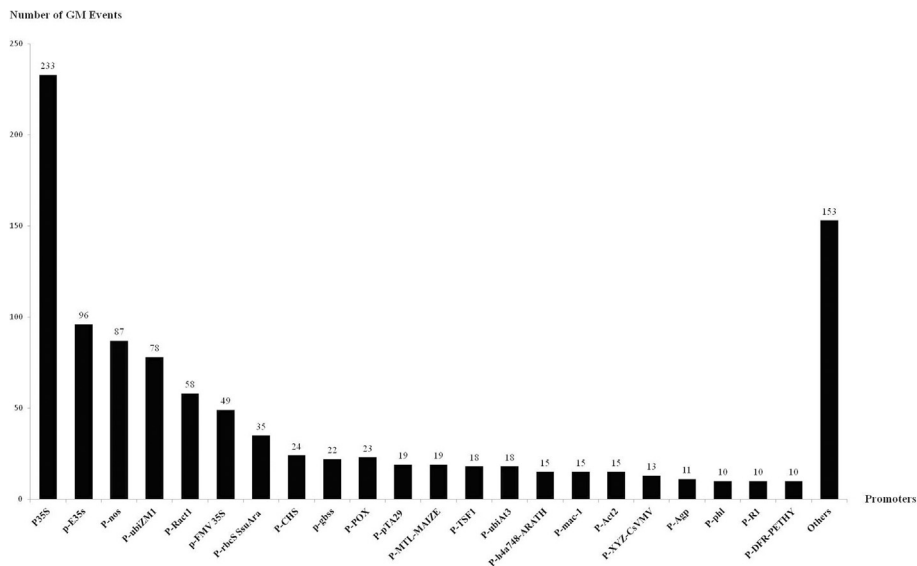


Fig. 3. Distribution of promoters used in plants' transformation. The chart shows the number of GM events that contain the respective promoter. The group indicated by "others" refers to the promoters that are present in less than 10 GM events, where 153 represents the total number of GM events that contain this group of promoters.

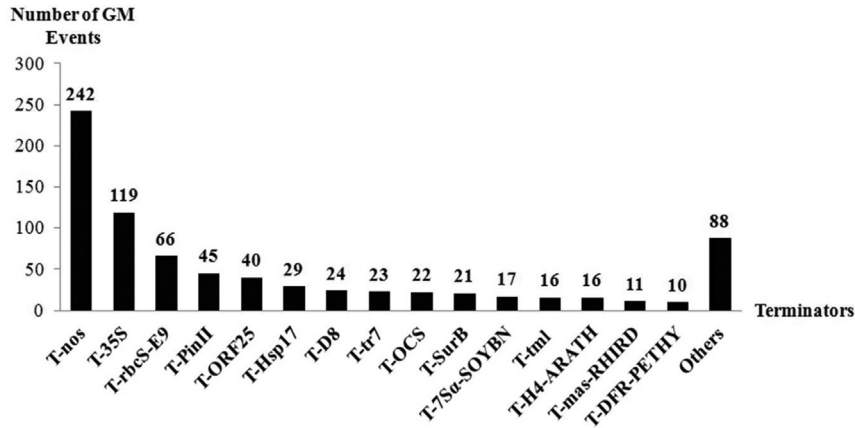


Fig. 4. Distribution of terminators used in plants' transformation. The chart represents the number of GM events that are positive to each of the compiled terminators. The group entitled "others" corresponds to the terminators that are present in less than 10 GM events, where 88 is the total number of GM events that contain this group of terminators.

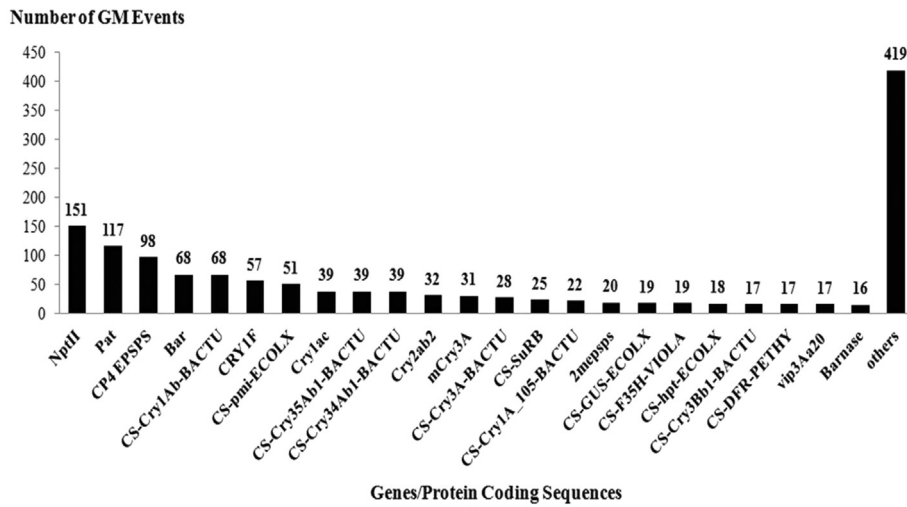


Fig. 5. Distribution of genes/protein coding sequences used in plants' transformation. The chart demonstrates the number of GM events that contains each of the collected transgenes. The group named "others" represents the transgenes that are available in less than 15 GM events, where 419 is the total number of GM events that contain this group of transgenes.

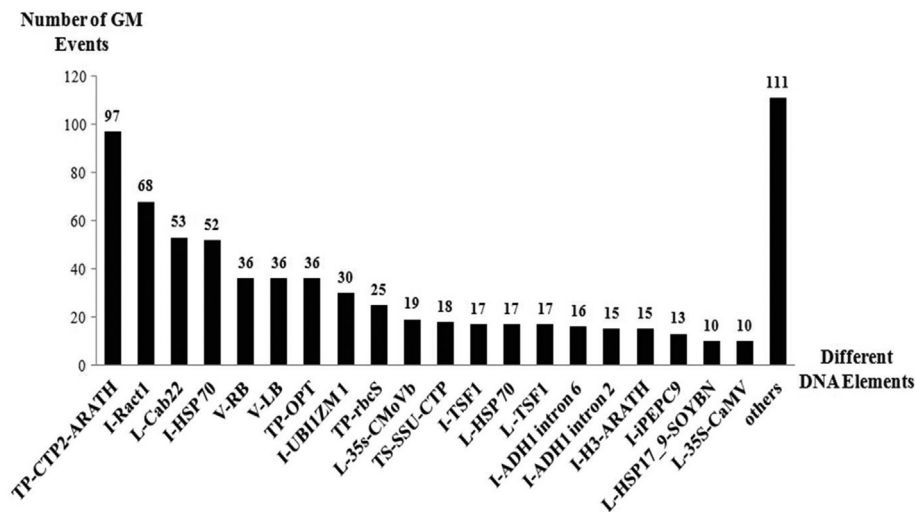


Fig. 6. Distribution of different categories of DNA elements used in plants' transformation. The chart represents the number of GM events that are positive to the collected elements. The last column titled "others" corresponds to the DNA elements that are present in less than 10 GM events, where 111 is the total number of GM events that contain this group of elements.

by “unknown” with a cell filled in blue.

4. Discussion

The increase of GM crops development and commercialization as well as the diversity of GM events in terms of genes and regulatory elements create challenges for GMOs analysis. In this line, pragmatic, affordable and reliable testing approaches become a requirement. To-date, the matrix approach represents the most appropriate strategy since it can be extended to include all known GM events and can be customized to different testing methodologies such as conventional and Real-Time PCR, according to the regulatory requirements and the available laboratory facilities.

In this connection, some genetic matrices of GM events have been previously published. They included Waiblinger's approach for testing 81 GM events with 5 GM targets (Waiblinger et al., 2010), and Gurinder's matrix for screening 141 GM events that are commercialized or under field trials in India (Randhawa, Morisset, Singh, & Žel, 2013). Two larger databases are also available. The GMO finder encompasses 324 GM events and 15 selected screening elements (Gerdes et al., 2012), and GMOseek includes more than 320 GM events and 240 GM targets (Morisset et al., 2014). The current paper provides an updated GMO matrix of genetic characterization that includes 508 GM events and 356 DNA elements. This matrix was constructed based on an extensive revision of the data registered in the main GMO databases, BCH, CERA-GM Crop Database and ISAAA (BCH Gene Registry, 2016; CERA GM Crop Database, 2016; ISAAA GM Approval Database, 2016). The revision shows inconsistencies among the databases at the level of registered GM plant species, recorded GM events and their nomenclature, as well as molecular characterization of GM events.

The inconsistent naming and coding of GM events complicated the search for a specific event among the databases. As a result, it may be falsely concluded that a certain GM event is absent from a specific database, if the name and/or code attributed by another database is used in the search. To avoid such false negative results, different searching methods were employed. For instance, the listing order of individual GM events was switched while looking for a stacked GM event such as 59122 × TC1507 × NK603 and TC1507 × 59122 × NK603, because not all stacked GM events have the same name or code in each database. In other cases, the first two or three letters which correspond to the applicant name were removed from events name/code such as MON for Monsanto or DAS for Dow AgroSciences. Some events were found by searching for both their name and code since not all events that have a unique identifier are designated by their codes in all databases. It is worth mentioning, that in some cases, even if the proper code/unique identifier is used, a typing or formatting mistake in the database may lead to a negative search results. These mistakes include an absent or additional space or hyphen in the event's code or name, or using of “0” or “O” instead of “Φ”. Finally, the extensions from the unique identifiers had to be excluded sometimes to be able to find the corresponding event due to inconsistencies at this level such as MST-FGØ72-2 and MST-FGØ72-3. Such types of inconsistencies should be resolved and a standardized nomenclature should be set up through a joint effort between all relevant authorities.

At the level of molecular characterization, the absence of a common way to nominate the DNA elements and attribute their abbreviations among the different databases, required deep attention while characterizing the GM events. Accordingly, comprehensive tables representing the DNA targets belonging to the four categories of elements (promoters, terminators, genes and others) with their names, abbreviations, alternatives and corresponding donor organisms have been provided in this paper. Again, it is crucial to adopt standardized nomenclature and codes in order

to facilitate the process of GM events' molecular characterization and the update of matrices in the future.

Moreover, the databases presented discrepancies in listing different DNA elements for some events as explained earlier in the results. Such conflicts in genetic characterization can be clarified experimentally by the use of event's specific methods and/or certified reference materials, if available. Otherwise, next generation sequencing or any other technique that fits the purpose may be adopted.

The DNA elements compiled in the genetic matrix show a significant expansion in the diversification of the DNA sequences used in plants' transformation. For instance, according to BATS reports in 2003, the number of foreign terminators, promoters and genes were 20, 29 and 40 respectively (BATS, 2003). However, this updated matrix shows a significant increase in the number of these elements to 55, 82 and 164 respectively, in addition to the inclusion of 55 new different DNA elements. Moreover, the updated frequencies of occurrence of DNA elements used in plants transformation were also determined in this study.

The second part of this study encompassed establishing, for the first time, a comprehensive regulatory GMOs matrix for all 508 compiled GM event. This novel table was also constructed based on a deep revision of the data registered in the three databases. The GM events are listed in this matrix following the same order as that of the genetic characterization, to allow for easier traceability. The regulatory matrix consists of three columns, each corresponding to one of these databases. For each GM event, the countries with regulatory approvals are listed chronologically and a color code was adopted for the different types of approvals, for easy comparison of data. The matrix included the page last update of all records, facilitating thereby its update upon the amendment or change of any regulation.

The discrepancies detected during this study justify the need for establishing a comprehensive and updated source of information for both the molecular characterization and regulatory approvals of GMOs. Accordingly, the matrices provided in this study, present a layout for establishing an automated and comprehensive tool for GMOs testing which would significantly facilitate GM events' identification process. In fact, the updated data provided in the genetic matrix permit designing streamline experimental screening strategies for an optimal coverage of GMOs by selecting the most informative DNA targets for the analysis. Furthermore, the regulatory matrix facilitates concluding the identity of potential GM events in the investigated sample by giving higher probability to those authorized in the countries of origin. Both genetic and regulatory databases should be updated on a regular basis, by including the upcoming GM events, additional GM target sequences and updated regulatory approvals.

Acknowledgment

We would like to thank Dr. Danielle Badro for her recommendations and for proofreading the manuscript.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.foodcont.2017.03.053>.

References

- Abdel Mawgood, A., Gassem, M., Alsadon, A., Alghamdi, S., & Al Doss, A. (2010). Monitoring of genetically modified food in Saudi Arabia. *African Journal of Food Science*, 4(8), 536–540.
- Al Hmoud, N., Al Rousan, H., Hayek, B., & Ibrahim, M. (2010). Detection of genetically modified maize and soybean food products in the Jordanian Market.

- Biotechnology*, 9(4), 499–505. <http://dx.doi.org/10.3923/biotech.2010.499.505>.
- Al Rousan, H., Al Hmoud, N., Hayek, B., & Ibrahim, M. (2010). A study on the occurrence of genetically modified soybean and maize feed products in the Jordanian market. *Journal of Cell and Molecular Biology*, 8(2), 87–94.
- Alexander, J. S., & Emilio, R. C. (2009). The global pipeline of new GM crops. In *Implications of asynchronous approval for international trade*. European Commission, Joint Research Center. EUR 23486 EN - 2009.
- Alexandra, P., Joana, S. A., Joana, C., Telmo, J. R. F., Maria Beatriz, P. P. O., Cristina, D.-M., et al. (2015). *Novel strategies for genetically modified organism detection*. Genetically modified organisms in food. Production, safety, regulation and public health. Elsevier. <http://dx.doi.org/10.1016/B978-0-12-802259-7.01001-0>. Retrieved from.
- Bakr, S., & Ayinde, O. (2013). Awareness of GM food proliferation in Saudi Arabia: A case study of Makkah city. *Journal of the Association of Arab Universities for Basic and Applied Sciences*, 13(1), 8–13. <http://dx.doi.org/10.1016/j.jaubas.2012.09.003>.
- BATS. (2003). *Genetically Modified (GM) Crops: molecular and regulatory details*. BATS. Version 2.
- BCH Gene Registry. (2016). *Biosafety clearing House*. from <http://bch.cbd.int/>.
- BCH LMO Registry. (2016). *Biosafety clearing House*. from <https://bch.cbd.int/database/lmo-registry/>.
- Biosafety Scanner. (2016). *Biosafety scanner*. from Genetics Rights Foundation <http://en.biosafetyscanner.org/>.
- CERA GM Crop Database. (2016). *Center for environmental Risk assessment*. from http://www.cera-gmc.org/?action=gm_crop_database.
- Clive, J. (2014). *Global status of commercialized biotech/GM crops: 2013* (Vol. 46). The International Service for the Acquisition of Agri-biotech Applications (ISAAA).
- DG Health and Food Safety. (2017). European Commission, Directorate General for Health and Food Safety, 2017, from http://ec.europa.eu/food/plant/gmo_en.
- El Sanhoty, R., Broll, H., Grohmann, L., Linke, B., Spiegelberg, A., Bogl, K. W., et al. (2002). Genetically modified maize and soybean on the Egyptian food market. *WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Nahrung Food*, 46(5), 360–363. doi: 10.1002/1521-3803(20020901)46:5<360::AID-FOOD360>3.0.CO;2-J.
- Gabrielle, J. P., & James, N. S. (1999). *Applications of biotechnology to Crops: Benefits and risks* (Vol. 12). Council for Agricultural Science and Technology.
- Gerdes, L., Busch, U., & Pecoraro, S. (2012). *GMOfinder—A GMO screening database*. *Food Analytical Methods*. <http://dx.doi.org/10.1007/s12161-012-9378-6>. ISSN 1936-9751.
- GMO-Compass. (2015). *GMO compass*. from <http://www.gmo-compass.org/eng/home/>.
- Herzallah, S. M. (2012). Detection of genetically modified material in feed and foodstuffs containing soy and maize in Jordan. *Journal of Food Composition and Analysis*, 26(1–2), 169–172. <http://dx.doi.org/10.1016/j.jfca.2012.01.007>.
- Holst-Jensen, A., Bertheau, Y., de Loose, M., Grohmann, L., Hamels, S., Hougs, L., et al. (2012). Detecting un-authorized genetically modified organisms (GMOs) and derived materials. *Biotechnology Advances*, 30(6), 1318–1335. <http://dx.doi.org/10.1016/j.biotechadv.2012.01.024>. Epub 2012 Feb 3.
- ISAAA GM Approval Database. (2016). *International service for the acquisition of agri-biotech applications*. from <http://www.isaaa.org/>.
- Kate, G., Lina, P., David, C., Nicky, W., & Kerry, R. E. (2003). *Review of technologies for detecting genetically modified materials in commodities and food*. Australian Government Analytical Laboratories, Research and Development Section.
- Morriset, D., Kralj Novak, P., Zupanic, D., Gruden, K., Lavrac, N., & Zel, J. (2014). *GMoseek: A user friendly tool for optimized GMO testing*. *BMC Bioinformatics*, 15(258). <http://dx.doi.org/10.1186/1471-2105-15-258>.
- OECD. (2006). *OECD guidance for the designation of a unique identifier for transgenic plants*. Organisation for Economic Co-operation and Development. ENV/JJM/MONO(2002)7/REV1(23).
- Oraby, H., Hassan, A., & Abou Mossallam, A. (2005). Screening food products for the presence of CaMV 35S promoter and NOS 3' terminator. *Journal of the Science of Food and Agriculture*, 85(12), 1974–1980. <http://dx.doi.org/10.1002/jsfa.2201>.
- Premanandh, J., Maruthamuthu, M., Sabbagh, A., & Al Muhairi, S. (2012). Prevalence of genetically modified foods (GM foods) in the United Arab Emirates. *Food Control*, 25(1), 10–12. <http://dx.doi.org/10.1016/j.foodcont.2011.10.001>.
- Querci, M., Van den Bulcke, M., Zel, J., Van den Eede, G., & Broll, H. (2010). New approaches in GMO detection. *Analytical Bioanalytical Chemistry*, 396, 1991–2002. <http://dx.doi.org/10.1007/s00216-009-3237-3>.
- Randhawa, G. J., Morisset, D., Singh, M., & Zel, J. (2013). *GMO matrix: A cost-effective approach for screening unauthorized genetically modified events in India*. *Food Control*, 38, 124–129. <http://dx.doi.org/10.1016/j.foodcont.2013.10.013>.
- Sakr, J., Mallah, N., Chalak, L., & Abou-Sleymane, G. (2014). *First comprehensive GMOs testing in Lebanon: Screening, identification and quantification of GM Soybean imports*. *Food Control*, 36, 146–152.
- Waiblinger, H.-U., Lutz, G., Mankertz, J., Engelbert, D., & Pietsch, K. (2010). A practical approach to screen for authorised and unauthorised genetically modified plants. *Anal Bioanal Chem*, 396, 2065–2072. <http://dx.doi.org/10.1007/s00216-009-3173-2>.
- Wentao, X., & Ying, S. (2015). *The detection techniques of genetically modified organisms*. Genetically modified organisms in food. Production, safety, regulation and public health ISBN: 978-0-12-802259-7 ed. Elsevier. <http://dx.doi.org/10.1016/B978-0-12-802259-7.01001-0>. Retrieved from
- WHO. (2017). *World Health Organization, Health topics, food*. Genetically modified Retrieved March 13, 2017, from http://www.who.int/topics/food_genetically_modified/en/.