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Development of a core collection of *Triticum* and *Aegilops* species for improvement of wheat for activity against chronic diseases

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Abstract

Background: The objective of this study was to develop a core collection of *Triticum* and *Aegilops* species as a resource for the identification and characterization of wheat lines with preventive activity against chronic diseases. Given that cancer is the leading cause of mortality in the world and shares risk factors with obesity, type-2 diabetes, and cardiovascular disease, and given that wheat has been reported to protect against these diseases, the core collection was developed based on cancer prevalence.

Methods: The Germplasm Resources Information Network (GRIN) database was used to identify *Triticum* and *Aegilops* species grown in regions of the world that vary in cancer prevalence based on the International Agency for Cancer Research GLOBOCAN world map of cancer statistics (2008). Cancer incidence data drove variety selection with secondary consideration of ploidy, center of origin, and climate.

Results: Analysis indicated that the geographic regions from which wheat is considered to have originated have a lower incidence of cancer than other geographic regions (P <0.01), so wheat lines from countries that comprise the 'Fertile Crescent' were highly represented in the core collection. A total of 188 lines were selected from 62,571 accessions maintained by GRIN. The accessions identified comprised two genera and 14 taxa of 10 species within 19 groups from 82 countries. The core collection is comprised of 153 spring, 25 winter, and five facultative selections of wheat.

Conclusions: A diverse core collection of wheat germplasm has been established from a range of regions worldwide. This core collection will be used to identify wheat lines with activity against chronic diseases using anticancer activity as a screening tool.

Keywords: *Aegilops*, Anticancer activity, Cancer, Core collection, *Triticum*, Wheat germplasm

Background

The consumption of whole grains has long been associated with a healthy lifestyle and chronic disease prevention; in particular, multiple studies have correlated whole-wheat consumption with protection against chronic diseases including cardiovascular disease, stroke, type 2 diabetes, and cancer at multiple sites [1-8]. However, these studies have failed to discriminate between the type of wheat that is consumed and the chronic disease protective effect observed. Specifically, the USDA has germplasm from 62,571 distinct wheat varieties; given the well-described differences in agronomic traits as a result of genetic polymorphisms within wheat species, as well as the recently characterized metabolite differences between and within wheat species and subspecies [9], further investigation of the chronic disease preventive capacity of individual wheat varieties is required.

In this paper, we propose that a neglected opportunity in the field of diet and chronic disease prevention is the use of staple food crops with defined bioactivity for daily consumption [10]. The rationale underlying this approach recognizes that societies have chosen their staple food crops, which are affordable and generally available to all individuals across socioeconomic strata, and that societies willingly consume these staples in large quantities on a

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daily basis. These consumption patterns thus provide a stable flow of health beneficial phytochemicals in much the same way that an oral drug is taken to maintain plasma concentrations of the active ingredient in a beneficial range [11]. Further research on bioactivity of specific varieties of these staple food crops is critical, given that major chronic diseases, including obesity, type-2 diabetes, cardiovascular disease, stroke, and cancer, account for over 60% of deaths worldwide [12,13], are interrelated at the molecular and cellular levels and share many common risk factors [14-16], and, most importantly, are also considered preventable through lifestyle choices of which diet is considered to play a prominent role [17-19].

While concern exists that the genetic factors driving the occurrence and progression of cancer and other chronic diseases are so powerful that diet can have little impact, most evidence indicates that the key strategy to conquering chronic diseases like cancer is through prevention particularly when the prevention strategy is routinized from 'womb to tomb' (reviewed in [20]). However, in addition to the general presumption that all varieties of a particular staple food crop are created equal with respect to health benefits, one of the challenges of this approach is the assumption that the ingredients which a food is processed into, rather than the food itself, is the most critical factor accounting for health benefits [10]. The work reported in this paper was initiated to provide a resource for evaluating the first premise, that is, that all botanically defined lines of wheat (*Triticum* and *Aegilops* species) have equivalent chronic disease fighting activity with anticancer activity providing a focal point for analysis. Cancer was chosen because among these chronic diseases, the prevalence of cancer continues to increase globally and cancer is now the leading cause of chronic disease related mortality in the world [21]; furthermore previously published reports have described an inverse association between wheat consumption and cancer incidence.

Wheat is ranked second, after rice, among all members of the Poaceae family in terms of the amount consumed by the global population [22]. Wheat is used in the preparation of a wide variety of foods for everyday use, including bread, pasta/macaroni/noodles, bulgur, cookies, biscuits, cakes, cereals, pizza, vermicelli, couscous, pastry, and chapatti/flatbread [23,24]. It is also fermented to make beer and other alcoholic beverages. Wheat's role as a primary human dietary component is due to its large grain size, agronomic adaptability, ease of storage, and nutritional quality. While a limited number of wheat lines account for most of wheat products consumed globally due to the emergence of global industrial food systems, some ancient wheat lines- such as einkorn and emmer- are still consumed as cereal substitutes in Middle Eastern countries, where wheat is considered to have originated [25]. These grains are very small and difficult to harvest and clean. As such, they are often used in porridge or soup without grinding or processing. In the Arab world (including Iraq, Syria, and Tunisia), soft green (immature) wheat grains, mostly domesticated tetraploid emmer, are sundried and roasted to make a food called Freekeh. In addition, people in Arab countries routinely mix Freekeh made from domesticated landraces of wheat grains with meat and spices in their daily foods.

As noted above, wheat is consumed in large amounts worldwide, but the type of wheat and the manner in which it is consumed differ markedly depending on geographic region. Because of the novel events underlying the domestication of wheat, there are major genetic differences among the types of wheat commonly consumed. As a result of this inherent diversity, the Germplasm Resources Information Network (GRIN) has accumulated over 62,571 wheat-related accessions [26]. The general approach to working with such a large resource is to devise a strategy by which to pick a representative sample of lines from the total resource (collection) that is small enough to manage for use in research yet large enough to capture the diversity of the population for the trait(s) of interest. The resulting subsample of germplasm is referred to as a core collection [27]. Herein, a core collection of wheat lines for future use in chronic disease prevention research is described.

Methods

Source of plant materials

The *Triticum* and *Aegilops* collections at GRIN (USDA/ARS, Aberdeen, Idaho) include 59,564 and 2,650 accessions, respectively [26]. Only *Triticum* and *Aegilops* were selected for establishing this core collection with the reasoning that these two genera comprise the majority of wheat lines that have emerged due to domestication through natural selection and polyploidization. The accessions chosen for inclusion in the core collection are described in Table 1. All available information was obtained on selected accessions, including passport information, characterization, and evaluation.

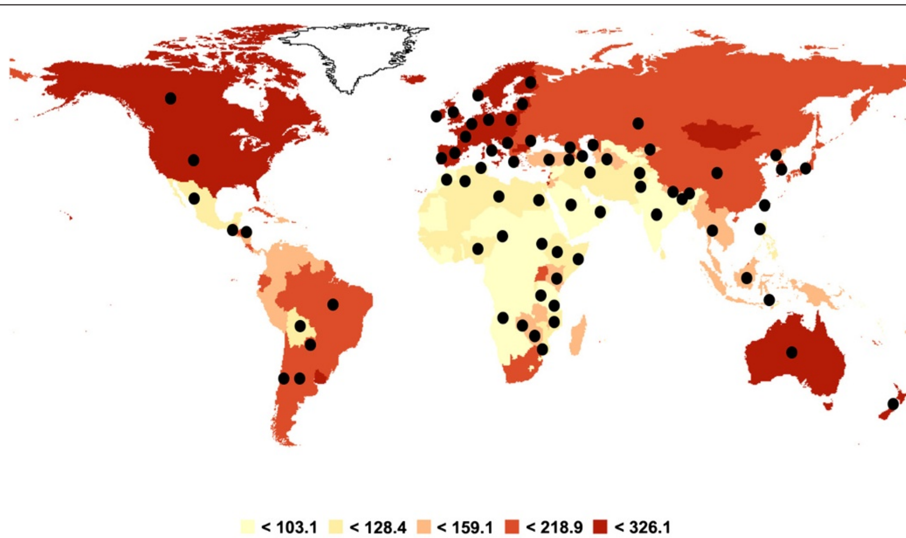
Criteria of selection

Cancer statistics

The data used were based on GLOBOCAN 2008 cancer statistics [21]. GLOBOCAN's cancer statistics are based on the incidence of all cancers using the age-standardized rate (ASR). Our intent was to select wheat lines attributed to specific countries identified in the GLOBOCAN global map (Figure 1) that showed wide variations in cancer incidence rates, under the presumption that these wheat lines, and their close relatives, are likely to be consumed in greater amounts in those countries.

Table 1 A summary of the *Triticum* and *Aegilops* species used for core collection

Species	Genome	Total active accessions at GRIN	Total number in core collection	Base species (%)
Aegilops speltoides var. *speltoides*	BB/GG	9	3	33.33
Aegilops speltoides var. *ligustica*	BB/GG	11	1	9.10
Aegilops tauschii	DD	200	1	0.50
Triticum aestivum subsp. *aestivum*	BBA^uA^uDD	46,225	80	0.17
Triticum aestivum subsp. *compactum*	BBA^uA^uDD	118	1	0.85
Triticum aestivum subsp. *spelta*	BBA^uA^uDD	1,292	6	0.46
Triticum hybrid	BBAADD	219	1	0.46
Triticum monococcum subsp. *aegilopoides*	A^mA^m	826	4	0.48
Triticum timopheevii subsp. *armeniacum*	GGA^uA^u	249	1	0.40
Triticum turgidum subsp. *carthlicum*	BBA^uA^u	95	2	2.11
Triticum turgidum subsp. *dicoccon*	BBA^uA^u	622	10	1.61
Triticum turgidum subsp. *dicoccoides*	BBA^uA^u	777	2	0.26
Triticum turgidum subsp. *durum*	BBA^uA^u	8,526	63	0.74
Triticum turgidum subsp. *paleocolchicum*	BBA^uA^u	4	1	25
Triticum turgidum subsp. *turanicum*	BBA^uA^u	108	1	0.93
Triticum turgidum subsp. *turgidum*	BBA^uA^u	1,054	6	0.57
Triticum urartu	A^uA^u	245	3	1.22
Triticosecale sp.	BBA^uA^uRR	1,985	1	0.05
Triticum zhukovskyi	$GGA^uA^uA^mA^m$	6	1	16.67
Total		**62,571**	**188**	**0.30**



Source: GLOBOCAN cancer statistics, 2008. Estimated age-standardized incidence rate per 100,000 residents for all cancers, excluding non-melanoma skin cancer, both sexes and all ages.

Figure 1 A world map of cancer incidence displaying geographic distribution of core collection of wheat germplasm. Estimated age-standardized incidence rate (ASR) per 100,000 residents for all cancers, excluding non-melanoma skin cancer, both sexes and all ages based on GLOBOCAN Cancer statistics, 2008. Each black dot represented a wheat growing country of the world. Four colors ranging from very light yellow to dark brown described the ASR from <103.1 to >326.1 per 100,000 individuals.

Centers of origin

Archeological evidence indicates that Armenia, Iran, Iraq, Lebanon, Israel, Jordan, Syria, and Turkey were the centers of origin for wheat germplasm [28]. Cancer statistics also indicated that the occurrence of cancer is very low in these areas, supporting the possibility that the wheat species cultivated and consumed locally provide anticancer protection. Wheat lines from these countries were highly represented in the core collection.

Regression analysis

To determine whether the relationship between wheat consumption and cancer incidence was related to geographic origin of wheat, data were collected from the Food and Agriculture Organization of the United Nations (FAOSTAT) from 2007, operationally defined as kg wheat products consumed per capita per year, and from the GLOBOCAN resource from 2008, operationally defined as ASR of cancer incidence at all sites excluding non-melanoma skin cancer. Countries without data for both parameters were excluded from analyses, resulting in a total of 165 countries for the global analysis (Figure 2A) and a subset of the global analysis using 19 Near Eastern countries which are geographically proximate to the origin of wheat (Figure 2B). The countries included in the latter analysis were Armenia, Azerbaijan, Cyprus, Egypt, Georgia, Iran, Israel, Jordan, Kuwait, Lebanon, Pakistan, Saudi Arabia, the Syrian Arab Republic, Tajikistan, Turkey, Turkmenistan, United Arab Emirates, Uzbekistan, and Yemen. No wheat consumption data were available for Iraq through FAOSTAT. Log_{10}-transformed ASRs were regressed on wheat consumption data (10 kg/capita/year) in linear regression analysis using GraphPad Prism vs. 5.02 (GraphPad Software, San Diego, CA, USA). Fit parameters for each analysis, including slope, Y-intercept, R^2, and line equations are provided in the figure legend (Figure 2).

Other considerations

The species of *Triticum* and *Aegilops* include germplasm with three ploidy levels: diploid with genomes A^m, B, D, and G; tetraploid with BA^u and GA^u genomes; and hexaploid with BA^uD genomes [28]. Selections within each genome and ploidy level were represented in the core collection.

Results and discussion

To our knowledge, there are no published core collections of wheat that have been specifically developed to permit the investigation of wheat for human health benefits and particularly for reducing chronic disease risk using anticancer activity as a screening tool. Thus, the approach used was necessarily descriptive in nature. Rather than enforcing established criteria usually implemented for the

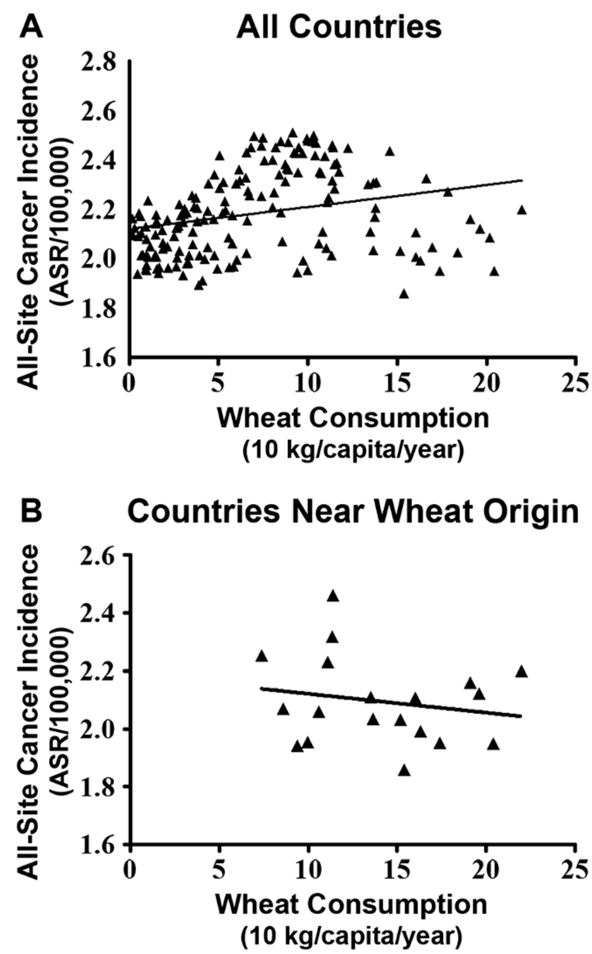


Figure 2 Linear regression analysis of association between wheat consumption and cancer incidence rates. To determine whether the relationship between wheat consumption and cancer incidence was related to geographic origin of wheat, 2007 wheat consumption data was collected from FAOSTAT, defined as kg wheat products consumed per capita per year, and from the GLOBOCAN resource from 2008, defined as age-standardized rates (ASR) per 100,000 of cancer incidence at all sites excluding non-melanoma skin cancer. ASRs were log_{10}-transformed to satisfy statistical criteria. Countries without data for both parameters were excluded from analyses. (**A**) All-site cancer incidence ASRs for 165 countries were regressed against yearly wheat consumption, which showed a slightly positive correlation between wheat consumption and cancer incidence. Slope = 0.008940 ± 0.002527; Y-intercept = 2.120 ± 0.02197; R^2 = 0.07131; line equation: Log_{10}-transformed ASR = 0.008940*wheat consumption + 2.120. (**B**) A subset of the global analysis, comprising ASRs for *n*=19 Near Eastern countries, which are geographically proximate to the origin of wheat, were regressed against wheat consumption data, which showed a slightly negative correlation between wheat consumption and cancer incidence. Slope = −0.006526 ± 0.008315; Y-intercept= 2.187 ± 0.1225; R^2 = 0.03497; line equation: Log_{10}-transformed ASR = −0.006526*wheat consumption + 2.187. Analyses were performed using the linear regression analysis function in GraphPad Prism vs. 5.02 (GraphPad Software, San Diego, CA, USA).

development of a core collection for agronomic traits such as disease or pest resistance, or post-harvest processing characteristics [27], cancer incidence data drove variety selection with secondary consideration of ploidy, center of origin, and climate.

Cancer statistics

A world map generated from the GLOBOCAN cancer database is shown (Figure 1) and was used to identify the countries from which germplasm was selected from the GRIN domain collection. Based on GLOBOCAN 2008 statistics, the lowest incidence rates of cancer occur in middle Africa, northern Africa, south central Asia, western Africa, eastern Africa, Central America, and western Asia. Interestingly, western Asia, or the Fertile Crescent region between the Tigris and Euphrates river basins, has been determined to be the geographic center of origin for wheat [28]. To explore the relationship between wheat consumption and cancer incidence as it relates to geographic origin of wheat, we used linear regression analysis. When cancer incidence rates for 165 countries were regressed on wheat consumption data in those countries, a slight positive correlation between these parameters was found (Figure 2A, slope = +0.0089 increase in $\log_{10}$-transformed ASR per 10 kg/capita/year increase in wheat consumption). This translates to an increase of 1.02% in cancer incidence for each 10 kg/capita/year increase in wheat consumption. Conversely, when this analysis was confined to 19 countries near the geographic origin of wheat, a slight negative correlation (Figure 2B, slope = −0.0065 increase in $\log_{10}$-transformed ASR per 10 kg/capita/year increase in wheat consumption). This translates to a reduction of 0.99% in cancer incidence for each 10 kg/capita/year increase in wheat consumption. Hence, the slightly positive association between global cancer incidence rates and wheat consumption is reversed when the analysis is restricted only to countries near the geographic origin of wheat ($P < 0.01$). Many other factors are likely involved in the observed correlations between global wheat consumption and cancer incidence rates. Thus, it is important to underscore that there is no evidence of a causal link between these parameters but rather these analyses support the use of cancer incidence by geographic locale as an objective albeit arbitrary tool to guide wheat line selection for the core collection.

The core collection of wheat germplasm was selected from regions with lower incidence rates of cancer, as well as regions such as North America, Europe, and Oceania (Australia and New Zealand) with higher incidence rates of cancer; evaluation of germplasm from regions of both low and high cancer rates is critical for assessing differences in the type of wheat consumed which may impact cancer activity. In choosing multiple selections from within a country, we were unable to follow the procedure of constant, proportional, and logarithmic selection, as all genotypes were not available in each country [27]. In addition, maintaining uniform diversity around the world was impossible as there are large differences in the total number of accessions in each country that was considered.

Characterization of selected lines

A total of 62,571 accessions at GRIN were designated as the source collection, which represented two genera and 14 taxa. From the source collection, 188 accessions were selected for the core collection, which is 0.3% of the source collection. The global distribution of the wheat lines in the core collection is shown (Figure 1, Table 1) and provides a summary of the *Triticum* and *Aegilops* species comprising the core collection. The core collection consisted of two genera and 14 taxa of 10 species and was comprised of 19 groups. These 188 accessions belonged to 82 different countries with three different climates (tropical, subtropical, and temperate). The plant introduction number, plant name, taxon, original source, selection criteria, growth habit, and probable market classes are shown (Table 2). Probable market classes were determined by visual observation of the germplasm using a grain color standard and may be changed during future evaluation.

Climate

There are several climates in which the domestication of wheat occurred: tropical, subtropical, and temperate, and three types of wheat resulted: winter, spring, and facultative. They differ in temperature response due to the presence and absence of dominant vernalization genes [29,30]. The three types of wheat are presented in the core collection.

Limitations

Cancer prevalence rates among countries are subject to a host of genetic and environmental determinants. Despite associations reported between wheat consumption and cancer risk, there is no direct causal evidence that a particular wheat variety reduces the cancer rate within a specific country [19]. Nonetheless, the overall cancer rate in a country provided an objective albeit arbitrary criterion for selecting wheat lines for inclusion in the core collection. The usefulness of this approach will be determined as screening for anticancer activity in laboratory model systems progresses. Another limitation is that many core collections of crop species are between 5% and 10% of the domain in size, and thus the core collection reported is relatively small in comparison (Table 1). However, there are examples of core collections <5% of the domain in size. For example, the international barley

Table 2 Detailed information for 188 *Triticum* and *Aegilops* germplasm collected from GRIN platform through USDA

No.	ID	Plant name	Taxon	Country	Selection criteria	Growth habit	Probable market class
1	PI 542274	84TK081-057	*A. speltoides var. speltoides*	Turkey	Center of origin	NA	NA
2	PI 560529	TU85-008-01	*A. speltoides var. speltoides*	Turkey	Center of origin	NA	NA
3	PI 449338	AE 081D	*A. speltoides var. speltoides*	Israel	Center of domestication	NA	NA
4	PI 560528	TU85-015-02-2	*A. speltoides var. ligustica*	Turkey	Center of origin	NA	NA
5	PI 603233	TA 1669	*A. tauschii*	Azerbaijan	D genome donor	NA	NA
6	Cltr 180	China	*T. aestivum subsp. aestivum*	China	Least breast cancer, highest producer of wheat	W	SRW
7	Cltr 14319	India Hybrid 65	*T. aestivum subsp. aestivum*	India	Least breast cancer, second highest producer of wheat	S	SWS
8	Cltr 15136	American 378	*T. aestivum subsp. aestivum*	Sudan	Northern Africa	S	SWS
9	PI 9871	Erivan	*T. aestivum subsp. aestivum*	Armenia	Center of origin	S	HRS
10	PI 9872	Galgalos	*T. aestivum subsp. aestivum*	Armenia	Center of origin	S	SWS
11	PI 52323	Little Joss	*T. aestivum subsp. aestivum*	UK	Northern Europe	W	SRW
12	PI 54431	Triminia	*T. aestivum subsp. aestivum*	Libya	Middle East	S	HRS
13	PI 62004	NA	*T. aestivum subsp. aestivum*	China	Least breast cancer	F	NA
14	PI 81791	Sapporo Haru Komugi Jugo	*T. aestivum subsp. aestivum*	Japan	Eastern Asia	S	SWS
15	PI 82469	Poubiru	*T. aestivum subsp. aestivum*	North Korea	Eastern Asia	S	HRS
16	PI 87117	Ejuiea	*T. aestivum subsp. aestivum*	South Korea	Eastern Asia	W	HRW
17	PI 94418	99	*T. aestivum subsp. aestivum*	Russia	Fourth highest producer of wheat	W	HRW
18	PI 116232	Solid Straw Tuscan	*T. aestivum subsp. aestivum*	NZ	High cancer incidence	W	SWW
19	PI 124818	Cross No. 7	*T. aestivum subsp. aestivum*	NZ	High cancer incidence	S	HRS
20	PI 139599	Egypt NA 101	*T. aestivum subsp. aestivum*	Egypt	Western Asia	S	SWS
21	PI 155315	Yemen	*T. aestivum subsp. aestivum*	Yemen	Western Asia	S	SRS
22	PI 165208	Sert Bolvadin	*T. aestivum subsp. aestivum*	Turkey	Center of origin	S	SWS
23	PI 178383	6256	*T. aestivum subsp. aestivum*	Turkey	Center of origin	W	SRW
24	PI 184994	Snogg II	*T. aestivum subsp. aestivum*	Norway	Northern Europe	S	HRS
25	PI 190451	Snogg	*T. aestivum subsp. aestivum*	Norway	Northern Europe	S	SRS
26	PI 191334	Marzuolo 87	*T. aestivum subsp. aestivum*	Italy	Southern Europe	W	HWW
27	PI 265482	Olympia	*T. aestivum subsp. aestivum*	Finland	Northern Europe	S	SWS
28	PI 266879	S995	*T. aestivum subsp. aestivum*	Iraq	Center of origin	S	HWS
29	PI 266880	S997	*T. aestivum subsp. aestivum*	Iraq	Center of origin	S	HRS
30	PI 274505	NA	*T. aestivum subsp. aestivum*	Thailand	South Eastern Asia	S	SWS
31	PI 283150	Horani Nawawi	*T. aestivum subsp. aestivum*	Jordan	Center of origin	S	SWS
32	PI 297005	AFRICA MAYO	*T. aestivum subsp. aestivum*	Kenya	Eastern Africa	S	HRS
33	PI 347003	White Shanazi	*T. aestivum subsp. aestivum*	Afghanistan	South Central Asia	S	SWS
34	PI 350308	DACIA	*T. aestivum subsp. aestivum*	Romania	Eastern Asia	W	HRW
35	PI 384399	Nigeria-2	*T. aestivum subsp. aestivum*	Nigeria	Western Africa	S	HWS
36	PI 406475	2	*T. aestivum subsp. aestivum*	Nepal	South Central Asia	S	HRS
37	PI 414975	No. 6	*T. aestivum subsp. aestivum*	Indonesia	South Central Asia	S	HRS
38	PI 480034	MG 31147	*T. aestivum subsp. aestivum*	Ethiopia	Eastern Africa	S	SWS
39	PI 487292	SY 270	*T. aestivum subsp. aestivum*	Jordan	Center of origin	S	HRS
40	PI 519554	PAKISTAN 20	*T. aestivum subsp. aestivum*	Kenya	Eastern Africa	S	SWS

Table 2 Detailed information for 188 *Triticum* and *Aegilops* germplasm collected from GRIN platform through USDA *(Continued)*

41	PI 532053	96	*T. aestivum subsp. aestivum*	Egypt	Northern Africa	S	SWS
42	PI 585019	15007	*T. aestivum subsp. aestivum*	Saudi Arabia	Western Asia	S	HRS
43	PI 585024	15063	*T. aestivum subsp. aestivum*	Saudi Arabia	Western Asia (a part of Core 95)	S	HRS
44	PI 603919	UCRBW98-2	*T. aestivum subsp. aestivum*	USA	DNA segment from Spelta and HWS Pavon (bread wheat), Northern America, a part of core 6	S	SWS
45	PI 648392	KUNDAN	*T. aestivum subsp. aestivum*	India	Least breast cancer, second highest producer of wheat	S	HWS
46	CItr 14352	II-50-25	*T. aestivum subsp. aestivum*	Paraguay	South America	S	HRS
47	PI 10611	Talimka	*T. aestivum subsp. aestivum*	Turkmenistan	South Central Asia	S	HWS
48	PI 61693	294	*T. aestivum subsp. aestivum*	Malawi	Eastern Africa	S	HWS
49	PI 91235	Cagayan	*T. aestivum subsp. aestivum*	Philippines	South East Asia	S	HRS
50	PI 125088	Ile de France	*T. aestivum subsp. aestivum*	France	Western Europe, more cancer	S	HWS
51	PI 174657	Ile de France	*T. aestivum subsp. aestivum*	France	Western Europe, more cancer	S	SRS
52	PI 182665	9915	*T. aestivum subsp. aestivum*	Lebanon	Western Asia	S	HWS
53	PI 191701	B 256 F.S. 1354	*T. aestivum subsp. aestivum*	Mozambique	Eastern Africa	F	SWS
54	PI 191744	FL S Aurora	*T. aestivum subsp. aestivum*	Mozambique	Eastern Africa	S	SWS
55	PI 203081	Sabanero	*T. aestivum subsp. aestivum*	Tanzania	Eastern Africa	S	HRS
56	PI 231115	II-2734-2c(1–2)x2T	*T. aestivum subsp. aestivum*	Guatemala	Central America	S	HRS
57	PI 234233	Idaho 1877 NR AE	*T. aestivum subsp. aestivum*	Zambia	Eastern Africa	S	HRS
58	PI 278386	Morocco 58	*T. aestivum subsp. aestivum*	Morocco	Northern Africa	S	HRS
59	PI 278395	Poland 2	*T. aestivum subsp. aestivum*	Poland	Eastern Europe	W	HRW
60	PI 313098	Quern	*T. aestivum subsp. aestivum*	Ireland	Northern Europe	S	HRS
61	PI 344018	Mistura Pinto	*T. aestivum subsp. aestivum*	Angola	Middle Africa, least cancers	S	SWS
62	PI 344019	Saraiva Vieira	*T. aestivum subsp. aestivum*	Angola	Middle Africa, least cancers	S	SWS
63	PI 351474	Reval	*T. aestivum subsp. aestivum*	Estonia	Northern Europe	W	HRW
64	PI 351870	10180-54-29	*T. aestivum subsp. aestivum*	Burundi	Eastern Africa	S	SWS
65	PI 374248	BOL-17	*T. aestivum subsp. aestivum*	Chad	Middle Africa, least cancers	S	HRS
66	PI 374249	BOL-19	*T. aestivum subsp. aestivum*	Chad	Middle Africa, least cancers	S	HRS
67	PI 374254	34335	*T. aestivum subsp. aestivum*	Mali	Western Africa	S	HWS
68	PI 384399	Nigeria-2	*T. aestivum subsp. aestivum*	Nigeria	Western Africa	S	HWS
69	PI 410425	ILICHEVKA	*T. aestivum subsp. aestivum*	Kazakhstan	South Central Asia	W	SRW
70	PI 428690	LEUCURUM 3	*T. aestivum subsp. aestivum*	Uzbekistan	South Central Asia	S	SRS
71	PI 470905	MG 18060	*T. aestivum subsp. aestivum*	Algeria	Northern Africa	S	SWS
72	PI 480481	R-124	*T. aestivum subsp. aestivum*	Bolivia	South America	S	SRS
73	PI 481713	41	*T. aestivum subsp. aestivum*	Bhutan	South Central Asia	W	HRW
74	PI 481715	Ka	*T. aestivum subsp. aestivum*	Bhutan	South Central Asia	S	SWS
75	PI 486155	CHIWORE	*T. aestivum subsp. aestivum*	Zimbabwe	Eastern Africa, least breast cancer	S	HRS
76	PI 486156	GWEBI	*T. aestivum subsp. aestivum*	Zimbabwe	Eastern Africa, least breast cancer	S	SWS
77	PI 486157	RUSAPE	*T. aestivum subsp. aestivum*	Zimbabwe	Eastern Africa, least breast cancer	S	HRS
78	PI 490405	Koira alkuna	*T. aestivum subsp. aestivum*	Mali	Western Africa	S	HWS
79	PI 494926	ZFA 3145	*T. aestivum subsp. aestivum*	Zambia	Eastern Africa	S	HRS
80	PI 532301	Alas	*T. aestivum subsp. aestivum*	Oman	Western Asia	S	SRS
81	PI 573754	NSGC 531	*T. aestivum subsp. aestivum*	Honduras	Central America	S	HRS

Table 2 Detailed information for 188 *Triticum* and *Aegilops* germplasm collected from GRIN platform through USDA *(Continued)*

82	PI 591964	EMBRAPA 16	*T. aestivum subsp. aestivum*	Brazil	South America	S	HRS
83	PI 639354	TJK03-128	*T. aestivum subsp. aestivum*	Tazikistan	South Central Asia	S	SWS
84	PI 648894	Dickson's No. 444	*T. aestivum subsp. aestivum*	Argentina	South America	S	HWS
85	Cltr 14108	Chinese Spring	*T. aestivum subsp. aestivum*	USA	Northern America	S	SRS
86	PI 434642	TINCURRIN	*T. aestivum subsp. compactum*	Australia	More cancer especially skin cancer	S	Club wheat
87	PI 190963	Spelta Hohenheim	*T. aestivum subsp. spelta*	Portugal	Southern Europe	S	Spelt
88	PI 348710	69Z6.894	*T. aestivum subsp. spelta*	Spain	Southern Europe	S	Spelt
89	PI 355625	Spelta 34	*T. aestivum subsp. spelta*	Belgium	Western Europe	S	Spelt
90	PI 591895	NA	*T. aestivum subsp. spelta*	Germany	Central Europe	W	Spelt
91	PI 367199	128	*T. aestivum subsp. spelta*	Afghanistan	Central Asia	W	Spelt
92	PI 538510	G2830	*T. monococcum subsp. aegilopoides*	Iraq	Center of origin, Western Asia	S	Wild einkorn
93	PI 167526	2485	*T. monococcum subsp. aegilopoides*	Turkey	Western Asia	S	Wild einkorn
94	PI 266844	87	*T. monococcum subsp. aegilopoides*	Uk	Northern Europe	S	Wild einkorn
95	PI 427990	G3114	*T. monococcum subsp. aegilopoides*	Lebanon	Center of domestication	W	Wild einkorn
96	PI 427304	G1764	*T. timopheevii subsp. armeniacum*	Armenia	Center of origin, Western Asia	W	Wild timopheevii
97	PI 538478	G2633	*T. timopheevii subsp. armeniacum*	Iraq	Center of domestication	W	Wild timopheevii
98	PI 70738	22	*T. turgidum subsp. carthlicum*	Iraq	Center of origin, Western Asia	S	Persian wheat
99	PI 532501	H83-1537	*T. turgidum subsp. carthlicum*	Soviet Union		S	Persian wheat
100	PI 471808	G-485-5 M	*T. turgidum subsp. dicoccoides*	Israel	Center of domestication	W	Wild emmer
101	PI 471778	G-40-1-2B-1 M	*T. turgidum subsp. dicoccoides*	Israel	Center of domestication	W	Wild emmer
102	PI 2789	Yaroslav Spring	*T. turgidum subsp. dicoccon*	Russia	Fourth highest producer of wheat	S	Cultivated emmer
103	PI 73388	2868	*T. turgidum subsp. dicoccon*	Armenia	Center of origin, Western Asia	S	Cultivated emmer
104	PI 79899	N-64	*T. turgidum subsp. dicoccon*	China	Least breast cancer, highest producer of wheat	S	Cultivated emmer
105	PI 190920	2323A	*T. turgidum subsp. dicoccon*	Portugal	Southern Europe	S	Cultivated emmer
106	PI 191390	Rufum	*T. turgidum subsp. dicoccon*	Ethiopia	Eastern Africa	S	Cultivated emmer
107	PI 308879	NA	*T. turgidum subsp. dicoccon*	Spain	Southern Europe	S	Cultivated emmer
108	PI 355483	T 563	*T. turgidum subsp. dicoccon*	Spain	Southern Europe	S	Cultivated emmer
109	PI 355485	T 567	*T. turgidum subsp. dicoccon*	Spain	Southern Europe	S	Cultivated emmer
110	PI 499973	KU 1533	*T. turgidum subsp. dicoccon*	Armenia	Center of origin, Western Asia	S	Cultivated emmer
111	PI 154582	NA	*T. turgidum subsp. dicoccon*	Taiwan	Eastern Asia	S	Cultivated emmer
112	Cltr 15185	Hudeiba 154	*T. turgidum subsp. durum*	Sudan	Northern Africa	S	Durum or macaroni
113	PI 9130	Saragolla	*T. turgidum subsp. durum*	Italy	Southern Europe	S	Durum or macaroni

Table 2 Detailed information for 188 *Triticum* and *Aegilops* germplasm collected from GRIN platform through USDA *(Continued)*

114	PI 54432	Tripshiro	*T. turgidum subsp. durum*	Libya	Northern Africa	S	Durum or macaroni
115	PI 67341	Huguenot	*T. turgidum subsp. durum*	Australia	More cancer especially skin cancer	S	Durum or macaroni
116	PI 78809	CI 10107	*T. turgidum subsp. durum*	Georgia	Western Asia	S	Durum or macaroni
117	PI 81792	Marching No. 8	*T. turgidum subsp. durum*	Japan	Eastern Asia	S	Durum or macaroni
118	PI 94701	390	*T. turgidum subsp. durum*	Ancient Palestine	Western Asia	S	Durum or macaroni
119	PI 133459	Durum H2	*T. turgidum subsp. durum*	Egypt	Center of origin, Northern Africa	S	Durum or macaroni
120	PI 153726	Sicilian	*T. turgidum subsp. durum*	N. Africa	Less cancers	S	Durum or macaroni
121	PI 157955	Francesone	*T. turgidum subsp. durum*	Italy	Southern Europe	S	Durum or macaroni
122	PI 174645	Huguenot	*T. turgidum subsp. durum*	Australia	More cancer especially skin cancer	S	Durum or macaroni
123	PI 182113	S-44	*T. turgidum subsp. durum*	Pakistan	South Central Asia	S	Durum or macaroni
124	PI 184532	Russia	*T. turgidum subsp. durum*	Russia	Europe	S	Durum or macaroni
125	PI 208908	Mendola	*T. turgidum subsp. durum*	Iraq	Center of origin	S	Durum or macaroni
126	PI 208910	Sin El-Jamil	*T. turgidum subsp. durum*	Iraq	Center of origin	S	Durum or macaroni
127	PI 210848	7979	*T. turgidum subsp. durum*	Iran	South Central Asia	S	Durum or macaroni
128	PI 221702	11	*T. turgidum subsp. durum*	Indonesia	Southern Eastern Asia	S	Durum or macaroni
129	PI 231380	Saragolla	*T. turgidum subsp. durum*	Italy	Oldest durum variety in Italy	S	Durum or macaroni
130	PI 261823	Namra	*T. turgidum subsp. durum*	Saudi Arabia	Western Asia	S	Durum or macaroni
131	PI 265017	796	*T. turgidum subsp. durum*	Serbia	Southern Europe	S	Durum or macaroni
132	PI 278223	Gartons Early Cone	*T. turgidum subsp. durum*	UK	Northern Europe	W	Durum or macaroni
133	PI 278258	Greece 1	*T. turgidum subsp. durum*	Greece	Southern Europe	S	Durum or macaroni
134	PI 278509	Valencia 6	*T. turgidum subsp. durum*	Spain	Southern Europe	S	Durum or macaroni
135	PI 278553	Tripolitco	*T. turgidum subsp. durum*	Cyprus	Western Asia	S	Durum or macaroni
136	PI 283853	China 34	*T. turgidum subsp. durum*	China	Least breast cancer, highest producer of wheat	S	Durum or macaroni
137	PI 306571	R.S.N.	*T. turgidum subsp. durum*	Italy	Southern Europe	S	Durum or macaroni
138	PI 325850	PW 3	*T. turgidum subsp. durum*	India	Least breast cancer, second highest producer of wheat	S	Durum or macaroni
139	PI 361149	Bijaga Yellow	*T. turgidum subsp. durum*	India	Least breast cancer, second highest producer of wheat	S	Durum or macaroni
140	PI 362046	C 1138/63	*T. turgidum subsp. durum*	Romania	Eastern Europe	W	Durum or macaroni

Table 2 Detailed information for 188 *Triticum* and *Aegilops* germplasm collected from GRIN platform through USDA *(Continued)*

141	PI 422295	QUILAFEN	*T. turgidum subsp. durum*	Chile	South America	S	Durum or macaroni
142	PI 422297	SINCAPE 90	*T. turgidum subsp. durum*	Italy	Southern Europe	S	Durum or macaroni
143	PI 422312	MACS-45	*T. turgidum subsp. durum*	India	Least breast cancer, second highest producer of wheat	S	Durum or macaroni
144	PI 428458	Egypt Local No. 8	*T. turgidum subsp. durum*	Egypt	Center of origin, Northern Africa	S	Durum or macaroni
145	PI 428468	JORDAN 38	*T. turgidum subsp. durum*	Jordan	Center of origin, Western Asia	S	Durum or macaroni
146	PI 428469	JORDAN 40	*T. turgidum subsp. durum*	Jordan	Center of origin, Western Asia	S	Durum or macaroni
147	PI 462107	172	*T. turgidum subsp. durum*	Yemen	Western Asia	S	Durum or macaroni
148	PI 480347	MG 31577	*T. turgidum subsp. durum*	Ethiopia	Eastern Africa	S	Durum or macaroni
149	PI 496260	MEDORA	*T. turgidum subsp. durum*	Canada	North America	S	Durum or macaroni
150	PI 519864	DURUM VARIETY 24	*T. turgidum subsp. durum*	Mexico	North America	S	Durum or macaroni
151	PI 520393	TUNISIAN DURUM 1	*T. turgidum subsp. durum*	Tunisia	Northern Africa	S	Durum or macaroni
152	PI 520394	TUNISIAN DURUM 8	*T. turgidum subsp. durum*	Tunisia	Northern Africa	S	Durum or macaroni
153	PI 520414	ICD 7780-5AP -OSH-OAP	*T. turgidum subsp. durum*	Syria	Center of origin, Western Asia	S	Durum or macaroni
154	PI 520415	SYRIAN DURUM 27	*T. turgidum subsp. durum*	Syria	Center of origin, Western Asia	S	Durum or macaroni
155	PI 542464	SHORT SARAGOLLA	*T. turgidum subsp. durum*	USA	High cancer incidence	S	Durum or macaroni
156	PI 585025	15017	*T. turgidum subsp. durum*	Saudi Arabia	Western Asia	S	Durum or macaroni
157	Cltr 14374	497-360	*T. turgidum subsp. durum*	Lebanon	Western Asia	S	Durum or macaroni
158	Cltr 14802	ELS 6404-122	*T. turgidum subsp. durum*	Eritrea	Eastern Africa	S	Durum or macaroni
159	PI 5465	Candeal	*T. turgidum subsp. durum*	Argentina	South America	F	Durum or macaroni
160	PI 5639	Kubanka	*T. turgidum subsp. durum*	Kazakhstan	South Central Asia, largest consumer of wheat	S	Durum or macaroni
161	PI 35314	1809a	*T. turgidum subsp. durum*	Kyrgyzstan	South Central Asia	F	Durum or macaroni
162	PI 50929	933	*T. turgidum subsp. durum*	Kyrgyzstan	South Central Asia	S	Durum or macaroni
163	PI 61108	6951	*T. turgidum subsp. durum*	Turkmenistan	South Central Asia	S	Durum or macaroni
164	PI 89642	NA	*T. turgidum subsp. durum*	Hondurus	Central America	S	Durum or macaroni
165	PI 278384	Morocco C10895	*T. turgidum subsp. durum*	Morocco	Northern Africa	W	Durum or macaroni
166	PI 286066	NA	*T. turgidum subsp. durum*	Poland	Eastern Europe	S	Durum or macaroni
167	PI 384401	Wurno 2	*T. turgidum subsp. durum*	Nigeria	Western Africa	S	Durum or macaroni

Table 2 Detailed information for 188 *Triticum* and *Aegilops* germplasm collected from GRIN platform through USDA *(Continued)*

168	PI 519759	D 73121	*T. turgidum subsp. durum*	Algeria	Northern Africa	S	Durum or macaroni
169	PI 520164	ALGERIA LINE 47	*T. turgidum subsp. durum*	Algeria	Northern Africa	S	Durum or macaroni
170	PI 532289	Musane	*T. turgidum subsp. durum*	Oman	Western Asia	S	Durum or macaroni
171	PI 565208	Chaggo	*T. turgidum subsp. durum*	Bolivia	South America	S	Durum or macaroni
172	PI 592019	VATAN	*T. turgidum subsp. durum*	Uzbekistan	South Central Asia	S	Durum or macaroni
173	PI 654290	TJK2006:296	*T. turgidum subsp. durum*	Tazikistan	South Central Asia	S	Durum or macaroni
174	Cltr 13165	Langdon	*T. turgidum subsp. durum*	USA	Northern America	W	Durum or macaroni
175	PI 330553	189	*T. turgidum subsp. paleocolchicum*	UK	Northern Europe	S	Cultivated emmer
176	PI 211708	Egypt	*T. turgidum subsp. turanicum*	Egypt	Center of origin, Northern Africa	S	Khorasan or oriental
177	PI 166591	Ak	*T. turgidum subsp. turgidum*	Turkey	Center of origin	S	Rivet or cone
178	PI 167867	4314	*T. turgidum subsp. turgidum*	Turkey	Center of origin	S	Rivet or cone
179	PI 481591	IQ 223	*T. turgidum subsp. turgidum*	Iraq	Center of origin	S	Rivet or cone
180	PI 502933	Fo Shou Mai	*T. turgidum subsp. turgidum*	China	Largest producer	S	Rivet or cone
181	PI 208912	Zerdakia	*T. turgidum subsp. turgidum*	Iraq	Center of origin	S	Rivet or cone
182	PI 438971	AKMOLINKA 2	*T. turgidum subsp. turgidum*	Kazakhstan	South Central Asia	S	Rivet or cone
183	PI 427328	G2264	*T. urartu*	Iraq	Center of origin	S	Wild einkorn
184	PI 428183	G1759	*T. urartu*	Armenia	Center of origin	S	Wild einkorn
185	PI 428279	G3162	*T. urartu*	Lebanon	Center of domestication	W	Wild einkorn
186	PI 355707	69Z5.72	*T. zhukovskyi*	Georgia	Donor for GG genome and cross between *T. timopheevi* and *T. monococcum*	W	Cultivated hexaploid
187	PI 429099	6A-696	*Triticosecale sp.*	Germany	Cross between *T. dicoccum* & *S. cereale*; hexaploid	F	*Tritical* (Rye and durum cross)
188	PI 574284	ASVM4*4654	*T. hybrid*	USA	High cancer incidence	S	*Aegilops squarrosa/T. dicoccum*

A, *Aegilops*; F, Facultative; HRW, Hard red winter; HRS, Hard red spring; HWS, Hard white spring; HWW, Hard white winter; NA, not available; S, Spring; W, Winter; SRS, Soft red spring; SRW, Soft red winter; SWS, Soft white spring; SWW, Soft white winter; T, *Triticum*.

core collection is approximately 0.3% of the world barley holding, and the ICRISAT (International Crops Research Institute for the Semi Arid Crops, Hyderabad, India) sorghum core collection is about 1.5% of the domain size [31,32]. As many of the lines shown (Table 2) are wild accessions, data are not available on genetic and metabolic markers, agronomic and morphological characteristics, thus limiting the descriptive information provided.

Future direction

Having established this core collection and obtained grain for each line from GRIN, the next step in the identification of distinct wheat lines with enhanced biomedical activity is the interrogation of these lines via phytochemical profiles using LC-TOF-MS analysis of wheat grain extracts according to our recently published procedures [9]. The chromatographic data that result will be subjected to advanced multivariate regression techniques that plot multidimensional relationships to define the chemical diversity within the core collection. The same extracts used for metabolic profiling will then be subjected to *in-vitro* biological analysis to assign a relative value for anticancer activity to each wheat line. For wheat lines with the greatest *in-vitro* activity, *in-vivo* testing in appropriate animal cancer models will be conducted. For wheat lines with *in-vivo* anticancer activity, the genetic and metabolomic traits that account for protection will be identified and appropriate experiments conducted to determine the extent to which environmental factors impact the stable expression of the traits of interest [10].

Conclusion

While there has been an active discussion of adding value to wheat through the enhancement of its human health benefits, no systematic approaches have been establish to advance this effort. The work reported herein constitutes the first essential step needed to examine wheat germplasm resources in order to identify health benefits that may exist and to develop them fully for the benefit of the consuming public.

Availability of supporting data

The datasets supporting the results of this article are available in the Germplasm Resources Information Network (GRIN) repository from the United States Department of Agriculture (USDA), http://www.ars-grin.gov/npgs/index.html; in the Food and Agriculture Organization of the United States (FAOSTAT) repository from the World Health Organization, http://faostat3.fao.org/home/index.html#COMPARE; and in the GLOBOCAN repository from the International Agency for Research on Cancer (IARC), http://globocan.iarc.fr.

Abbreviations

ASR: Age-standardized rate per 100,000 individuals; CC: Core collection; GRIN: Germplasm Resources Information Network; mt: Metric tons; PI: Plant introduction.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MS directed the selection of specific species from GRIN, SM participated in data analysis and germplasm selection, and HT provided overall direction and specific guidance relative to interpretation of the cancer prevalence data. All authors participated in writing the manuscript. All authors read and approved the final manuscript.

Authors' information

MS is a Research Associate in the Department of Soil and Crop Sciences, SM is a doctoral candidate in the Cell and Molecular Biology Program, and HT directs the Cancer Prevention Laboratory at Colorado State University.

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