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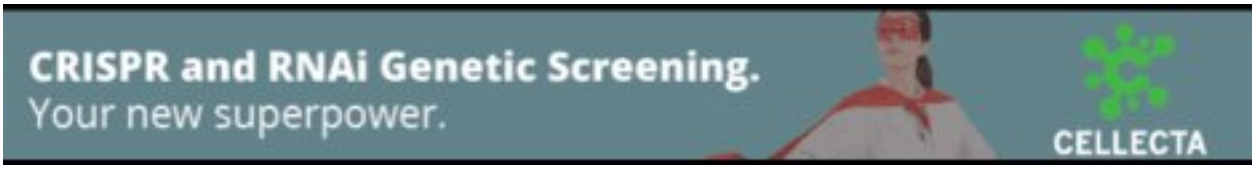

LETTER

A Collection of 1814 Human Chromosome 7-Specific STSs

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An established goal of the ongoing Human Genome Project is the development and mapping of sequence-tagged sites (STSs) every 100 kb, on average, across all human chromosomes. En route to constructing such a physical map of human chromosome 7, we have generated 1814 chromosome 7-specific STSs. The corresponding PCR assays were designed by the use of DNA sequence determined in our laboratory (79%) or generated elsewhere (21%) and were demonstrated to be suitable for screening yeast artificial chromosome (YAC) libraries. This collection provides the requisite landmarks for constructing a physical map of chromosome 7 at <100-kb average spacing of STSs.

The relevant information about these STSs is available electronically in the STS Division of GenBank (dbSTS) and the Genome Database (GDB) as well as in a summary table available at http://www.cshl.org/gr or http://www.nchgr.nih.gov/DIR/GTB/CHR7.

A central activity of the Human Genome Project is the construction of highly annotated physical maps of all human chromosomes. These maps will in turn be used as an organizational framework for generating the first-generation sequence of the human genome. The widely adopted paradigm for constructing physical maps of human DNA is based on the use of sequence-tagged sites (STSs) as the mapping landmarks (Olson et al. 1989). STSs and their corresponding PCR assays have been found to be well suited for analyzing various mapping reagents, particularly yeast artificial chromosomes (YACs) (Green and Olson 1990a; Green and Green 1991) and, increasingly, radiation hybrid cell lines (Cox et al. 1990; Walter et al. 1994; Gyapay et al. 1996).[1]

A programmatic goal of the Human Genome Project in the United States is the mapping of STSs at roughly 100-kb spacing across the human genome (Collins and Galas 1993). This will require the generation and mapping of at least 30,000 STSs, each of which will be associated with a unique PCR assay. Not surprisingly, a major effort in recent years has been directed toward the large-scale development of STSs from human DNA. In addition to numerous reports of establishing small numbers of STSs, large sets of STSs have been developed in a targeted approach for individual human chromosomes [including chromosomes 3 (Naylor et al. 1996), 4 (Goold et al. 1993), 5 (Grady et al. 1996), 7 (Green et al. 1991a), 10 (Zheng et al. 1994), 11 (Smith et al. 1993; James et al. 1994; Quackenbush et al. 1995), 12 (Krauter et al. 1995), 21 (Chumakov et al. 1992), 22 (Hudson et al. 1994; Bell et al. 1995; Collins et al. 1995), X (Ciccodicola et al. 1994; Nelson et al. 1995), and Y (Foote et al. 1992; Vollrath et al. 1992)] as well as in a more genome-wide fashion [including from random sequences (Hudson et al. 1995), short tandem repeat polymorphisms (Weissenbach et al. 1992; Buetow et al. 1994; Gyapay et al. 1994; Murray et al. 1994; Sheffield et al. 1995; Utah Marker Development Group 1995; Dib et al. 1996; Sunden et al. 1996), and expressed-sequence tags (ESTs) (Polymeropoulos et al. 1993; Berry et al. 1995)].

Our interest has focused on constructing a YAC-based STS-content map of human chromosome 7 (Green et al. 1991a, 1994, 1995a), a genomic segment that contains a predicted ~170 Mb of DNA

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STS Name	Alias	Source	STS Accession	Source GenBank Accession	GDB Accession	GDB Cross-Reference
sWSS10	PGY1	Gene	G19985	M29423	GDB:583426	GDB:120712
sWSS143		Lambda Clone	L10545		GDB:204758	
sWSS604		Alu-PCR Product	G00315		GDB:1317156	
sWSS858		Random Probe	G19996	X16414	GDB:375879	GDB:178549
sWSS874		Random YAC Insert	L23747		GDB:269356	
sWSS1017		YAC End (yWSS598-R)	G12531		GDB:1317242	
sWSS1147	AFM032xa1	Genetic Marker	G18243	Z16455	GDB:307649	GDB:187853
sWSS2535	HUM0S15D12	EST	G18339	D12064	GDB:3754594	GDB:214548

Figure 1 Representative sample of the electronic summary table containing relevant information about the chromosome 7-specific STSs. The 1814 STSs reported here are summarized in an electronic table that can be accessed through the World Wide Web at http://www.cshl.org/gr or http://www.nchgr.nih.gov/DIR/GTB/CHR7. For each STS, the following information is provided: STS name (in each case starting with the prefix "sWSS" followed by a unique number), relevant alias (such as the name of the corresponding genetic marker or gene/EST, if one exists), source of the sequence from which the STS was derived [(Gene) known gene; (Lambda Clone) chromosome 7-specific lambda clone; (Alu-PCR Product) *Alu*-PCR product generated from chromosome 7 DNA; (Random Probe) random chromosome 7-specific DNA probe; (Random YAC Insert) random DNA segment derived from YAC; (YAC End) isolated YAC insert end; (Genetic Marker) short tandem repeat polymorphism, and (EST) expressed-sequence tag], STS accession no. in GenBank, source GenBank accession no. (for those STSs developed from sequences with other GenBank records), GDB accession no., and relevant cross-reference GDB accession no. (if one exists). Note that for STSs developed from YAC insert ends, the clone from which the STS was derived is indicated in parenthesis [with its name starting with the prefix "yWSS" followed by a unique number (Green et al. 1995a)] along with an L or R (corresponding to the left/centric or right/acentric insert end of the YAC, respectively). The complete table is sorted by STS name and contains "hotlinks" (shown in blue) to the corresponding GenBank and GDB records or field definitions. An electronic tool that allows searching of the table by STS name, alias, source, or relevant accession no. (GenBank or GDB) is also available at http://www.nchgr.nih.gov/DIR/GTB/CHR7.

(Trask et al. 1989; Morton 1991) and corresponds to ~5% of the human genome. Thus, the generation of a 100-kb STS map of this chromosome will necessitate the targeted development of at least 1700 STSs. Previously we have described methods for the generation of chromosome-specific STSs (Green et al. 1991a; Green 1993) and have reported the development of the first 100 chromosome 7-specific STSs (Green et al. 1991a) as well as much smaller sets of STSs from specific regions of the chromosome (Green et al. 1995b; Johnson et al. 1995; Keen et al. 1995; Torigoe et al. 1995; Hoglund et al. 1996; McGuire et al. 1996). Here we report a comprehensive update of our efforts, which has to date resulted in the development of 1814 chromosome 7-specific STSs.

RESULTS AND DISCUSSION

As part of a large-scale effort to construct a YAC-based STS-content map of human chromosome 7, we have developed a set of 1814 STS-specific PCR assays corresponding to chromosome 7 DNA. These efforts have involved the generation of STSs from a diversity of sources, including completely random sequences as well as those selectively chosen based on their putative location on the evolving physical map, close proximity to a marker on the genetic map, or presence in a gene or EST. In general, our strategies for STS generation were tailored for the establishment of PCR assays suitable for screening YAC libraries, as described (Green and Olson 1990b; Green 1995).

The majority (79%) of the STSs reported here were developed using DNA sequence data generated in our laboratory, primarily from YACs (in particular, YAC insert ends), lambda clones, and *Alu*-PCR products derived from monochromosomal human–hamster hybrid cell lines (containing chromosome 7 as their only human DNA). Of note, the availability of a chromosome 7-specific YAC library, constructed from such a hybrid cell line and containing a low fraction of chimeric clones (Green et al. 1991b, 1995a), allowed us to emphasize the development of STSs from YAC insert ends. The latter STSs facilitate the establishment of long-range clone coverage by maximizing the likelihood that overlaps among YACs will be identified (Green and Green 1991; Palazzolo et al. 1991; Kere et al. 1992). As a result, our largest class of STSs corresponds to YAC insert ends.

For the remaining STSs (21%), the corresponding PCR assays were designed using DNA sequence data generated in other laboratories. Most of these STSs reflect genomic landmarks that allow integration of our physical map with other maps of the chromosome, such as genetic maps and transcript (or gene/EST) maps. In particular, we have made a concerted effort to establish PCR assays corresponding to short tandem repeat polymorphisms mapped

by others to chromosome 7. We have found that, in most instances, it is best to design pairs of oligonucleotide primers that anneal on the same side of the polymorphic tract (rather than flanking it) (Green et al. 1994). The resulting PCR assays tend to be more robust and, therefore, more suitable for screening YAC libraries.

In summary, we have extended our earlier STS-development efforts (Green et al. 1991a, 1995b; Johnson et al. 1995; Keen et al. 1995; Torigoe et al. 1995; Hoglund et al. 1996; McGuire et al. 1996) and now report the establishment of 1814 human chromosome 7-specific STSs. To our knowledge, this is the largest single set of STSs developed for any individual human chromosome. These STSs are being used to construct a YAC-based STS-content map of chromosome 7 (G.G. Bouffard, J.R. Idol, V.V. Braden, L.M. Iyer, A.F. Cunningham, L.A. Weintraub, J.W. Touchman, R.M. Mohr-Tidwell, D.C. Peluso, R.S. Fulton, et al., in prep.). The relevant information about all of these STSs has been deposited into both the STS Division of GenBank (dbSTS) and the Genome Database (GDB), with a summary table available electronically at http://www.cshl.org/gr or http://www.nchgr.nih.gov/DIR/GTB/CHR7. A representative sample from this electronic summary table is provided in Figure 1.

METHODS

The development and characterization of PCR assays corresponding to chromosome 7-specific STSs have been described (Green et al. 1991a; Green 1993). In brief, single-pass DNA sequence was acquired either in our laboratory (mostly from YACs, lambda clones, or *Alu*-PCR products derived from chromosome 7 DNA) or from other investigators (mostly from short tandem repeat polymorphisms and genes/ESTs). In almost all instances, oligonucleotide primers suitable for PCR were selected using the program OSP (Hillier and Green 1991). For inclusion among the STSs reported here, the corresponding PCR assay must have amplified the appropriate-sized product from human genomic DNA, the DNA from human–rodent hybrid cell lines containing (but not those devoid of) human chromosome 7, and yeast DNA containing small amounts of human genomic DNA (Green et al. 1991a; Green 1993), but not from yeast DNA alone.

All relevant information about the STSs reported here has been deposited into the STS Division of GenBank (dbSTS) at the National Center for Biotechnology Information as well as into GDB. For those STSs developed using sequence data generated in other laboratories, appropriate cross-references to the original sequences are included in the GenBank and GDB records.

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