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Table S1: **Accession numbers** of deep sequencing reads datasets from *H. sapiens* of Gene Expression Omnibus (GEO) and Sequence Read Archive (SRA) database at NCBI. These datasets were used to predict structural clusters from deep sequencing reads (red and green paths, Figure 1).

| Database | Accession numbers                      |
|----------|----------------------------------------|
| GEO      | GSE10829,     GSE13483,    GSE13370,  |
|          | GSE14362                                             |
| SRA      | SRR015446,   SRR015447,   SRR015448,               |
|          | SRR038852,   SRR038853,   SRR038854,               |
|          | SRR038855,   SRR038856,   SRR038857,               |
|          | SRR038858,   SRR038859,   SRR038860,               |
|          | SRR038861,   SRR038862,   SRR038863 |
| Class                          | # genes | subclasses                                      |
|-------------------------------|---------|------------------------------------------------|
| Cellular Processes            | 1154    | 413 Cell Communication                         |
|                               |         | 305 Cell Growth and Death                      |
|                               |         | 214 Cell Motility                              |
|                               |         | 431 Transport and Catabolism                   |
| Environmental Information Processing | 1548    | 68 Membrane Transport                          |
|                               |         | 784 Signaling Molecules and Interaction        |
|                               |         | 907 Signal Transduction                        |
| Genetic Information Processing | 699     | 279 Folding, Sorting and Degradation           |
|                               |         | 119 Replication and Repair                     |
|                               |         | 192 Transcription                              |
|                               |         | 128 Translation                                |
| Human Diseases                | 1216    | 380 Cancers                                    |
|                               |         | 181 Cardiovascular Diseases                    |
|                               |         | 224 Immune System Diseases                     |
|                               |         | 326 Infectious Diseases                        |
|                               |         | 105 Metabolic Diseases                         |
|                               |         | 323 Neurodegenerative Diseases                 |
| Metabolism                    | 1486    | 262 Amino Acid Metabolism                      |
|                               |         | 317 Carbohydrate Metabolism                    |
|                               |         | 163 Energy Metabolism                          |
|                               |         | 225 Glycan Biosynthesis and Metabolism         |
|                               |         | 339 Lipid Metabolism                           |
|                               |         | 187 Metabolism of Cofactors and Vitamins       |
|                               |         | 23 Metabolism of Terpenoids and Polyketides    |
|                               |         | 186 Nucleotide Metabolism                      |
|                               |         | 108 Xenobiotics Biodegradation and Metabolism  |
|                               |         | 104 Metabolism of Other Amino Acids            |
|                               |         | 11 Biosynthesis of Other Secondary Metabolites |
| Organismal systems            | 1890    | 197 Circulatory System                         |
|                               |         | 150 Development                                |
|                               |         | 423 Endocrine System                           |
|                               |         | 13 Environmental Adaptation                    |
|                               |         | 126 Excretory System                           |
|                               |         | 801 Immune System                              |
|                               |         | 213 Nervous System                             |
|                               |         | 448 Sensory System                             |

**Table S2**: Description of KEGG classes used for Figures 3, S1, S2. For each class (first column), the number of genes in the class (second column) and in the corresponding subclasses (third and fourth column) are reported.
| Chromosome | #predictions with paralogs | #predictions from deep sequencing data | #predictions with paralogs / deep sequencing data combination |
|------------|---------------------------|--------------------------------------|------------------------------------------------------------|
|            | #total | in intronic regions | in intergenic regions | #total | in intronic regions | in intergenic regions | #total | in intronic regions | in intergenic regions |
| 1          | 11     | 8                   | 6                     | 14     | 8                   | 6                     | 2       | 1                   | 1                     |
| 2          | 27     | 13                  | 14                    | 7       | 4                   | 3                     | 1       | 1                   | 0                     |
| 3          | 20     | 8                   | 12                    | 6       | 4                   | 2                     | 1       | 1                   | 0                     |
| 4          | 17     | 6                   | 11                    | 1       | 1                   | 0                     | 1       | 1                   | 0                     |
| 5          | 11     | 7                   | 4                     | 7       | 2                   | 5                     | 0       | 0                   | 0                     |
| 6          | 21     | 7                   | 14                    | 2       | 2                   | 0                     | 0       | 0                   | 0                     |
| 7          | 20     | 15                  | 5                     | 5       | 5                   | 0                     | 6       | 1                   | 2                     |
| 8          | 16     | 9                   | 7                     | 7       | 7                   | 0                     | 0       | 0                   | 0                     |
| 9          | 16     | 7                   | 9                     | 3       | 1                   | 2                     | 1       | 1                   | 0                     |
| 10         | 17     | 6                   | 11                    | 3       | 3                   | 0                     | 2       | 0                   | 2                     |
| 11         | 9      | 5                   | 4                     | 5       | 5                   | 0                     | 0       | 0                   | 0                     |
| 12         | 15     | 6                   | 9                     | 3       | 3                   | 0                     | 0       | 0                   | 0                     |
| 13         | 11     | 6                   | 5                     | 3       | 2                   | 1                     | 0       | 0                   | 0                     |
| 14         | 6      | 2                   | 4                     | 7       | 3                   | 4                     | 1       | 0                   | 1                     |
| 15         | 10     | 5                   | 5                     | 3       | 1                   | 2                     | 0       | 0                   | 0                     |
| 16         | 16     | 6                   | 10                    | 6       | 6                   | 0                     | 0       | 0                   | 0                     |
| 17         | 7      | 3                   | 4                     | 6       | 4                   | 2                     | 0       | 0                   | 0                     |
| 18         | 3      | 1                   | 2                     | 1       | 0                   | 1                     | 0       | 0                   | 0                     |
| 19         | 10     | 4                   | 6                     | 4       | 2                   | 2                     | 1       | 0                   | 1                     |
| 20         | 6      | 4                   | 2                     | 1       | 0                   | 1                     | 1       | 0                   | 1                     |
| 21         | 7      | 6                   | 1                     | 0       | 0                   | 0                     | 0       | 0                   | 0                     |
| 22         | 4      | 3                   | 1                     | 2       | 2                   | 0                     | 3       | 1                   | 2                     |
| X          | 20     | 8                   | 12                    | 3       | 1                   | 2                     | 0       | 0                   | 0                     |
| Total      | 300    | 142                 | 158                   | 99      | 66                  | 35                    | 20      | 10                  | 10                   |

**Table S3: Predictions on human chromosomes: details of Table 1.** For each human chromosome, the total number of predictions, the number of predictions in intronic regions and the number of predictions in intergenic regions obtained with the three kinds of input proposed by the algorithm are reported. Predictions made using the *ab initio* method (black path, Figure 1) are filtered with RepeatMasker and/or with EST data. All predictions are filtered with genomic information and do not overlap neither CDS nor exons (on either strands). (Notice that in genbank files, a gene, identified with "gene" tag, is derived by automated computational analysis using gene prediction methods and it is decomposed in exons ("exon" tags are used) or in CDSs ("CDS" tags).) When two structural clusters overlap on each strand, only one is counted in the table.
| Chromosome | #SC in first 5% of chromosome | #SC in last 5% of chromosome | Percentage of SC in terminal chromosomal regions |
|------------|-------------------------------|------------------------------|-----------------------------------------------|
| 1          | 8                             | 1                            | 33.33%                                        |
| 2          | 4                             | 11                           | 42.86%                                        |
| 3          | 3                             | 8                            | 40.74%                                        |
| 4          | 7                             | 5                            | 63.16%                                        |
| 5          | 4                             | 5                            | 50.00%                                        |
| 6          | 3                             | 5                            | 34.78%                                        |
| 7          | 9                             | 9                            | 58.06%                                        |
| 8          | 8                             | 6                            | 60.87%                                        |
| 9          | 1                             | 3                            | 20.00%                                        |
| 10         | 5                             | 4                            | 40.91%                                        |
| 11         | 4                             | 0                            | 28.57%                                        |
| 12         | 3                             | 4                            | 38.89%                                        |
| 13         | 0                             | 8                            | 57.14%                                        |
| 14         | 0                             | 4                            | 28.57%                                        |
| 15         | 0                             | 0                            | 0.00%                                         |
| 16         | 3                             | 6                            | 39.13%                                        |
| 17         | 3                             | 4                            | 53.85%                                        |
| 18         | 0                             | 4                            | 100.00%                                       |
| 19         | 1                             | 2                            | 20.00%                                        |
| 20         | 1                             | 3                            | 50.00%                                        |
| 21         | 0                             | 4                            | 57.14%                                        |
| 22         | 0                             | 5                            | 55.56%                                        |
| X          | 11                            | 0                            | 52.38%                                        |

**Table S4: Number of structural clusters (SC) located in terminal regions of human chromosomes.** The number of SC located in the first 5% (second column) and last 5% (third column) of each chromosome are reported together with the corresponding percentage of SC located in terminal regions (fourth column).
Table S5: Analysis of reads overlapping miRNA/miRNA* in structural clusters. For each human chromosome, the number of reads overlapping miRNAs and miRNA*s (where a read and a miRNA/miRNA* share at least a nucleotide), the number of reads “contained” in stretched miRNAs and miRNA*s (where, following (Friedländer et al. 2008), the alignment can extend the miRNA or the miRNA* on the 5’-end by at most 2nt and the 3’-end by at most 5nt), the percentage of reads contained in stretched miRNAs or miRNA*s (computed as the sum of the fourth and fifth columns divided by the seventh column in this table), the number of reads in structural clusters (SC), and the mean number of reads in SCs are given. Notice that when a miRNA and its miRNA* are close to a loop and a read covers the loop, then it might overlap both sequences. The same might hold for miRNA1/miRNA1* and miRNA2/miRNA2* lying in the same structural cluster, where a read might overlap some nucleotides in both pairs. In chromosome 16, notice that there is a single miRNA overlapping many reads (3686) with a large part of them (2805) that include the miRNA. In chromosome 17, there is a structural cluster that contains essentially all reads of the chromosome overlapping some SC (that is more than 41000); such reads do not lie exactly on a miRNA but they overlap it. In particular, notice that our method chooses miRNA sequences based on best energy matching and not on reads multiplicity. We fall very close to reads accumulation nevertheless. The situation is analogous for chromosome 15 containing 2 structural clusters that behave as the one in chromosome 17.
**Table S6: Analysis of reads overlapping miRNA/miRNA* in structural clusters.** Analysis reported in Table S5, continued. The number of SCs overlapped by a variable number of reads is reported.

| Chromosome | < 100 | ≥ 100& < 500 | ≥ 500& < 1000 | ≥ 1000& < 2000 | ≥ 2000& < 3000 | ≥ 3000& < 4000 | ≥ 4000& < 5000 | ≥ 5000 |
|------------|-------|--------------|---------------|----------------|----------------|----------------|----------------|-------|
| 1          | 10    | 1            | 0             | 0              | 0              | 0              | 2              | 1     |
| 2          | 7     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 3          | 6     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 4          | 1     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 5          | 4     | 1            | 2             | 0              | 0              | 0              | 0              | 0     |
| 6          | 2     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 7          | 5     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 8          | 7     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 9          | 3     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 10         | 3     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 11         | 5     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 12         | 2     | 0            | 0             | 0              | 0              | 0              | 0              | 1     |
| 13         | 1     | 0            | 0             | 0              | 0              | 0              | 0              | 2     |
| 14         | 2     | 0            | 0             | 4              | 0              | 0              | 0              | 1     |
| 15         | 3     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 16         | 5     | 0            | 0             | 0              | 0              | 1              | 0              | 0     |
| 17         | 4     | 0            | 0             | 0              | 0              | 0              | 1              | 1     |
| 18         | 1     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 19         | 4     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 20         | 1     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 21         | 0     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| 22         | 2     | 0            | 0             | 0              | 0              | 0              | 0              | 0     |
| X          | 0     | 0            | 2             | 0              | 0              | 0              | 0              | 1     |
| **Total**  | **78**| **2**        | **2**         | **6**          | **0**          | **1**          | **3**          | **7** |

**Table S7: Structural clusters** predicted from deep sequencing data and constituted by reads coming from the same experiment. The names refer to the nomenclature used in file SLSCs.xls where a description of their localisation along the chromosomes is given. File SLSCs.xls reports the experimental dataset where reads in a structural cluster were found.
| class                          | subclass                                      | pathway                           | # genes | % chromosomes | % covered genes | P-value |
|-------------------------------|-----------------------------------------------|-----------------------------------|---------|---------------|-----------------|---------|
| hsa04540 Cellular Processes   | Cell Communication                           | Gap junction                      | 90      | 42.69         | 72.22           | 0.008   |
| hsa04210 Cellular Processes   | Cell Growth and Death                         | Apoptosis                         | 87      | 21.53         | 44.82           | 0.032   |
| hsa04144 Cellular Processes   | Transport and Catabolism                      | Endocytosis                        | 201     | 24.78         | 45.77           | 0.014   |
| hsa04142 Cellular Processes   | Transport and Catabolism                      | Lysosome                          | 121     | 42.69         | 69.42           | 0.028   |
|                               | Cellular Processes                            | Transport and Catabolism           | 431     | 24.78         | 45.01           | 0.001   |
| hsa04340 Environmental        | Signal Transduction                           | Hedgehog signaling pathway        | 56      | 55.80         | 83.92           | 0.048   |
| Information Processing        |                                               |                                   |         |               |                 |         |
| hsa04330 Environmental        | Signal Transduction                           | Notch signaling pathway           | 47      | 10.46         | 38.29           | 0.017   |
| Information Processing        |                                               |                                   |         |               |                 |         |
| hsa04310 Environmental        | Signal Transduction                           | Wnt signaling pathway             | 150     | 27.86         | 52.66           | 0.015   |
| Information Processing        |                                               |                                   |         |               |                 |         |
| hsa03440 Genetic Information  | Replication and Repair                        | Homologous recombination          | 28      | 42.69         | 75              | 0.082   |
| Processing                     |                                               |                                   |         |               |                 |         |
| hsa03040 Genetic Information  | Replication and Repair                        | all                               | 119     | 48.79         | 73.1            | 0.058   |
| Processing                     |                                               |                                   |         |               |                 |         |
| hsa05216 Human Diseases       | Cancers                                       | Thyroid cancer                    | 20      | 33.52         | 68.96           | 0.055   |
|                              |                                               |                                   |         |               |                 |         |
| hsa05416 Human Diseases       | Cardiovascular Diseases                       | Viral myocarditis                 | 70      | 27.86         | 68.57           | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05330 Human Diseases       | Immune System Diseases                        | Allograft rejection               | 35      | 27.86         | 80              | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05310 Human Diseases       | Immune System Diseases                        | Asthma                            | 28      | 40.54         | 96.42           | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05332 Human Diseases       | Immune System Diseases                        | Graft-versus-host disease         | 37      | 27.86         | 81.08           | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05322 Human Diseases       | Immune System Diseases                        | Systemic lupus erythematosus      | 138     | 30.79         | 68.84           | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05130 Human Diseases       | Immune System Diseases                        | all                               | 224     | 36            | 65.17           | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05131 Human Diseases       | Infectious Diseases                           | Pathogenic Escherichia coli infection | 58     | 27.86         | 63.79           | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05131 Human Diseases       | Infectious Diseases                           | Shigellosis                       | 63      | 40.54         | 73.01           | 0.005   |
|                              |                                               |                                   |         |               |                 |         |
| hsa04940 Human Diseases       | Metabolic Diseases                            | Type 1 diabetes mellitus          | 41      | 27.86         | 73.17           | <0.001  |
|                              |                                               |                                   |         |               |                 |         |
| hsa05016 Human Diseases       | Neurodegenerative Diseases                    | Huntington's disease              | 177     | 18.11         | 37.85           | 0.035   |
|                              |                                               |                                   |         |               |                 |         |
| hsa0516 Human Diseases        | Neurodegenerative Diseases                    | all                               | 323     | 18.11         | 34.98           | 0.072   |

**Table S8**: KEGG’s pathways or KEGG’s subclasses whose genes are covered by structural cluster regions in a highly non random manner. For each pathway or subclass, the corresponding curve is reported in Figures S1. The P-value associated to the best point in the curve is given. The coordinates of this point are described. Only pathways or subclasses with associated P-values < 0.1 are listed.
| class | subclass | pathway | # genes | % chromosomes | % covered genes | P-value |
|-------|----------|---------|---------|--------------|----------------|---------|
| hsa00053 | Metabolism | Carbohydrate Metabolism | Ascorbate and aldarate metabolism | 25 | 36 | 88 | <0.001 |
| hsa00051 | Metabolism | Carbohydrate Metabolism | Fructose and mannose metabolism | 34 | 33.52 | 67.64 | 0.007 |
| hsa00049 | Metabolism | Carbohydrate Metabolism | Pentose and glucuronate interconversions | 28 | 40.54 | 89.28 | <0.001 |
| hsa00534 | Metabolism | Glycan Biosynthesis and Metabolism | Glycosaminoglycan biosynthesis - heparan sulfate | 26 | 33.52 | 65.38 | 0.092 |
| hsa00511 | Metabolism | Glycan Biosynthesis and Metabolism | Other glycan degradation | 16 | 10.46 | 50 | 0.02 |
| hsa00140 | Metabolism | Lipid Metabolism | Steroid hormone biosynthesis | 55 | 58.90 | 94.54 | <0.001 |
| hsa00860 | Metabolism | Metabolism of Co-factors and Vitamins | Porphyrin and chlorophyll metabolism | 42 | 40.54 | 69.04 | 0.055 |
| hsa00830 | Metabolism | Metabolism of Co-factors and Vitamins | Retinol metabolism | 64 | 38.35 | 70.31 | 0.011 |
| hsa00900 | Metabolism | Metabolism of Terpenoids and Polyketides | Terpenoid backbone biosynthesis | 15 | 14.46 | 53.33 | 0.029 |
| hsa00230 | Metabolism | Nucleotide Metabolism | Purine metabolism | 159 | 30.79 | 52.83 | 0.093 |
| hsa00982 | Metabolism | Xenobiotics Biodegradation and Metabolism | Drug metabolism - cytochrome P450 | 72 | 52.46 | 84.72 | <0.001 |
| hsa00983 | Metabolism | Xenobiotics Biodegradation and Metabolism | Drug metabolism - other enzymes | 51 | 42.69 | 82.35 | <0.001 |
| hsa00980 | Metabolism | Xenobiotics Biodegradation and Metabolism | Metabolism of xenobiotics by cytochrome P450 | 70 | 52.46 | 85.71 | 0.003 |
| Metabolism | Metabolism | Xenobiotics Biodegradation and Metabolism | all | 108 | 52.46 | 83.33 | 0.001 |
| hsa04360 | Organismal Systems | Development | Axon guidance | 129 | 33.52 | 58.13 | 0.012 |
| Organismal Systems | Development | all | 150 | 33.52 | 56.66 | 0.041 |
| hsa04916 | Organismal Systems | Endocrine System | Melanogenesis | 101 | 42.69 | 69.3 | 0.064 |
| hsa04962 | Organismal Systems | Excretory System | Vasopressin-regulated water reabsorption | 44 | 33.52 | 65.9 | 0.072 |
| hsa04612 | Organismal Systems | Immune System | Antigen processing and presentation | 83 | 30.79 | 63.85 | 0.039 |
| hsa04062 | Organismal Systems | Immune System | Chemokine signaling pathway | 189 | 42.69 | 66.66 | 0.063 |
| hsa04610 | Organismal Systems | Immune System | Complement and coagulation cascades | 69 | 57.38 | 84.05 | 0.023 |
| hsa04672 | Organismal Systems | Immune System | Intestinal immune network for IgA production | 46 | 36 | 76.08 | 0.001 |
| hsa04660 | Organismal Systems | Immune System | T cell receptor signaling pathway | 108 | 63.02 | 85.18 | 0.094 |
| Organismal Systems | Immune System | all | 801 | 36 | 55.43 | 0.025 |
| hsa04740 | Organismal Systems | Sensory System | Olfactory transduction | 386 | 44.80 | 84.45 | <0.001 |
| hsa04742 | Organismal Systems | Sensory System | Taste transduction | 51 | 63.02 | 92.15 | 0.028 |

Table S8 continued.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR captured genes |
|-----|-------------|--------------|-----------------------------------------------|
|     |            |              | captured | all | with genes | all | TSHB H3F3A IL10 C1QA C1QC C1QB FCER1A FCER1G FCGR2A FCGR3A FCGR2C FCGR3B FCGR2B HIST3H3 HIST3H2A HIST3H2BB |
| 1   | 16          | 36           | 6(10)    | 16(27) | 32.65      |     | CD8A CD8B TPO CD28 CTLA4 ICOS |
| 2   | 6           | 10           | 2(2)     | 15(27) | 39.15      |     | LOC644950 CD80 CD86 |
| 3   | 3           | 4            | 0(0)     | 11(19) | 27.33      |     | LOC651868 RNase3 ACTN3 TRIM21 PRG2 |
| 4   | 0           | 2            | 1(2)     | 10(18) | 26.39      |     | LOC651868 RNase3 ACTN3 TRIM21 PRG2 |
| 5   | 6           | 13           | 2(2)     | 10(18) | 26.39      |     | LOC651868 RNase3 ACTN3 TRIM21 PRG2 |
| 6   | 74          | 74           | 3(5)     | 15(23) | 41.15      |     | LOC651868 RNase3 ACTN3 TRIM21 PRG2 |
| 7   | 1           | 2            | 1(2)     | 10(31) | 36.14      |     | LOC651868 RNase3 ACTN3 TRIM21 PRG2 |
| 8   | 0           | 1            | 0(0)     | 10(23) | 35.41      |     | LOC644950 CD80 CD86 |
| 9   | 2           | 15           | 2(4)     | 12(20) | 44.80      |     | C5 C8G |
| 10  | 4           | 5            | 3(3)     | 13(22) | 45.38      |     | DCLRE1C BLNK H2AFY2 PRF1 |
| 11  | 3           | 9            | 3(8)     | 8(14)  | 32.19      |     | ACTN3 TRIM21 PRG2 |
| 12  | 9           | 12           | 2(4)     | 11(18) | 42.27      |     | GRIN2B HIST1H4H H2AFJ CD4 C1S C1R AICDA KLRD1 KLR1C |
| 13  | 2           | 2            | 1(1)     | 5(14)  | 23.82      |     | LOC644950 CD80 CD86 |
| 14  | 3           | 5            | 2(3)     | 7(14)  | 32.66      |     | LOC644950 CD80 CD86 |
| 15  | 0           | 0            | 0(0)     | 9(13)  | 43.30      |     | LOC644950 CD80 CD86 |
| 16  | 1           | 3            | 1(2)     | 9(23)  | 51.49      |     | LOC644950 CD80 CD86 |
| 17  | 2           | 4            | 2(2)     | 8(13)  | 45.16      |     | LOC644950 CD80 CD86 |
| 18  | 0           | 1            | 0(0)     | 1(4)   | 7.82       |     | LOC644950 CD80 CD86 |
| 19  | 8           | 10           | 4(9)     | 8(15)  | 58.42      |     | IL2RG C3 KIR2DL3 KIR2DL1 KIR3DL1 KIR3DL2 ACTN4 CD79A |
| 20  | 2           | 3            | 2(2)     | 5(8)   | 41.28      |     | SNRPB CD40 |
| 21  | 1           | 1            | 1(6)     | 2(7)   | 26.28      |     | SNRPB CD40 |
| 22  | 1           | 3            | 1(1)     | 3(8)   | 32.99      |     | SNRPB CD40 |
| 23  | 2           | 9            | 2(5)     | 9(23)  | 30.67      |     | SNRPB CD40 |

**Table S9: Immune System Diseases (subclass).** For each chromosome, the list of genes belonging to the KEGG’s subclass and localized within structural cluster regions (SCR) are given. The SCRs correspond to the best point in the curve of Figs S1-8, whose coordinates are reported in Table S8. The total number of genes in the subclass, the number of genes covered by some SCR, the number of SCR capturing some gene in the subclass (the number of SCs covering these genes is reported in parenthesis), the number of SCRs within the chromosome (the total number of SCs is reported in parenthesis) and the list of genes in the class lying in some SCR are given.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|-------------|--------------|-------------------------------|----------------|
| 1   | 3           | 3(2)         | 37.39                         | FCER1A FCER1G IL10 |
| 2   | 0           | 0(0)         | 43.82                         |
| 3   | 0           | 0(0)         | 45.02                         |
| 4   | 0           | 0(0)         | 30.46                         |
| 5   | 5           | 5(1)         | 28.78                         | IL3 IL5 IL13 IL4 IL9 |
| 6   | 13          | 13(4)        | 47.00                         | TNF HLA-DRA HLA-DRB5 HLA-DRB1 HLA-DQA1 HLA-DQB1 HLA-DQA2 HLA-DOB HLA-DMB HLA-DMA HLA-DOA HLA-DPA1 HLA-DPB1 |
| 7   | 0           | 0(0)         | 39.91                         |
| 8   | 0           | 0(0)         | 39.46                         |
| 9   | 0           | 0(0)         | 48.62                         |
| 10  | 0           | 0(0)         | 52.66                         |
| 11  | 1           | 1(2)         | 37.75                         | PRG2 |
| 12  | 0           | 0(0)         | 46.05                         |
| 13  | 0           | 0(0)         | 27.77                         |
| 14  | 1           | 1(2)         | 36.89                         | RNASE3 |
| 15  | 0           | 0(0)         | 47.72                         |
| 16  | 0           | 0(0)         | 57.12                         |
| 17  | 2           | 2(2)         | 52.78                         | EPX CCL11 |
| 18  | 0           | 0(0)         | 8.48                          |
| 19  | 0           | 0(0)         | 63.13                         |
| 20  | 1           | 1(1)         | 47.57                         | CD40 |
| 21  | 0           | 0(0)         | 29.48                         |
| 22  | 0           | 0(0)         | 36.01                         |
| X   | 1           | 1(4)         | 35.51                         | CD40LG |

**Table S10: Asthma (pathway).** See Figure S1-7 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
| 1   | 63         | 65           | 6(15)                         | OR4F5 OR4F16 TAS1R3 GN1B CALML6 TAS1R1 OR2B11 OR2C3 OR2G2 OR2G3 OR13G1 OR6F1 OR1C1 OR5AT1 OR11L1 OR2W3 OR2T8 OR2L13 OR2L8 OR2AK2 OR2L2 OR2L3 OR2M5 OR2M2 OR2M3 OR2M4 OR2T33 OR2T32 OR2M7 OR5BF1 OR2T6 OR2T1 OR2T2 OR2T3 OR2T5 OR2T29 OR2T34 OR2T10 OR2T11 OR2T27 OR5BU1 GNT2 OR10J3 OR10J1 OR10J5 PKRCAB CLCA2 CLCA1 CLCA4 OR10T2 OR10K2 OR10K1 OR10R2 OR6Y1 OR1X1 OR10Z1 OR6K2 OR6K3 OR6K6 OR6N1 OR6N2 |
| 2   | 4          | 6            | 3(15)                         | OR1G3 OR1G2 OR1G1 OR1G10 |
| 3   | 8          | 9            | 4(5)                          | 15(27)                       |
| 4   | 2          | 4            | 2(3)                          | 10(19)                       |
| 5   | 5          | 6            | 2(6)                          | 9(18)                       |
| 6   | 18         | 19           | 2(5)                          | 13(23)                       |
| 7   | 2          | 28           | 5(2)                          | 8(31)                       |
| 8   | 0          | 1            | 0(0)                          | 9(23)                       |
| 9   | 24         | 27           | 4(8)                          | 11(20)                       |
| 10  | 3          | 5            | 3(4)                          | 12(22)                       |
| 11  | 135        | 161          | 6(12)                         | 8(14)                       |
| 12  | 32         | 32           | 3(7)                          | 10(18)                       |
| 13  | 1          | 1            | 1(8)                          | 5(14)                       |
| 14  | 22         | 22           | 3(4)                          | 6(14)                       |
| 15  | 2          | 7            | 2(3)                          | 7(13)                       |
| 16  | 6          | 6            | 3(12)                         | 8(23)                       |
| 17  | 15         | 18           | 4(10)                         | 7(13)                       |
| 18  | 0          | 1            | 0(0)                          | 1(4)                        |
| 19  | 22         | 23           | 3(4)                          | 7(15)                       |
| 20  | 2          | 2            | 2(4)                          | 5(8)                        |
| 21  | 0          | 0            | 0(0)                          | 2(7)                        |
| 22  | 1          | 2            | 1(1)                          | 3(8)                        |
| X   | 3          | 3            | 3(16)                         | 9(23)                       |

Table S11: Sensory System (subclass). See Figure S1-9 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|------------------------------|----------------|
|     | captured   | all          | with genes                  | all            |
| 1   | 5          | 5            | 3(10)                       | 12(27)         | 62.05 | TAS1R3 GNBI TAS1R1 TAS1R2 PRKACB |
| 2   | 0          | 1            | 0(0)                        | 12(35)         | 69.84 |
| 3   | 0          | 0            | 0(0)                        | 12(27)         | 70.86 |
| 4   | 0          | 0            | 0(0)                        | 7(19)          | 50.36 |
| 5   | 0          | 1            | 0(0)                        | 5(18)          | 37.13 |
| 6   | 2          | 2            | 1(4)                        | 11(23)         | 81.57 | ITPR3 GRM4 |
| 7   | 9          | 10           | 3(13)                       | 7(31)          | 64.47 | TAS2R3 TAS2R4 TAS2R5 TAS2R38 TAS2R39 TAS2R40 TAS2R60 TAS2R41 GNAT3 |
| 8   | 0          | 1            | 0(0)                        | 6(23)          | 54.91 |
| 9   | 2          | 2            | 2(11)                       | 6(20)          | 68.17 | CACNA1B PRKACG |
| 10  | 0          | 0            | 0(0)                        | 9(22)          | 79.98 |
| 11  | 2          | 2            | 2(7)                        | 7(14)          | 57.61 | GNG3 TRPM5 |
| 12  | 16         | 16           | 2(10)                       | 6(18)          | 64.40 | ADCY6 SCNN1A GNBI TAS2R7 TAS2R8 TAS2R9 TAS2R10 TAS2R13 TAS2R14 TAS2R50 TAS2R49 TAS2R48 TAS2R44 TAS2R46 TAS2R43 TAS2R42 |
| 13  | 0          | 0            | 0(0)                        | 5(14)          | 53.39 |
| 14  | 1          | 1            | 1(3)                        | 5(14)          | 60.54 | ADCY4 |
| 15  | 1          | 1            | 1(2)                        | 4(13)          | 65.12 | PLCB2 |
| 16  | 3          | 3            | 2(12)                       | 6(23)          | 81.73 | GNG13 SCNN1G SCNN1B |
| 17  | 1          | 1            | 1(1)                        | 7(13)          | 81.17 | ACCN1 |
| 18  | 0          | 0            | 0(0)                        | 1(4)           | 12.75 |
| 19  | 2          | 2            | 1(6)                        | 4(15)          | 80.96 | CACNA1A PRKACA |
| 20  | 2          | 2            | 2(4)                        | 4(8)           | 78.80 | KCNB1 GNAS |
| 21  | 0          | 0            | 0(0)                        | 2(7)           | 50.25 |
| 22  | 0          | 0            | 0(0)                        | 2(5)           | 55.63 |
| X   | 1          | 1            | 1(11)                       | 8(23)          | 64.33 | PRKX |

**Table S12**: Taste transduction (pathway). See Figure S1-5 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|-----------------|
|     |            |              |                               |                 |
| 1   | 59         | 60           | 5(14)                         | 15(27)          |
|     |            |              |                               |                 |
|     |            |              |                               |                 |
| 2   | 4          | 5            | 3(15)                         | 18(35)          |
|     |            |              |                               |                 |
| 3   | 6          | 6            | 2(2)                          | 15(27)          |
|     |            |              |                               |                 |
| 4   | 0          | 2            | 0(0)                          | 10(19)          |
|     |            |              |                               |                 |
| 5   | 4          | 4            | 2(6)                          | 9(18)           |
|     |            |              |                               |                 |
| 6   | 16         | 17           | 2(5)                          | 13(23)          |
|     |            |              |                               |                 |
| 7   | 1          | 17           | 1(4)                          | 8(31)           |
|     |            |              |                               |                 |
| 8   | 0          | 0            | 0(0)                          | 9(23)           |
|     |            |              |                               |                 |
| 9   | 23         | 26           | 3(5)                          | 11(20)          |
|     |            |              |                               |                 |
| 10  | 3          | 5            | 3(4)                          | 12(22)          |
|     |            |              |                               |                 |
| 11  | 133        | 158          | 5(10)                         | 8(14)           |
|     |            |              |                               |                 |
| 12  | 16         | 16           | 2(4)                          | 10(18)          |
|     |            |              |                               |                 |
| 13  | 0          | 0            | 0(0)                          | 5(14)           |
|     |            |              |                               |                 |
| 14  | 21         | 21           | 2(3)                          | 6(14)           |
|     |            |              |                               |                 |
| 15  | 0          | 5            | 0(0)                          | 7(13)           |
|     |            |              |                               |                 |
| 16  | 3          | 3            | 2(4)                          | 8(23)           |
|     |            |              |                               |                 |
| 17  | 13         | 14           | 2(4)                          | 7(13)           |
|     |            |              |                               |                 |
| 18  | 0          | 1            | 0(0)                          | 1(4)            |
|     |            |              |                               |                 |
| 19  | 21         | 22           | 3(4)                          | 7(15)           |
|     |            |              |                               |                 |
| 20  | 0          | 0            | 0(0)                          | 5(8)            |
|     |            |              |                               |                 |
| 21  | 0          | 0            | 0(0)                          | 2(7)            |
|     |            |              |                               |                 |
| 22  | 1          | 2            | 1(1)                          | 3(8)            |
|     |            |              |                               |                 |
| X   | 2          | 2            | 2(16)                         | 9(23)           |

Table S13: Olfactory transduction (pathway). See Figure S1-5 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
| 1   | 56         | 99           | 16(27)                        | 32.65          |
|     |            |              |                               | AKT2 NRFL3 IL6R ADAR SHC1 CD1D CD1A CD1C CD1B CD1E AIM2 FCERL1 CD48 FCD44 F1R LFCER1 GFCGR2A HPAG FCGR3A FCGR2C FCGR5B FCGR2B SH2D1B TLR5 ISG15 GN1B PRKCCZ LOC646821 F3 CSF3 IRKBE RASSF5 IL10 P1GR C14B C14B PCB3 CS52 CR2 CR1 CD46 CD34 GNG5 BLC10 CLDN19 P1K3R3 RAP1A NRAS SKE CD247 XCL2 XCL1 C1QA C1QG C1QB DDEFL1 WASP2 |
| 2   | 22         | 40           | 14(30)                        | 39.06          |
|     |            |              |                               | IL8R8 IL8RA ARPC2 STATT1 NRCC1 CD26 CTLA4 ICOS CREB1 ADCY3 PDCD1 CD18 CD8B TPPO PRKCE INPP5D PROC CASP10 CASP8 NCX2 DDEF2 ROCK2 |
| 3   | 27         | 48           | 8(20)                         | 39.15          |
|     |            |              |                               | GP9 CD80 GSK3B CD86 ADCY5 CCR9 CXCR6 CCR1 CCR1 CCR3 FL173802 CCR5 TRELX1 RHN A2G2 GTP G1F2 PAK2 DLG1 ARPC4 RAI1 CCR4 MYD88 CX3CR1 CCR8 CTNBN1 THPO |
| 4   | 17         | 42           | 7(9)                          | 27.33          |
|     |            |              |                               | TLR2 TXX TEC MYL5 SH3BP2 GRK1 TLR6 TLR6 FGB PGA FGG KIT CLDN22 CASP3 TLR3 KLB1 F11 |
| 5   | 20         | 32           | 6(18)                         | 36.14          |
|     |            |              |                               | F12 GRK6 CTNNA1 TMEM73 CD14 IL5 IL5 IL4 HS4P1A CXCL14 CSF1R CD74 IL12B CANX MAPK9 DOWN2 LCP2 |
| 6   | 45         | 63           | 8(15)                         | 39.14          |
|     |            |              |                               | CCR6 MLLT4 HLA-F HLA-G HLA-A HLA-E HLA-C HLA-D MICB LTA TWF NFCR3 HSA1PIL HSA1AP1 HSA1A HSA1B C2 CFB CFB4 C4A HLA-DRA HLA-DRB5 HLA-DRB1 HLA-DQA1 HLA-DQB1 HLA-DOB TAP2 TAP1 HLA-DMB HLA-DMA HLA-DOA HLA-DPA1 HLA-DBP1 TAPPB ATG5 FOXO3 E2R PLG RIPK1 MAP3K7 NFV A NCR2 POLR1C HSP90A1 NF2BE |
| 7   | 20         | 32           | 6(18)                         | 36.14          |
|     |            |              |                               | ARFC1A ARPC1B GN2B EPO TRIPS SERPINE1 CLDN15 MYL2CPL NCF1 CCL26 CCL24 GNT1 GNT1 CLDN 3 CLDN 4LIMK1 CARD11 ACTB RAC1 IL6 |
| 8   | 12         | 18           | 6(13)                         | 35.41          |
|     |            |              |                               | PTK2 CDLN23 PLAT IRKBP PLOR3D P5P3CC TNCR1 NFCR3 HSA1PIL HSA1AP1 HSA1A HSA1B C2 CFB CFB4 C4A HLA-DRA HLA-DRB5 HLA-DRB1 HLA-DQA1 HLA-DQB1 HLA-DOB TAP2 TAP1 HLA-DMB HLA-DMA HLA-DOA HLA-DPA1 HLA-DBP1 TAPPB ATG5 FOXO3 E2R PLG RIPK1 MAP3K7 NFV A NCR2 POLR1C HSP90A1 NF2BE |
| 10  | 12         | 22           | 5(5)                          | 32.39          |
|     |            |              |                               | BIRC3 BIRC2 SERPING1 CTNND1 IFTM1 IHRAS IRF7 TOLLIP CD81 GNG3 PLCB3 RASGRP2 SIPA1 RELA CFL1 ACTN3 ADRBK1 RPS6KB2 FADD F2 |
| 11  | 20         | 45           | 6(12)                         | 32.19          |
|     |            |              |                               | BIRC3 BIRC2 SERPING1 CTNND1 IFTM1 IHRAS IRF7 TOLLIP CD81 GNG3 PLCB3 RASGRP2 SIPA1 RELA CFL1 ACTN3 ADRBK1 RPS6KB2 FADD F2 |
| 12  | 23         | 38           | 4(8)                          | 42.27          |
|     |            |              |                               | TBK1 IRAK4 RAPGEF3 ADCY6 ITGB7 ITGA5 VWF CD9 LTBR CD4 GN B3 PTPN6 C1S C1R C3A1 AICDA A2M KLDR1 KLRK1 KLRK4 KLRC3 KLRC2 KLC1 |
| 13  | 5          | 11           | 2(9)                          | 23.82          |
|     |            |              |                               | RXFAP TNSRF13B F7 F10 GRK1 |
| 14  | 13         | 23           | 5(11)                         | 32.66          |
|     |            |              |                               | ARHGA5P CDF2 NFKB1A HSPA9A1 RAF1 P5P3CC TNCR1 NFCR3 HSA1PIL HSA1AP1 HSA1A HSA1B C2 CFB CFB4 C4A HLA-DRA HLA-DRB5 HLA-DRB1 HLA-DQA1 HLA-DQB1 HLA-DOB TAP2 TAP1 HLA-DMB HLA-DMA HLA-DOA HLA-DPA1 HLA-DBP1 TAPPB ATG5 FOXO3 E2R PLG RIPK1 MAP3K7 NFV A NCR2 POLR1C HSP90A1 NF2BE |
| 15  | 13         | 16           | 5(7)                          | 43.30          |
|     |            |              |                               | MAP2K1 RASGRP1 PAK6 PLCB2 CHP PLAG24B PLAG4E PLA2G4D PLA2G4F PDLA3 C3K ANPEP PSTIP1 |
| 17  | 26         | 56           | 7(12)                         | 45.16          |
|     |            |              |                               | TNFRSF13B MAP2K3 TRIM25 TBKBP1 GNT2 ITGA3 CRK SERPIN2 ACTG1 RAC3 CD7 CCL5 CCL16 CCL14 CCL15 CCL23 CCL18 CCL3 CCL4 CCL53 CCL61 CCL63 CCL64 CCL62 CSF3 CCR7 SHP1K |
| 18  | 1          | 6            | 1(4)                          | 7.82           |
|     |            |              |                               | NFATC1 |
| 19  | 43         | 57           | 7(14)                         | 58.42          |
|     |            |              |                               | PPAP2C SHC2 MADCAM1 CFD GNG7 PIK51C MAP2K2 TICAM1 CD37 FLT3L4 IRF3 CD33 PRKCCZ LILRB3 KIR3DL3 KIR2DL3 KIR2DL1 KIR2DL4 KIR3DL4 KIR2DL4S KIR2DL2 NCR1 IL11 DNM2 EPRO CALR PRKACA ACTN4 NFkB1B PAK4 AKT2 TGFBI CD79A GSK3A PLAUR C3 VAV1 FCE2L MAP2K7 CCL25 LOC646048 PIN1 ICAM1 |
| 20  | 8          | 15           | 4(5)                          | 41.28          |
|     |            |              |                               | MAV5 PLCB1 PLCB4 PK7 THBD MMP9 CD40 PREX1 |
| 21  | 2          | 10           | 1(6)                          | 26.28          |
|     |            |              |                               | ICOSLG ITG5B |
| 22  | 11         | 18           | 3(8)                          | 32.99          |
|     |            |              |                               | MAPK12 MAPK1I GRAP2 PLOR3H TNFRSF13C BID CLDN5 GIP1BB SERPIN1 CRLK1 MAPK1 |
| X   | 10         | 26           | 7(20)                         | 30.67          |
|     |            |              |                               | CXCR3 C5PS2RA IL3RA CD99 PRXK MAPK7IP3 CD40LG PK3 DDX3X CLDN2 |

Table S14: Immune System (subclass). See Figure S1-8 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
| 1   | 7          | 16           | 30.13                         | NRAS EFNA4 EFNA3 EFNA1 SEMA4A SRGAP2 EPHB2 |
| 2   | 6          | 10           | 36.30                         | DPYS5 NCK2 NGEF EP4A4 ROCK2 SEMA4F |
| 3   | 13         | 18           | 35.89                         | GSK3B SEMA5B EPHA3 PXLNA1 PXLNB1 RHOA SEMA3F GNA12 |
|     |            |              |                               | SEMA3B EPHA6 SRGAP3 PAK2 |
| 4   | 1          | 5            | 25.69                         | ABLM2 |
| 5   | 3          | 7            | 24.85                         | UNC5A SL1T3 ABLM3 |
| 6   | 2          | 4            | 38.22                         | EPHA7 NOTCH1 |
| 7   | 5          | 13           | 34.25                         | RAC1 CDK5 LIMK1 EPHB4 EGFR |
| 8   | 4          | 5            | 33.01                         | DPYS2 PTK2 PWWIL2 PWWCC |
| 9   | 3          | 5            | 41.99                         | ABL1 SEMA1D NOTCH1 |
| 10  | 7          | 8            | 41.69                         | ITGB1 NR1P1 CXCL12 SLIT1 UNC5B PWW3CB SEMA1G |
| 11  | 3          | 9            | 29.40                         | HRAS CFL1 RHOD |
| 12  | 6          | 7            | 39.96                         | RND1 ETV6 PWWIL1 PWWNC1 PNT4 SRGAP1 |
| 13  | 0          | 1            | 21.85                         | |
| 14  | 2          | 3            | 30.55                         | NFATC4 CFL2 |
| 15  | 7          | 8            | 40.63                         | SEMA4B MAP2K1 CPEB1 FES PAK6 CHF SEMA7A |
| 16  | 6          | 9            | 48.46                         | CHP2 NFATC3 NFAT5 MAPK3 NTN2L SPIRE2 |
| 17  | 1          | 2            | 41.36                         | RAC3 |
| 18  | 1          | 2            | 7.49                          | NFATC1 |
| 19  | 4          | 4            | 55.56                         | NOTCH3 EFNA2 SEMA6B PAK4 |
| 20  | 1          | 2            | 37.68                         | PAK7 |
| 21  | 0          | 1            | 24.68                         | |
| 22  | 2          | 5            | 31.49                         | PLEXB2 MAPK1 |
| X   | 1          | 5            | 28.25                         | PAK3 |

**Table S15:** Development (subclass). See Figure S1-8 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-----------------------------|----------------|
|     | captured   | all with genes | all |                        |                 |
| 1   | 7          | 14 (4)       | 16 (27) | 30.13 | NRAS EFNA4 EFNA3 EFNA1 SEMA4A SRGAP2 EPHB2 |
| 2   | 6          | 9 (6)        | 19 (35) | 36.30 | DPYSL5 NCK2 NGEF EPHA4 ROCK2 SEMA4F |
| 3   | 13         | 18 (8)       | 15 (27) | 35.89 | GSK3B SEMA5B EPHA3 PLXNA1 PLXNB1 RHOA SEMA3F GNA12 SEMA3B EPHB3 EPHA6 SRGAP3 PAK2 |
| 4   | 1          | 5 (1)        | 11 (19) | 25.69 | ABLIM2 |
| 5   | 3          | 7 (3)        | 10 (18) | 24.85 | UNC5A SLIT3 ABLIM3 |
| 6   | 1          | 2 (1)        | 15 (23) | 38.22 | EPHA7 |
| 7   | 4          | 12 (4)       | 10 (31) | 34.25 | RAC1 CDK5 EPHB4 LIMK1 |
| 8   | 3          | 4 (3)        | 11 (23) | 33.01 | DPYSL2 PTK2 PPP3CC |
| 9   | 2          | 4 (2)        | 13 (20) | 41.99 | ABL1 SEMA1D |
| 10  | 7          | 8 (5)        | 13 (22) | 41.69 | ITGB1 NRPI CXCL12 SLITI UNC5B PPP3CB SEMA1G |
| 11  | 3          | 7 (2)        | 8 (14)  | 29.40 | HRAS CFL1 RHOD |
| 12  | 4          | 5 (3)        | 13 (18) | 39.96 | RND1 SRGAP1 PLXNC1 NTN4 |
| 13  | 0          | 1 (0)        | 5 (14)  | 21.85 |                 |
| 14  | 2          | 2 (1)        | 7 (14)  | 30.55 | NFATC4 CFL2 |
| 15  | 5          | 6 (4)        | 9 (13)  | 40.63 | PAK6 CHF SEMA4B SEMA7A FES |
| 16  | 5          | 5 (4)        | 9 (23)  | 48.46 | CHF2 NFATC3 NFAT5 MAPK3 NYT2L |
| 17  | 1          | 3 (1)        | 8 (13)  | 41.36 | RAC3 |
| 18  | 1          | 3 (1)        | 1 (4)   | 7.49  | NFATC1 |
| 19  | 3          | 3 (1)        | 8 (15)  | 55.56 | EFNA2 SEMA6B PAK4 |
| 20  | 1          | 2 (1)        | 5 (8)   | 37.68 | PAK7 |
| 21  | 0          | 0 (0)        | 2 (7)   | 24.68 |                 |
| 22  | 2          | 4 (2)        | 3 (8)   | 31.49 | PLXNB2 MAPK1 |
| X   | 1          | 5 (1)        | 9 (23)  | 28.25 | PAK3 |

**Table S16**: Axon guidance (pathway). See Figure S1-4 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
| 1   | 13         | 36           | 18.40                         | F11R, FCGR2A, FCGR3A, FCGR2C, FCGR3B, IL10, CD247, ARF1, ATP6V0B, PK3R3, SHC1, ARHGEF2, TLR5 |
| 2   | 14         | 24           | 22.33                         | STAT1, NCK2, IL8RB, IL8RA, ARPC2, TUBA1A, ADAM17, YWHAQ, ATP6V1C2, ROCK2, CFLAR, CASP8, PFN4, ADY3 |
| 3   | 7          | 19           | 21.90                         | SEC61A1, CTNNB1, PFN2, RHOA, HCLS1, CAV3, ARPC3 |
| 4   | 4          | 12           | 16.39                         | ATP6V0B, PIK3R3, SHC1, ARHGEF2, TLR5 |
| 5   | 13         | 17           | 15.85                         | TUBB2A, TUBB2B, TUBB, ATP6V1G2, TNF, HLA-DRA, HLA-DRB5, HLA-DRB1, HLA-DQA1, HLA-DQB1, HLA-DQB2, HLA-DOB, ATG5 |
| 6   | 13         | 27           | 24.27                         | IL6, NCF1, ACTB, ARPC1A, ARPC1B, SERPINE1, PDIA4, ATP6V0E2, RAC1, KDEL, SEC61G, EGRF |
| 7   | 12         | 25           | 24.37                         | PPP2R2A, IKBKB, PPP2CB, PTK2, ATP6V1B |
| 8   | 5          | 12           | 21.91                         | TUBB2C, PRKACG, TJP2, DN1M, ARPC5L, SHC3 |
| 9   | 6          | 16           | 27.90                         | TUBB2C, PRKACG, TJP2, DN1M, ARPC5L, SHC3 |
| 10  | 3          | 12           | 25.31                         | PPP2R2D, TUBB5, DOCK1 |
| 11  | 6          | 18           | 25.31                         | PLCB3, RELA, RHOG, CTTN, MUC2, KCNQ1 |
| 12  | 7          | 14           | 18.24                         | PLCB3, RELA, RHOG, CTTN, MUC2, KCNQ1 |
| 13  | 0          | 1            | 13.97                         | AKT1, NFKBIA, FOS |
| 14  | 1          | 7            | 18.82                         | CSK, SMAD3, PLCB2, TJP1 |
| 15  | 4          | 11           | 26.65                         | CYBA, TUBB3, ATP6V0D1, CDH1, ATP6V0C, GNAO1, MAP3K, SEPT1 |
| 16  | 8          | 14           | 32.95                         | CRK, ACTG1 |
| 17  | 2          | 17           | 25.39                         | PLCB1, PLCB4 |
| 18  | 0          | 4            | 6.18                          | PLCB1, PLCB4 |
| 19  | 11         | 18           | 37.24                         | GNA11, GNA15, TICAM1, NFKBIA, AKT2, PPP2R1A, PRKCG, SHC2, CALR, PRKACA, THGB1 |
| 20  | 2          | 6            | 24.27                         | PLCB1, PLCB4 |
| 21  | 2          | 5            | 18.29                         | U2AF1, TTGB2 |
| 22  | 3          | 10           | 22.17                         | MAPK12, MAPK11, CLTCL1 |
| X   | 0          | 6            | 17.75                         | MAPK12, MAPK11, CLTCL1 |

**Table S17:** Infectious Diseases (subclass). See Figure S1-8 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|--------------------------------|----------------|
|     | captured   | all          | with genes | all |                  |
| 1   | 3          | 8            | 3(10)     | 16(27) | 24.66 | PKLR PFK3R3 PRKCZ |
| 2   | 3          | 10           | 3(3)      | 20(35) | 29.42 | HK2 PTPRN CD28 |
| 3   | 3          | 10           | 2(9)      | 15(27) | 28.92 | CD80 CD86 HES1 |
| 4   | 0          | 4            | 0(0)      | 11(19) | 21.18 |                  |
| 5   | 3          | 4            | 3(6)      | 11(18) | 20.74 | IL12B HK3 MAPK9 |
| 6   | 20         | 20           | 2(4)      | 15(23) | 31.98 | HLA-F HLA-G HLA-A HLA-E HLA-C HLA-B LTA TNF HLA-DRA HLA-DRB5 HLA-DRB1 HLA-DQA1 HLA-DQB1 HLA-DQA2 HLA-DOB HLA-DMB HLA-DMA HLA-DOA HLA-DPA1 HLA-DPB1 |
| 7   | 3          | 7            | 3(13)     | 11(31) | 30.17 | PTPRN2 BHLHB8 MNX1 |
| 8   | 2          | 3            | 2(7)      | 11(23) | 27.74 | MAFA IKKB |
| 9   | 1          | 1            | 1(3)      | 14(20) | 35.34 | CACNA1B |
| 10  | 3          | 7            | 3(4)      | 13(22) | 33.71 | PRF1 HHEX GAD2 |
| 11  | 1          | 4            | 1(4)      | 8(14)  | 23.82 | INS |
| 12  | 2          | 5            | 2(2)      | 13(18) | 33.38 | CACNA1C IAPP |
| 13  | 1          | 2            | 1(8)      | 5(14)  | 17.91 | IHS2 |
| 14  | 1          | 2            | 1(1)      | 8(14)  | 25.59 | GZMB |
| 15  | 1          | 2            | 1(2)      | 10(13) | 34.07 | PFKM2 |
| 16  | 1          | 2            | 1(2)      | 10(23) | 41.34 | MAPK3 |
| 17  | 3          | 5            | 3(3)      | 8(13)  | 33.74 | CACNA1G SOCS3 HNF1B |
| 18  | 0          | 0            | 0(0)      | 2(4)   | 6.84 |                  |
| 19  | 2          | 4            | 2(3)      | 9(15)  | 48.48 | CACNA1A INSR |
| 20  | 2          | 3            | 1(1)      | 5(8)   | 30.47 | NKKX2-2 FOXA2 |
| 21  | 0          | 0            | 0(0)      | 3(7)   | 21.49 |                  |
| 22  | 0          | 1            | 0(0)      | 4(8)   | 27.20 |                  |
| X   | 0          | 1            | 0(0)      | 11(23) | 23.24 |                  |

**Table S18: Metabolic Diseases (subclass).** See Figure S1-8 and Table S8.
| Chr | # of genes captured | # of SCR(SC) all | % of chromosome covered by SCR | captured genes |
|-----|---------------------|-----------------|-------------------------------|----------------|
| 1   | 9                   | 30 (5)          | 15.26                         | CAPN2 UBE2J2 CALML6 NCSTN NDUFS2 TOMM40L SDHC ATP6 PSEN2 |
| 2   | 10                  | 19 (7)          | 18.56                         | DCTN1 HTRA2 NDUFA10 POLR2D NDUFS1 ADAM17 COX7A2L NDUFS3 CASP8 ALS2 |
| 3   | 6                   | 15 (4)          | 18.39                         | GSK3B NDUFB4 UQCRCl IFT57 AP2M1 POLR2H |
| 4   | 3                   | 15 (2)          | 13.78                         | CASP3 SLC25A4 HTT |
| 5   | 8                   | 17 (6)          | 13.33                         | LOC727947 SDHA SLC6A3 NDUFS6 NDUFA2 VDAC1 CLTB DCTN4 |
| 6   | 6                   | 16 (5)          | 20.18                         | PRPH2 TBP TNF HSPA1A UBE2J1 SOD2 |
| 7   | 6                   | 15 (5)          | 21.35                         | RAC1 HIP1 POLR2J POLR2J3 IL6 CYCS |
| 8   | 5                   | 12 (4)          | 18.49                         | PPP3CC VDAC3 NEFM NEPL CYC1 |
| 9   | 6                   | 13 (5)          | 23.50                         | PRKAGC C5 NOTCH1 C8G GRIN1 HSPA5 |
| 10  | 4                   | 11 (2)          | 20.88                         | IDE |
| 11  | 8                   | 26 (2)          | 15.45                         | POLR2L AP2A2 TH COX8A STIP1 PLCB3 BAD CAPN1 |
| 12  | 9                   | 18 (7)          | 21.56                         | LRRK2 SP1 ATP5G2 GRIN2B NDUFA9 TNFRSF1A GAPDH APAF1 PRPH |
| 13  | 0                   | 1 (0)           | 12.00                         | |
| 14  | 3                   | 7 (3)           | 14.87                         | CALM1 DNAL1 RCOR1 |
| 15  | 4                   | 7 (3)           | 22.17                         | COX5A SIN3A PLCB2 CHP |
| 16  | 6                   | 13 (4)          | 28.14                         | NDUFB10 DNH3 UQCRCl POLR2C ATP2A1 MAPK3 |
| 17  | 1                   | 20 (1)          | 20.94                         | CDK5R1 |
| 18  | 0                   | 5 (0)           | 5.85                          | |
| 19  | 7                   | 24 (4)          | 31.36                         | MAP2K2 CREB3L3 POLR2E ATP5D NDUFS7 COX6B2 NDUFA7 |
| 20  | 3                   | 8 (2)           | 19.66                         | TAF4 PLCB1 PLCB4 |
| 21  | 3                   | 8 (2)           | 16.23                         | UBE2G2 BACE2 NDUFV3 |
| 22  | 6                   | 13 (3)          | 19.16                         | MAPK12 MAPK11 EP300 NDUFA6 CLTCL1 SEPT5 |
| X   | 3                   | 10 (2)          | 15.01                         | SLC25A6 SLC25A5 NDUFA1 |

**Table S19**: Neurodegenerative Diseases (subclass). See Figure S1-9 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
|     | captured   | all          | with genes                   | all            |
| 1   | 4          | 5            | 3(3)                         | 16(27)         | 30.13 NRAS TPM3 NTRK1 RXRG |
| 2   | 1          | 2            | 1(1)                         | 19(35)         | 36.30 TCF7L1               |
| 3   | 3          | 3            | 3(7)                         | 15(27)         | 35.89 PPARG CTNNB1 TFG     |
| 4   | 0          | 1            | 0(0)                         | 11(19)         | 25.69                       |
| 5   | 1          | 1            | 1(1)                         | 10(18)         | 31.85 TCF7                 |
| 6   | 1          | 1            | 1(2)                         | 15(23)         | 38.22 RXRB                 |
| 7   | 0          | 1            | 0(0)                         | 10(31)         | 34.25                       |
| 8   | 0          | 1            | 0(0)                         | 11(23)         | 33.01                       |
| 9   | 1          | 1            | 1(3)                         | 13(20)         | 41.99 RXRA                 |
| 10  | 2          | 4            | 2(2)                         | 13(22)         | 41.69 RET NCOA4            |
| 11  | 2          | 2            | 2(5)                         | 8(14)          | 29.40 CCND1 HRAS           |
| 12  | 0          | 1            | 0(0)                         | 13(18)         | 39.96                       |
| 13  | 0          | 0            | 0(0)                         | 5(14)          | 21.85                       |
| 14  | 0          | 0            | 0(0)                         | 7(14)          | 30.55                       |
| 15  | 1          | 1            | 1(1)                         | 9(13)          | 40.63 MAP2K1               |
| 16  | 2          | 2            | 2(3)                         | 9(23)          | 48.46 CDH1 MAPK3           |
| 17  | 0          | 1            | 0(0)                         | 8(13)          | 41.36                       |
| 18  | 0          | 0            | 0(0)                         | 1(4)           | 7.49                        |
| 19  | 1          | 1            | 1(2)                         | 8(15)          | 55.56 MAP2K2               |
| 20  | 0          | 0            | 0(0)                         | 5(8)           | 37.68                       |
| 21  | 0          | 0            | 0(0)                         | 2(7)           | 24.68                       |
| 22  | 1          | 1            | 1(1)                         | 3(8)           | 31.49 MAPK1                |
| X   | 0          | 0            | 0(0)                         | 9(23)          | 28.25                       |

**Table S20:** Thyroid Cancer (pathway). See Figure S1-7 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
| 1   | 5          | 12           | 24.66%                        | WNT9A WNT3A VANGL2 DVL1 WNT2B |
| 2   | 4          | 7            | 29.42%                        | ROCK2 FZD7 WNT6 WNT10A |
| 3   | 6          | 10           | 28.92%                        | CTNNB1 DVL3 SENP2 RUVBL1 GSK3B RHOA |
| 4   | 1          | 8            | 21.18%                        | CTBP1 |
| 5   | 8          | 10           | 20.74%                        | TCF7 SKP1 PPP2CA CAMK2A FBXW1 MAPK9 WNT8A NDK2 |
| 6   | 4          | 6            | 31.98%                        | CCND3 PPP2R5D CSNK2B MAP3K7 |
| 7   | 3          | 8            | 30.17%                        | RAC1 CUL1 FZD9 |
| 8   | 4          | 8            | 27.71%                        | PPP3CC PPP2CB SFRP1 DKK4 |
| 9   | 1          | 3            | 35.34%                        | PRKACG |
| 10  | 9          | 12           | 33.71%                        | CTBP2 PPP3CB CAMK2G BTRC FZD8 DKK1 FRAT1 FRAT2 SFRP5 |
| 11  | 4          | 9            | 23.82%                        | PLCB3 PPP2R5B FOSL1 MMP7 |
| 12  | 6          | 9            | 33.38%                        | FZD10 WNT10B WNT1 LRP6 WNT3B CCND2 |
| 13  | 1          | 1            | 17.91%                        | |
| 14  | 4          | 6            | 25.59%                        | PSEN1 PPP2R5C CHD8 NFATC4 |
| 15  | 3          | 3            | 23.82%                        | PLCB2 CHP SMAD3 |
| 16  | 5          | 9            | 41.34%                        | AXIN1 CREBBP NFATC3 NFAT5 CSNK2A2 |
| 17  | 1          | 9            | 33.71%                        | RAC9 |
| 18  | 1          | 4            | 6.84%                         | NFATC1 |
| 19  | 4          | 4            | 48.48%                        | PRKACA APC2 PPP2R1A PRKCG |
| 20  | 2          | 4            | 30.17%                        | PLCB1 PLCB4 |
| 21  | 0          | 0            | 21.49%                        | |
| 22  | 3          | 5            | 27.20%                        | RBX1 EP300 WNT7B |
| X   | 1          | 3            | 23.24%                        | PRKX |

**Table S21: Wnt (pathway).** See Figure S1-4 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
| 1   | 4          | 4(8)         | 8.85                          | PSEN2 HES5 NCSTN DVL1 |
| 2   | 0          | 0(0)         | 10.46                         |                |
| 3   | 2          | 2(2)         | 10.66                         | DVL3 HES1      |
| 4   | 1          | 1(1)         | 8.08                          | CTBP1          |
| 5   | 1          | 1(2)         | 7.44                          | MAML1          |
| 6   | 2          | 2(2)         | 11.58                         | PTCRA DLL1    |
| 7   | 1          | 1(1)         | 13.40                         | LFNG           |
| 8   | 0          | 0(0)         | 10.89                         |                |
| 9   | 1          | 1(1)         | 12.74                         | NOTCH1         |
| 10  | 1          | 1(1)         | 11.87                         | CTBP2          |
| 11  | 0          | 0(0)         | 9.07                          |                |
| 12  | 0          | 0(0)         | 11.91                         |                |
| 13  | 0          | 0(0)         | 7.87                          |                |
| 14  | 1          | 1(3)         | 9.95                          | JAG2           |
| 15  | 1          | 1(1)         | 11.90                         | DLL4           |
| 16  | 0          | 0(0)         | 16.52                         |                |
| 17  | 1          | 1(4)         | 12.06                         | RFNG           |
| 18  | 0          | 0(0)         | 3.90                          |                |
| 19  | 2          | 2(4)         | 18.33                         | DLL3 NUMBL    |
| 20  | 0          | 0(0)         | 11.35                         |                |
| 21  | 0          | 0(0)         | 10.91                         |                |
| 22  | 0          | 0(0)         | 11.93                         |                |
| X   | 0          | 0(0)         | 8.31                          |                |

**Table S22**: Notch (pathway). See Figure S1-4 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
|     | captured   | all          | with genes                   | all            |                |
| 1   | 8          | 8            | 6(10)                        | 13(27)         | 53.45 BMP8A BMP8B PTCH2 WNT4 WNT9A WNT3A WNT2B PRKACB |
| 2   | 4          | 6            | 1(2)                         | 14(35)         | 60.73 STK36 WNT6 WNT10A IHH |
| 3   | 3          | 3            | 3(6)                         | 14(27)         | 64.32 GSK3B WNT7A WNT5A |
| 4   | 0          | 1            | 0(0)                         | 7(19)          | 43.01          |
| 5   | 4          | 4            | 4(13)                        | 6(18)          | 35.34 FBXW11 CSNK1A1 WNT8A CSNK1G3 |
| 6   | 3          | 3            | 2(4)                         | 11(23)         | 68.93 BMP5 RAB23 BMP6 |
| 7   | 1          | 5            | 1(10)                        | 7(31)          | 55.03 SHH |
| 8   | 0          | 0            | 0(0)                         | 8(23)          | 52.22          |
| 9   | 3          | 3            | 2(10)                        | 8(20)          | 62.06 PRKACG GAS1 PTCH1 |
| 10  | 3          | 3            | 2(4)                         | 11(22)         | 72.52 SUFU WNT8B BTRC |
| 11  | 1          | 1            | 1(1)                         | 8(14)          | 52.96 WNT11 |
| 12  | 5          | 5            | 2(10)                        | 6(18)          | 58.74 WNT5B WNT10B WNT1 DHH GLI1 |
| 13  | 1          | 2            | 1(1)                         | 5(14)          | 43.54 CSNK1A1L |
| 14  | 0          | 1            | 0(0)                         | 5(14)          | 53.24          |
| 15  | 1          | 1            | 1(5)                         | 5(13)          | 60.11 CSNK1G1 |
| 16  | 0          | 0            | 0(0)                         | 6(23)          | 74.96          |
| 17  | 3          | 3            | 2(6)                         | 7(13)          | 72.68 WNT3 WNT9B CSNK1D |
| 18  | 0          | 0            | 0(0)                         | 1(4)           | 11.11          |
| 19  | 2          | 2            | 1(6)                         | 4(15)          | 76.69 CSNK1G2 PRKACA |
| 20  | 2          | 2            | 2(4)                         | 5(8)           | 66.79 BMP7 BMP2 |
| 21  | 0          | 0            | 0(0)                         | 2(7)           | 42.26          |
| 22  | 2          | 2            | 1(7)                         | 2(8)           | 48.09 CSNK1E WNT7B |
| X   | 1          | 1            | 1(11)                        | 8(23)          | 54.22 PRKX |

Table S23: Hedgehog (pathway). See Figure S1-4 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|--------------------------------|----------------|
|     |            |              |                                | all            |
| 1   | 20         | 42           | 11(22)                         | 16(27)         | ATP6V0B PRDX1 SH3GLB1 PMVK GBA NTRK1 DDEF1 ATP4C HMGCL FUCAL LDLRAP1 ABCD3 ATG4C AP4B1 CTSE PEX19 HSPA6 RAB4A CENTB5 PRKCB1 PEX10 |
| 2   | 16         | 24           | 10(21)                         | 20(35)         | RAB11FIP5 STAMBP DDEF2 EHD3 XDH AGXT ATG3B ACSL3 AP1S3 CENTG2 VPS24 LAPTM4A IL8RB IL8RA SLC11A1 PEX13 |
| 3   | 14         | 28           | 8(18)                          | 16(27)         | RHOA CHMP2B ACOX2 LAMP3 AP2M1 EHHAHD RAB7A PIK3R4 GLB1 PDCD6IP CENTB2 TFRC CAV3 ATG7 |
| 4   | 8          | 16           | 6(11)                          | 12(19)         | GRK4 FSAPL1 ACOX3 IDUA FGFR3 ACSL1 CTSO CENTD1 |
| 5   | 8          | 22           | 4(8)                           | 11(18)         | FSD2 CENTD3 RUFY1 CSF1R GM2A CLTB FGFR4 GRK6 |
| 6   | 16         | 23           | 6(10)                          | 15(23)         | HLA-F HLA-G HLA-A PEX6 HLA-E HLA-C HLA-B HSAF1L HSPA1A HSPA1B NF1 PPT2 PEC1 SOD2 IGFR2 ATG5 |
| 7   | 5          | 13           | 3(7)                           | 13(31)         | RHOA CHMP2B ACOX2 LAMP3 AP2M1 EHHAHD RAB7A PIK3R4 GLB1 PDCD6IP CENTB2 TFRC CAV3 ATG7 |
| 8   | 4          | 18           | 4(10)                          | 11(23)         | GRK4 FSAPL1 ACOX3 IDUA FGFR3 ACSL1 CTSO CENTD1 |
| 9   | 9          | 27           | 6(9)                           | 17(20)         | GRK4 FSAPL1 ACOX3 IDUA FGFR3 ACSL1 CTSO CENTD1 |
| 10  | 6          | 15           | 6(9)                           | 13(22)         | GRK4 FSAPL1 ACOX3 IDUA FGFR3 ACSL1 CTSO CENTD1 |
| 11  | 14         | 29           | 5(9)                           | 9(14)          | FOLR3 FOLR1 FOLR2 CENTD2 PRDX5 EHD1 CTSW CTSF PEX16 HRAS AP2A2 CTSF INS TSG101 |
| 12  | 7          | 26           | 6(10)                          | 13(18)         | PEK5 ULC1 PXMP2 SLC11A2 M6PR ABCD2 IQSEC3 |
| 13  | 2          | 5            | 1(8)                           | 5(14)          | LAM1 GRK1 |
| 14  | 7          | 11           | 3(3)                           | 8(14)          | LAM1 GRK1 |
| 15  | 11         | 18           | 7(9)                           | 10(13)         | LAM1 GRK1 |
| 16  | 11         | 16           | 5(17)                          | 10(23)         | CLN3 GALNS DCER2 RAB11FIP3 GNPTG ATP6V0C ATP6V0D1 PARD6A PLA2G15 VPS4A MPV17L |
| 17  | 9          | 31           | 5(8)                           | 8(13)          | GDNF Nepf SMAD6 SMAD7 SMAD4 AP3B2 SH3GL3 |
| 18  | 1          | 9            | 1(3)                           | 2(4)           | GDNF Nepf SMAD6 SMAD7 SMAD4 AP3B2 SH3GL3 |
| 19  | 14         | 25           | 8(14)                          | 9(15)          | NUDT19 ECH1 PEX1G MCOLN1 RAB11B ACP5 MAN2B1 DNASE2 PIK3K1 CH3GL1 NAPSA TGFBR1 EPN1 CHMP2A |
| 20  | 3          | 11           | 3(5)                           | 6(8)           | ARFGAP1 CTS8 HAO1 |
| 21  | 0          | 1            | 0(0)                           | 3(7)           | ARFGAP1 CTS8 HAO1 |
| 22  | 6          | 10           | 3(6)                           | 4(8)           | SLC25A17 NAGA ARFGAP3 PEX26 CLTCL1 ARSA |

**Table S24:** Transport and Catabolism (subclass). See Figure S1-9 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
|     | captured   | all with genes | all                          |                |
| 1   | 3          | 11            | 3(10)                        | 16(27)         | 18.40 | DFFB CAPN2 PIK3R3 |
| 2   | 3          | 7             | 1(1)                         | 22(35)         | 22.33 | CFLAR CASP10 CASP8 |
| 3   | 3          | 8             | 3(6)                         | 17(27)         | 21.90 | ENDOGL1 IRAK2 PRKAR2A |
| 4   | 1          | 4             | 1(2)                         | 12(19)         | 16.39 | CASP3 |
| 5   | 0          | 2             | 0(0)                         | 12(18)         | 18.85 |                |
| 6   | 2          | 2             | 2(5)                         | 16(23)         | 24.27 | RIPK1 TNF |
| 7   | 2          | 4             | 2(7)                         | 15(31)         | 24.37 | CYCS PRKAR1B |
| 8   | 6          | 6             | 2(4)                         | 11(23)         | 21.91 | IKKBK PPP3CC TNFRSF10B TNFRSF10C TNFRSF10D TNFRSF10A |
| 9   | 3          | 4             | 3(5)                         | 17(20)         | 27.90 | PRKACG ENDOG TRAF2 |
| 10  | 1          | 4             | 1(1)                         | 13(22)         | 25.31 | PPP3CB |
| 11  | 5          | 8             | 2(3)                         | 9(14)          | 18.24 | BIRC3 BIRC2 BAD CAPN1 RELA |
| 12  | 3          | 4             | 3(3)                         | 14(18)         | 26.09 | APAF1 TNFRSF1A IRAK4 |
| 13  | 0          | 0             | 0(0)                         | 5(14)          | 13.97 |                |
| 14  | 2          | 2             | 2(5)                         | 8(14)          | 19.82 | AKT1 NFKBIA |
| 15  | 1          | 1             | 1(1)                         | 11(13)         | 26.65 | CHP |
| 16  | 1          | 2             | 1(1)                         | 11(23)         | 32.95 | TRADD |
| 17  | 0          | 4             | 0(0)                         | 8(13)          | 26.28 |                |
| 18  | 0          | 1             | 0(0)                         | 2(4)           | 6.18  |                |
| 19  | 2          | 4             | 2(3)                         | 9(15)          | 37.24 | AKT2 PRKACA |
| 20  | 0          | 1             | 0(0)                         | 6(8)           | 23.27 |                |
| 21  | 0          | 0             | 0(0)                         | 3(7)           | 18.89 |                |
| 22  | 0          | 2             | 0(0)                         | 4(8)           | 22.17 |                |
| X   | 1          | 6             | 1(11)                        | 11(23)         | 17.75 | IL3RA |

**Table S25: Apoptosis (pathway).** See Figure S1-4 and Table S8.
Table S26: Replication and Repair (subclass). See Figure S1-9 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-----------------------------|----------------|
| 1   | 29         | 38 (24)      | 58.81                       | CEPT1 ETNK2 HSD11B1 PLA2G2E PLA2G2A PLA2G5 PLA2G2D PLA2G2F PLA2G2C LYPLA2 HMGCCL PAFAH2 MECR DEGS1 GN-PAT AKR1A1 CYP4A11 CYP4A22 GPX7 SCP2 CPT2 ACOT7 GBA HSD1B7 ALDH9A1 PPAP2B CYP2J2 OXCT2 PPT1 |
| 2   | 25         | 28 (28)      | 66.66                       | HADHA HADHB SELI LYCAT SRD5A2 CYP1B1 NEU2 DGKD UGT1A8 UGT1A10 UGT1A9 UGT1A7 UGT1A6 UGT1A5 UGT1A4 UGT1A3 UGT1A1 NEU4 PECR CYP27A1 SGPP2 ACSL3 ACADL MBOAT2 SMPD4 |
| 3   | 13         | 15 (19)      | 68.35                       | MGLL GPD1L GLBI ACAA1 CYP8B1 GPX1 GLYCTK PTPLB PCYT1A BDHI ACOX2 EHHDH DGK |
| 4   | 16         | 35 (16)      | 47.72                       | DGKQ ACOX3 UGT8 ENP16 ACSL1 SRD5A3 UGT2B17 UGT2B15 UGT2B10 UGT2A3 UGT2B7 UGT2B11 UGT2B8 UGT2B4 UGT2A1 SULT1E1 |
| 5   | 6          | 11 (15)      | 36.58                       | LPCAT1 SRD5A1 ALDH7A1 ACSL6 LTG1S GPX3 |
| 6   | 16         | 16 (18)      | 76.83                       | ACAT2 AGPAT4 ELOVL2 MBOAT1 SMPD2 PEC1 GPX6 GPX5 NEU1 CYP4A2 PPT2 AGPAT1 HSD1B8 CYP39A1 PLA2G7 ELOVL5 |
| 7   | 12         | 13 (18)      | 60.69                       | AKRIB1 AKRIB10 DGKI AKR1D1 TBXAS1 AGK CYP51A1 CYP53A5 CYP3A7 CYP3A4 CYP3A43 ACHE |
| 8   | 11         | 14 (19)      | 54.22                       | CYP1B1 CYP1B2 DGAT1 FDFT1 LYPLA1 AGPAT6 CYP7A1 CYP7B1 ASAH1 LPL EPHX2 |
| 9   | 11         | 12 (15)      | 60.03                       | VGGC STPLC1 HSD17B3 BAAT ALDH1B1 PTGS1 PTGES2 PTGES CEL AGPAT2 PTGDS |
| 10  | 25         | 30 (19)      | 77.02                       | ALOX5 ASAH2C ACADSB CHAT ASAH2 SGMS1 LIPF CH25H LIPA CYP2C18 CYP2C19 CYP2C9 CYP2CS SCD CYP17A1 SGPL1 PLA2G12B OLAH PTPLA AKR1C1 AKR1C2 AKR1C3 AKR1C4 ECHS1 CYP2E1 |
| 11  | 15         | 17 (12)      | 55.75                       | DAK ACAT1 FADS1 FADS2 TM7F2 CHKA CPT1A HSD1B12 DGRZ DHCR7 NEU3 DGAT2 PHCA PTDSS2 SMPD1 |
| 12  | 9          | 13 (13)      | 62.14                       | GPD1 SOAT2 DGKA HSD17B6 CYP2B1 MBOAT5 LTA4H CHPT1 ETK1 |
| 13  | 0          | 1 (0)        | 49.45                       | GALC CYP4A6I DEGS2 ACOT1 ACOT2 ACOT4 SPTLC2 |
| 14  | 7          | 9 (8)        | 58.18                       | GALT CYP4A6I DEGS2 ACOT1 ACOT2 ACOT4 SPTLC2 |
| 15  | 7          | 8 (10)       | 63.13                       | AGPAT7 PLA2G8B PLA2G4A LIPC CYP1A1 CYP1A2 PLA2G1A |
| 16  | 10         | 10 (23)      | 79.48                       | LPCAT2 HSD17B2 CDIPT HSD3B7 HSD11B2 LCAT PLA2G15 SMPD3 PLA2G10 DCI |
| 17  | 17         | 21 (13)      | 78.39                       | PEMT ALDH3A2 HSD17B1 PHOSPH01 ACOX1 SPHK1 PGSI ENP7 PCYT2 FASN ACACA DGKE PAFAH1B1 GGT6 ALOX5 PLD2 ALOX12 |
| 18  | 0          | 4 (0)        | 12.09                       | SULT2B1 SPHK2 CPT1C LEN4 SLC27A5 CYP2B6 PAFAH1B3 PPAP2C GPX4 ACER1 GCDH GPSN2 CYP4F3 CYP4F2 |
| 19  | 14         | 14 (14)      | 79.39                       | PTGIS CDS2 CRKL1 |
| 20  | 3          | 4 (2)        | 73.99                       | GPL15 CDS2 CRKL1 |
| 21  | 4          | 4 (6)        | 47.05                       | CBRI CBRI3 AGPAT3 LSS |
| 22  | 10         | 13 (2)       | 52.62                       | PLA2G6 MCAT PNPLA3 CERK CPT1B CHKB ARSA COMT GGT1A1 GGT1 |
| X   | 6          | 9 (15)       | 60.31                       | DGAT2L4 GLA ACSL4 PCY1T1B GK STS |

**Table S27:** Lipid Metabolism (subclass). See Figure S1-8 and Table S8.
| Chr | # of genes | # of SCR(SC) | % of chromosome covered by SCR | captured genes |
|-----|------------|--------------|-------------------------------|----------------|
| 1   | 14         | 15           | 6(12) 13(27)                  | 49.81 MGST3 UCK2 DPYD GSTM4 GSTM2 GSTM1 GSTM5 GSTM3 EPHX1 |
| 2   | 12         | 13           | 4(10) 17(35)                  | 56.62 CYP1B1 UGT1A8 UGT1A10 UGT1A9 UGT1A7 UGT1A6 UGT1A5 UGT1A4 UGT1A3 UGT1A1 XDH AOX1 |
| 3   | 2          | 3            | 2(4) 14(27)                  | 60.41 UMPS IMPDH2 |
| 4   | 9          | 17           | 1(1) 8(19)                    | 39.87 UGT2B17 UGT2B15 UGT2B10 UGT2A3 UGT2B7 UGT2B11 UGT2B28 UGT2B4 UGT2A1 |
| 5   | 0          | 0            | 0(0) 8(18)                    | 34.22 |
| 6   | 6          | 6            | 2(3) 11(23)                  | 63.67 TPMT GSTA2 GSTA1 GSTA5 GSTA3 GSTA4 |
| 7   | 4          | 8            | 1(5) 7(31)                    | 51.25 CYP3A5 CYP3A7 CYP3A4 CYP3A3 |
| 8   | 2          | 3            | 1(3) 8(23)                    | 49.72 NAT1 NAT2 |
| 9   | 1          | 1            | 1(3) 10(20)                  | 59.21 UCK1 |
| 10  | 11         | 11           | 4(13) 11(22)                  | 68.83 CYP2C19 CYP2C18 CYP2C29 CYP2C8 CYP2E1 AKR1C1 AKR1C2 AKR1C3 AKR1C4 GSTO1 GSTO2 |
| 11  | 3          | 3            | 1(2) 8(14)                    | 50.14 GSTP1 ALDH3B2 ALDH3B1 |
| 12  | 1          | 1            | 1(4) 8(18)                    | 56.45 MGST1 |
| 13  | 0          | 0            | 0(0) 5(14)                    | 39.59 |
| 14  | 1          | 1            | 1(1) 5(14)                    | 49.58 GSTZ1 |
| 15  | 2          | 3            | 1(3) 6(13)                    | 57.73 CYP1A1 CYP1A2 |
| 16  | 4          | 4            | 2(3) 7(23)                    | 71.58 TK2 CES2 CES1 CES7 |
| 17  | 2          | 2            | 2(6) 7(13)                    | 68.87 ALDH3A1 TK1 |
| 18  | 0          | 0            | 0(0) 1(4)                     | 10.45 |
| 19  | 7          | 7            | 2(8) 5(15)                    | 73.56 CYP2A6 CYP2A7 CYP2B6 CYP2A13 CYP2F1 CYP2S1 DHDH |
| 20  | 2          | 2            | 2(4) 5(8)                     | 61.98 ITPA UCKL1 |
| 21  | 0          | 0            | 0(0) 2(7)                     | 39.06 |
| 22  | 4          | 5            | 2(8) 2(8)                     | 45.07 CYP2D6 ECGF1 GSTT2 GSTT1 |
| X   | 3          | 3            | 2(5) 8(23)                    | 50.02 MAOA MAOB HPRT1 |

**Table S28**: Xenobiotics Biodegradation and Metabolism (subclass). See Figure S1-9 and Table S8.
| class                  | subclass                          | pathway                        | # genes | % chromosomes | % covered genes | P-value |
|------------------------|-----------------------------------|--------------------------------|---------|---------------|-----------------|---------|
| hsa04210               | Cellular Processes                | Apoptosis                      | 87      | 7.48          | 27.58           | 0.014   |
| hsa04114               | Cellular Processes                | Oocyte meiosis                  | 113     | 54.43         | 74.33           | 0.05    |
| hsa04810               | Cellular Processes                | Regulation of actin cytoskeleton| 214     | 11.31         | 28.97           | 0.029   |
| hsa04144               | Cellular Processes                | all                            | 214     | 11.31         | 28.97           | 0.029   |
| hsa02010               | Environmental Information Processing | Membrane Transport            | 44      | 49.68         | 75.00           | 0.082   |
| hsa04020               | Environmental Information Processing | Signal Transduction            | 178     | 60.84         | 81.46           | <0.001  |
| hsa04010               | Environmental Information Processing | Signal Transduction            | 270     | 63.11         | 77.77           | 0.091   |
| hsa04330               | Environmental Information Processing | Signal Transduction            | 47      | 5.05          | 27.65           | 0.03    |
| hsa04070               | Environmental Information Processing | Signal Transduction            | 78      | 47.83         | 71.79           | 0.016   |
| hsa04370               | Environmental Information Processing | Signal Transduction            | 75      | 62.50         | 90.66           | 0.036   |
| hsa04310               | Environmental Information Processing | Signal Transduction            | 150     | 54.01         | 73.33           | 0.019   |
| Environmental Information Processing | Signal Transduction | 907     | 55.23         | 67.25           | 0.035           |

Table S29-1: KEGG’s pathways or KEGG’s subclasses whose genes are covered by structural cluster regions, defined on non-isolated structural clusters as described in Methods, in a highly non random manner. For each subclass (corresponding to lines having “all” as pathway column), the corresponding curve is reported in Figs. S2. The P-value associated to the best point in the curve is given. The coordinates of this point are described. Only pathways or subclasses with associated P-values < 0.1 are listed. They belong to the classes “Cellular Processes” and “Environmental Information Processing”.
| class     | subclass     | pathway                          | # genes | % chromosomes | % covered genes | P-value |
|-----------|--------------|----------------------------------|---------|---------------|-----------------|---------|
| hsa05215  | Human Diseases | Cancers                          | 89      | 46.88         | 69.66           | 0.07    |
| hsa05416  | Human Diseases | Cardiovascular Diseases          | 70      | 9.50          | 41.42           | 0.001   |
|           | Human Diseases | Cardiovascular Diseases          | all     | 33.12         | 53.59           | 0.061   |
| hsa05330  | Human Diseases | Immune System Diseases           | 35      | 10.42         | 54.28           | 0.002   |
| hsa05310  | Human Diseases | Immune System Diseases           | 28      | 28.83         | 82.14           | <0.001  |
| hsa05320  | Human Diseases | Immune System Diseases           | 50      | 10.42         | 38.00           | 0.022   |
| hsa05332  | Human Diseases | Immune System Diseases           | 37      | 9.50          | 62.16           | <0.001  |
| hsa05322  | Human Diseases | Immune System Diseases           | 138     | 12.18         | 57.24           | <0.001  |
|           | Human Diseases | Immune System Diseases           | all     | 11.31         | 43.75           | <0.001  |
| hsa05140  | Human Diseases | Infectious Diseases              | 70      | 11.31         | 42.85           | 0.003   |
| hsa05130  | Human Diseases | Infectious Diseases              | 58      | 21.22         | 50.00           | 0.012   |
| hsa05131  | Human Diseases | Infectious Diseases              | 63      | 9.50          | 36.50           | 0.012   |
|           | Human Diseases | Infectious Diseases              | all     | 326           | 9.50            | 27.30   | 0.002   |
| hsa04940  | Human Diseases | Metabolic Diseases               | 41      | 10.42         | 53.65           | <0.001  |
|           | Human Diseases | Metabolic Diseases               | all     | 105           | 9.50            | 30.47   | 0.048   |
| hsa05010  | Human Diseases | Neurodegenerative Diseases       | 161     | 21.98         | 49.06           | 0.005   |
| hsa05014  | Human Diseases | Neurodegenerative Diseases       | 53      | 41.26         | 71.69           | 0.026   |
| hsa05016  | Human Diseases | Neurodegenerative Diseases       | 177     | 30.09         | 53.10           | 0.063   |
| hsa05012  | Human Diseases | Neurodegenerative Diseases       | 118     | 29.46         | 51.69           | 0.074   |
|           | Human Diseases | Neurodegenerative Diseases       | all     | 323           | 21.98           | 44.27   | 0.002   |

Table S29-2 continued. Pathways or subclasses with associated P-values < 0.1 and belonging to the class "Human diseases" are listed.
| class | subclass | pathway | # genes | % chromosomes | % covered genes | P-value |
|-------|----------|---------|---------|---------------|-----------------|---------|
| hsa00330 | Metabolism | Amino Acid Metabolism | Arginine and proline metabolism | 54 | 79.26 | 94.44 | 0.078 |
| hsa00290 | Metabolism | Amino Acid Metabolism | Valine, leucine and isoleucine biosynthesis | 11 | 59.82 | 90.90 | 0.071 |
| hsa00232 | Metabolism | Biosynthesis of Other Secondary Metabolites | Caffeine metabolism | 7 | 15.57 | 100.00 | <0.001 |
| Metabolism | Biosynthesis of Other Secondary Metabolites | all | 11 | 15.57 | 72.72 | 0.025 |
| hsa00053 | Metabolism | Carbohydrate Metabolism | Ascorbate and aldarate metabolism | 25 | 9.50 | 40.00 | 0.005 |
| hsa00049 | Metabolism | Carbohydrate Metabolism | Pentose and glucuronate interconversions | 28 | 9.50 | 39.28 | 0.008 |
| hsa00030 | Metabolism | Carbohydrate Metabolism | Pentose phosphate pathway | 27 | 65.40 | 81.48 | 0.097 |
| hsa00511 | Metabolism | Glycan Biosynthesis and Metabolism | Other glycan degradation | 16 | 33.12 | 75.00 | 0.02 |
| hsa00592 | Metabolism | Lipid Metabolism | alpha-Linolenic acid metabolism | 18 | 48.30 | 83.33 | 0.033 |
| hsa00590 | Metabolism | Lipid Metabolism | Arachidonic acid metabolism | 57 | 48.30 | 71.92 | 0.073 |
| hsa00561 | Metabolism | Lipid Metabolism | Glycerolipid metabolism | 49 | 51.90 | 73.46 | 0.051 |
| hsa00564 | Metabolism | Lipid Metabolism | Glycerophospholipid metabolism | 78 | 48.30 | 70.51 | 0.028 |
| hsa00591 | Metabolism | Lipid Metabolism | Linoleic acid metabolism | 28 | 12.18 | 46.42 | 0.01 |
| hsa00140 | Metabolism | Lipid Metabolism | Steroid hormone biosynthesis | 55 | 24.17 | 58.18 | <0.001 |
| Metabolism | Lipid Metabolism | all | 339 | 24.17 | 41.88 | 0.005 |
| hsa00860 | Metabolism | Metabolism of Cofactors and Vitamins | Porphyrin and chlorophyll metabolism | 42 | 40.20 | 59.52 | 0.036 |
| hsa00830 | Metabolism | Metabolism of Cofactors and Vitamins | Retinol metabolism | 64 | 12.18 | 42.18 | <0.001 |
| hsa00903 | Metabolism | Metabolism of Terpenoids and Polyketides | Limonene and pinene degradation | 8 | 51.90 | 87.50 | 0.096 |
| hsa00230 | Metabolism | Nucleotide Metabolism | Purine metabolism | 159 | 47.36 | 64.15 | 0.057 |
| Metabolism | Nucleotide Metabolism | all | 186 | 45.40 | 60.21 | 0.073 |
| hsa00982 | Metabolism | Xenobiotics Biodegradation and Metabolism | Drug metabolism - cytochrome P450 | 72 | 12.18 | 34.72 | 0.011 |
| hsa00983 | Metabolism | Xenobiotics Biodegradation and Metabolism | Drug metabolism - other enzymes | 51 | 9.50 | 39.21 | <0.001 |
| hsa00980 | Metabolism | Xenobiotics Biodegradation and Metabolism | Metabolism of xenobiotics by cytochrome P450 | 70 | 18.84 | 47.14 | <0.001 |
| Metabolism | Xenobiotics Biodegradation and Metabolism | all | 108 | 19.64 | 42.59 | 0.006 |

Table S29-3 continued. Pathways or subclasses with associated P-values < 0.1 and belonging to the class "Metabolism" are listed.
| class        | subclass       | pathway                                      | # genes | % chromosomes | % covered genes | P-value |
|--------------|----------------|----------------------------------------------|---------|---------------|-----------------|---------|
| hsa04270     | Organismal Sys-| Circulatory System                           | 125     | 54.43         | 75.20           | 0.038   |
|              | tems            | Vascular smooth muscle contraction           |         |               |                 |         |
| hsa04920     | Organismal Sys-| Circulatory System                           | 197     | 56.01         | 75.12           | 0.042   |
|              | tems            | all                                          |         |               |                 |         |
| hsa04912     | Organismal Sys-| Endocrine System                             | 67      | 44.39         | 67.16           | 0.043   |
|              | tems            | Adipokine signaling pathway                  |         |               |                 |         |
| hsa04910     | Organismal Sys-| Endocrine System                             | 137     | 48.77         | 72.26           | 0.006   |
|              | tems            | Insulin signaling pathway                    |         |               |                 |         |
| hsa04962     | Organismal Sys-| Endocrine System                             | 44      | 34.77         | 68.18           | 0.006   |
|              | tems            | Vasopressin-regulated water reabsorption     |         |               |                 |         |
| hsa04612     | Organismal Sys-| Immune System                                | 83      | 10.42         | 45.78           | <0.001  |
|              | tems            | Antigen processing and presentation          |         |               |                 |         |
| hsa04664     | Organismal Sys-| Immune System                                | 78      | 48.30         | 76.92           | <0.001  |
|              | tems            | Fc epsilon RI signaling pathway              |         |               |                 |         |
| hsa04666     | Organismal Sys-| Immune System                                | 93      | 61.86         | 88.17           | 0.025   |
|              | tems            | Fc gamma R-mediated phagocytosis             |         |               |                 |         |
| hsa04649     | Organismal Sys-| Immune System                                | 85      | 18.04         | 41.17           | 0.092   |
|              | tems            | Hematopoietic cell lineage                   |         |               |                 |         |
| hsa04672     | Organismal Sys-| Immune System                                | 46      | 16.40         | 50.00           | 0.007   |
|              | tems            | Intestinal immune network for IgA production|         |               |                 |         |
| hsa04650     | Organismal Sys-| Immune System                                | 134     | 9.50          | 31.34           | 0.029   |
|              | tems            | Natural killer cell mediated cytotoxicity    |         |               |                 |         |
| hsa04660     | Organismal Sys-| Immune System                                | 108     | 8.51          | 26.85           | 0.078   |
|              | tems            | T cell receptor signaling pathway            |         |               |                 |         |
|              |                 | all                                          | 801     | 12.18         | 29.08           | <0.001  |
| hsa04720     | Organismal Sys-| Nervous System                               | 70      | 60.50         | 85.71           | 0.035   |
|              | tems            | Long-term potentiation                       |         |               |                 |         |
| hsa04722     | Organismal Sys-| Nervous System                               | 126     | 53.19         | 72.22           | 0.059   |
|              | tems            | Neurotrophin signaling pathway               |         |               |                 |         |
| hsa04740     | Organismal Sys-| Sensory System                               | 386     | 21.98         | 65.02           | <0.001  |
|              | tems            | Olfactory transduction                       |         |               |                 |         |
| hsa04744     | Organismal Sys-| Sensory System                               | 29      | 35.86         | 68.96           | 0.024   |
|              | tems            | Phototransduction                            |         |               |                 |         |
| hsa04742     | Organismal Sys-| Sensory System                               | 51      | 38.04         | 86.27           | <0.001  |
|              | tems            | Taste transduction                           |         |               |                 |         |
|              |                 | all                                          | 448     | 21.98         | 63.16           | <0.001  |

Table S29-4 continued. Pathways or subclasses with associated P-values < 0.1 and belonging to the class "Organismal Systems" are listed.
|       | % of FS coverage | % of SCR coverage | FS-SCR overlapping |
|-------|------------------|-------------------|--------------------|
|       |                  |                   | %FS    | %SCR    |
| chr1  | 56.00            | 23.16             | 21.10  | 51.01   |
| chr2  | 27.72            | 27.74             | 26.20  | 26.19   |
| chr3  | 11.93            | 27.23             | 30.34  | 13.29   |
| chr4  | 22.32            | 20.88             | 21.01  | 23.39   |
| chr5  | 33.21            | 19.63             | 23.63  | 39.98   |
| chr6  | 17.92            | 30.27             | 40.41  | 23.90   |
| chr7  | 38.80            | 29.94             | 53.63  | 71.95   |
| chr8  | 23.16            | 26.43             | 18.52  | 16.23   |
| chr9  | 19.11            | 33.63             | 10.84  | 6.16    |
| chr10 | 38.63            | 31.76             | 35.14  | 42.75   |
| chr11 | 24.99            | 23.67             | 30.00  | 33.35   |
| chr12 | 34.64            | 31.66             | 23.93  | 26.18   |
| chr13 | 24.88            | 16.96             | 17.82  | 26.13   |
| chr14 | 12.69            | 24.35             | 0.00   | 0.00    |
| chr15 | 9.47             | 32.39             | 41.86  | 12.23   |
| chr16 | 16.21            | 39.44             | 46.04  | 18.92   |
| chr17 | 6.85             | 31.91             | 0.00   | 0.00    |
| chr18 | 22.86            | 6.68              | 0.00   | 0.00    |
| chr19 | 72.89            | 45.96             | 60.60  | 96.11   |
| chr20 | 10.09            | 28.74             | 46.99  | 16.50   |
| chr21 | 0.00             | 20.72             | 0.00   | 0.00    |
| chr22 | 32.99            | 26.00             | 58.91  | 74.76   |
| chrX  | 14.60            | 21.68             | 0.00   | 0.00    |
| Total | 26.38            | 26.40             | 28.56  | 28.54   |

**Table S30**: Coverage of fragile sites (FS, first column) and of structural cluster regions (SCR, second column) on human chromosomes. The overlapping region is described by the proportion of FS shared with SCR (%FS) and the proportion of SCR shared by FS (%SCR). See also Figure S13. Notice that SCRs are defined with respect to a global chromosomal coverage of 26.40%.
Table S31: Coverage of genes associated to different biological pathways by structural cluster regions (SCR) and fragile sites (FS) on human chromosomes. Structural cluster regions cover 26.40% of the human genome (see Methods). We only consider those pathways that appeared to be statistically meaningful in the analysis, and whose corresponding curves are plotted in Figures S1. Bold values indicate best coverage (line by line). The number of genes for each pathway (third column) and the percentage of genes captured in regions where SCR and FS overlap (FS-SCR) (sixth column) are also indicated.
Table S32: Comparison of cancer gene coverage between structural cluster regions (SCR) and fragile sites (FS). Cancer gene datasets are analyzed with a similar chromosome coverage considered for SCR (26.40%, see Methods) and FS (26.38%). The percentage of cancer genes in the dataset located in SCR and FS is reported. Best values are indicated in bold. Regions where structural cluster regions and fragile sites overlap (FS-SCR) are also reported. Overlapping regions cover 7.53% of the human chromosomes. The number of genes contained in each dataset is also reported.