

## Supplementary Information

### Nongenetic cancer-risk SNPs affect oncogenes, tumor suppressor genes and immune function

M. Fagny<sup>1</sup>, J. Platig<sup>2,3</sup>, M.L. Kuijjer<sup>4,5,6</sup>, X. Lin<sup>5</sup>, and J. Quackenbush<sup>2,4,5,7</sup>

<sup>1</sup>Genetique Quantitative et Evolution - Le Moulon, Institut National de la Recherche agronomique, Universite Paris-Sud, Centre National de la Recherche Scientifique, AgroParisTech, Universite Paris-Saclay, France

<sup>2</sup>Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA

<sup>3</sup>Harvard Medical School, Boston, Massachusetts, USA

<sup>4</sup>Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, Massachusetts, USA

<sup>5</sup>Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

<sup>6</sup>Centre for Molecular Medicine Norway, University of Oslo, Oslo, Norway

<sup>7</sup>Department of Cancer Biology, Dana-Farber Cancer Institute, Boston, Massachusetts, USA

## Supplementary Figures

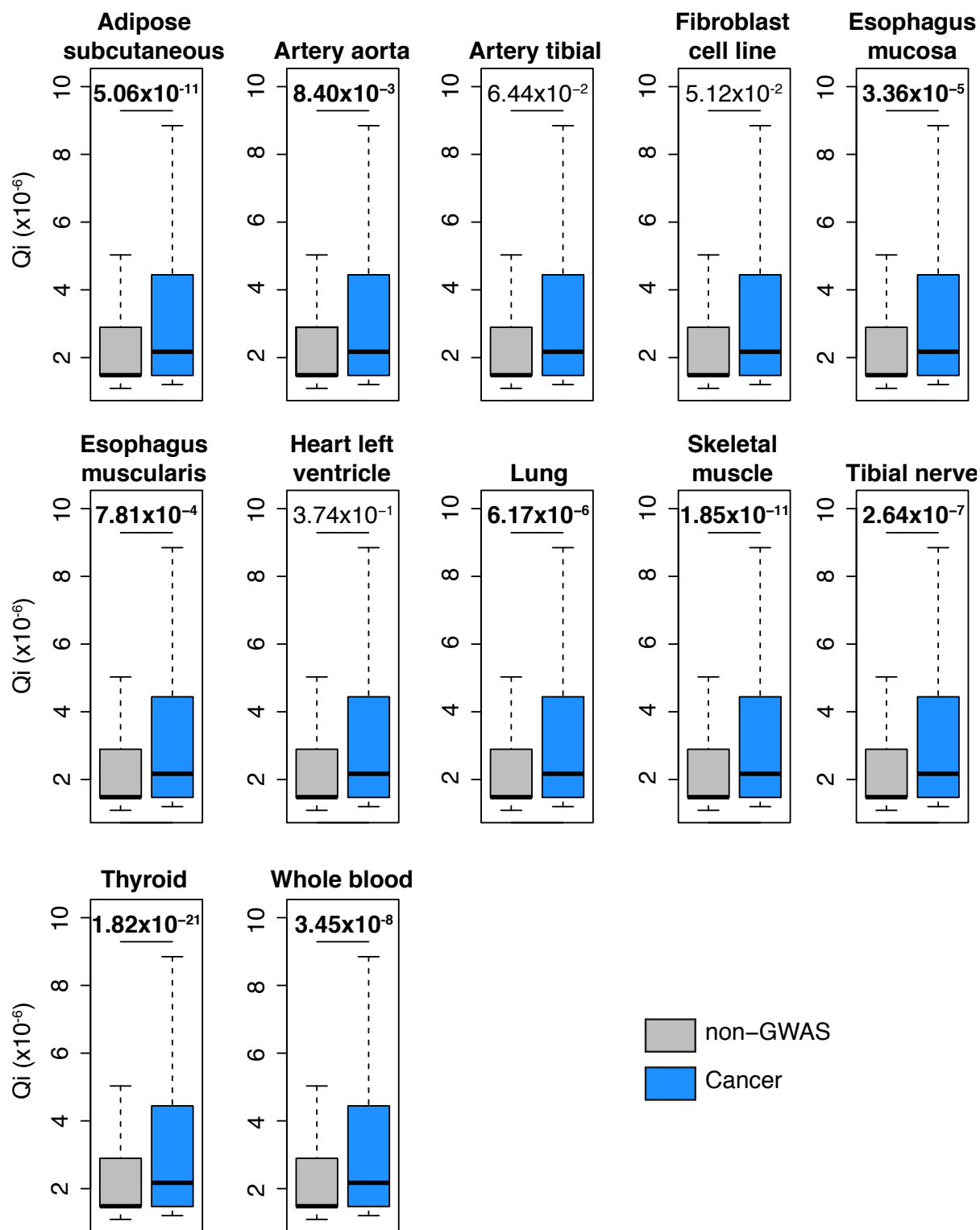


**Figure S1:** Related to Figure 2. SNPs associated in GWAS with a increased risk of developing cancer have higher network core scores than non-cancer SNPs. This enrichment is significant in ten of thirteen tissues; significant p-values are indicated in bold text. The lack of significance in tibial artery and heart left ventricle may reflect the rarity of cancers in these tissues. The failure to reach significance in fibroblast cell lines may be due to alteration of normal cellular functions in culture.

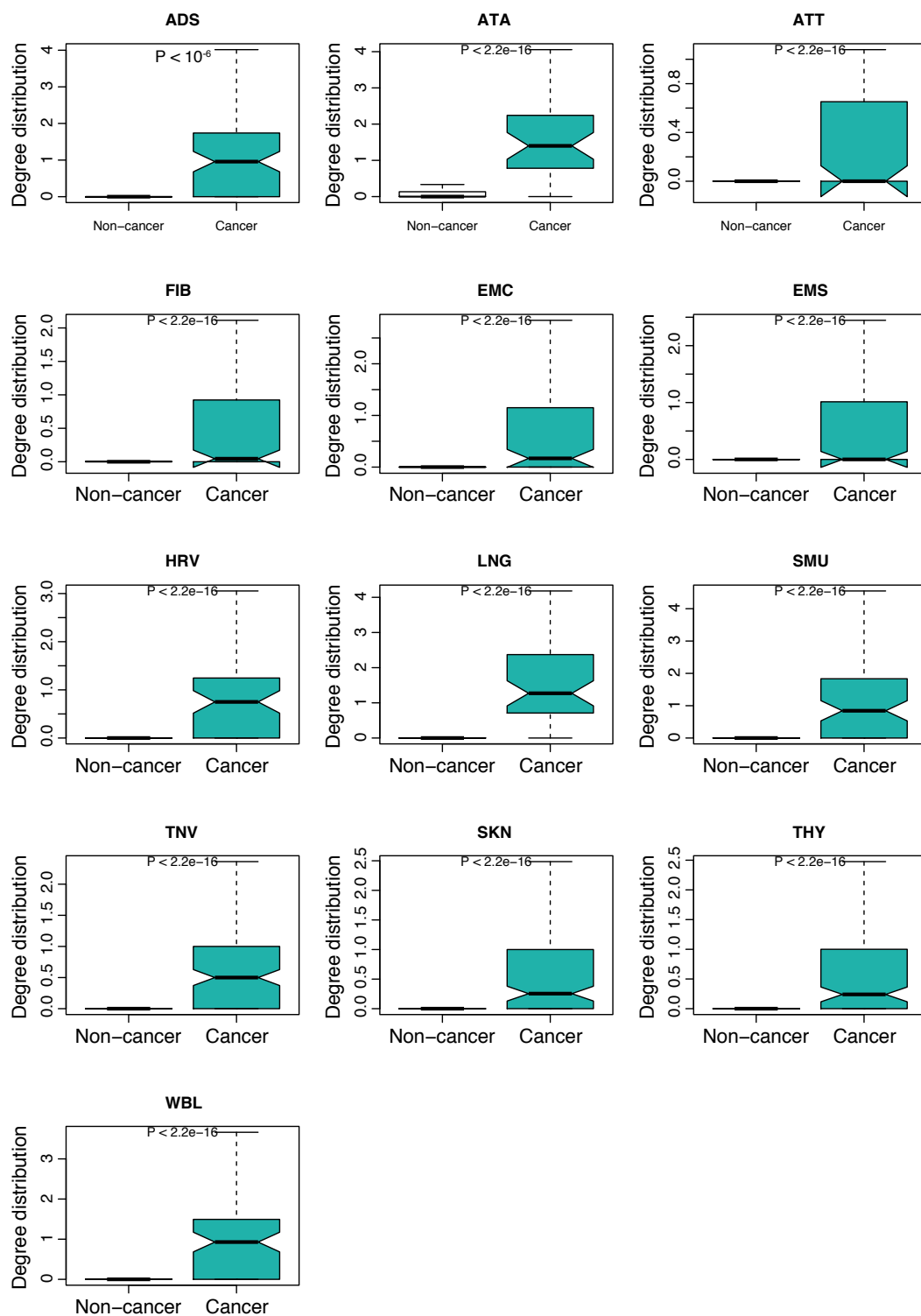


**Figure S2:** Cancer risk SNPs preferentially target oncogenes and tumor suppressor genes. In each panel, box plots present distributions of the number of tumor suppressor genes and oncogenes associated with cancer-risk SNPs and with other SNPs in each tissue-specific network. P values were obtained using  $10^6$  resamplings, taking into account global differences in degree distribution between cancer-risk SNPs and other SNPs.

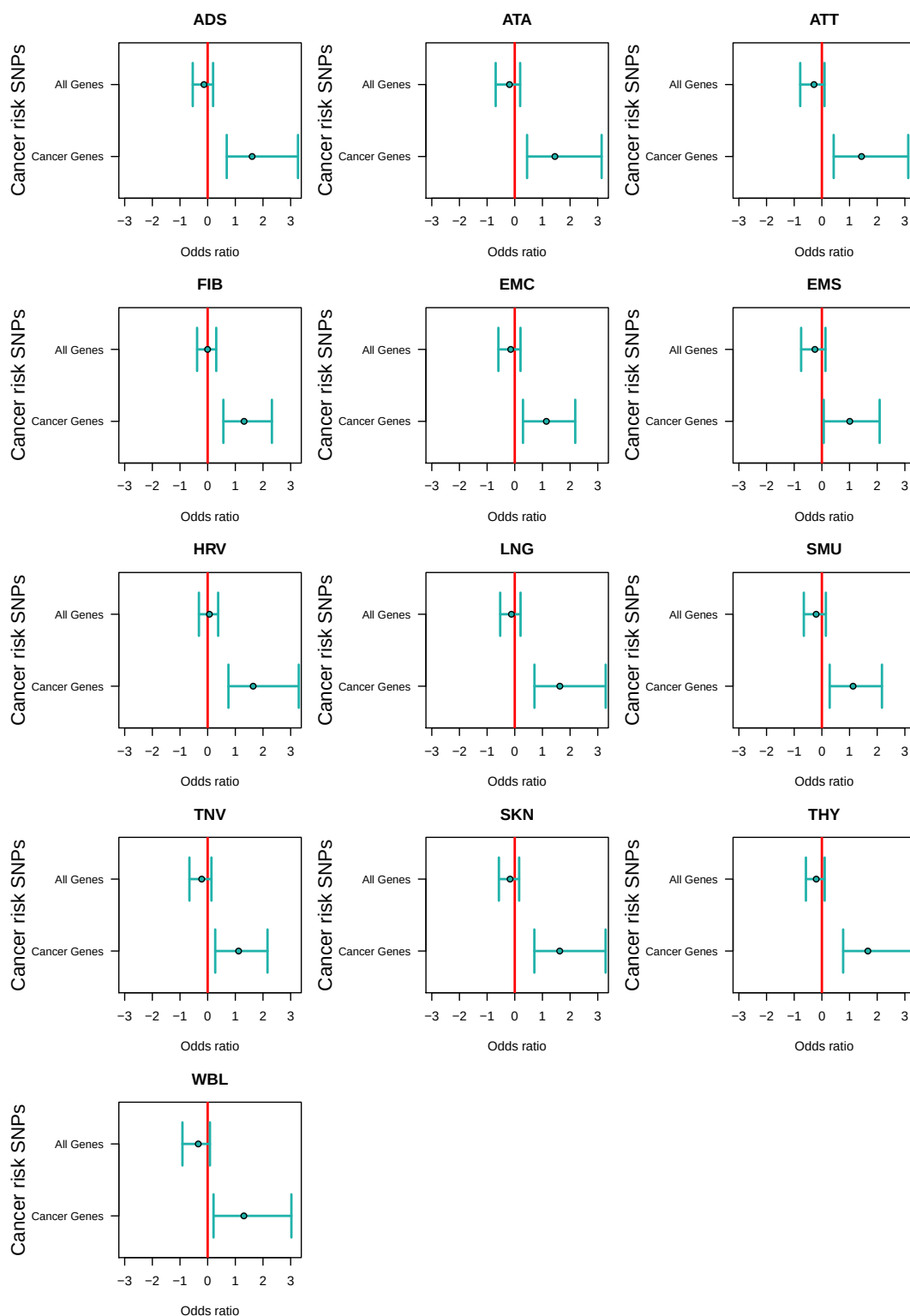


**Figure S3:** Cancer-risk SNPs associated with gene expression levels in eQTL analyses are preferentially located in the promoters of oncogenes and tumor suppressor genes, independent of tissue. The Odds ratio measures the enrichment in cancer-risk SNPs among all genes' promoters (top) or oncogenes and tumor suppressor genes' promoters (bottom) compared to other SNPs.

## Supplementary Tables

**Table S1:** Summary of data: tissues and number of samples.

| Tissue names         | Abbreviation | GTEX tissues                         | Samples |
|----------------------|--------------|--------------------------------------|---------|
| Adipose subcutaneous | ADS          | Adipose - Subcutaneous               | 313     |
| Aorta                | ATA          | Artery - Aorta                       | 216     |
| Artery tibial        | ATT          | Artery - Tibial                      | 303     |
| Fibroblast           | FIB          | Skin cells - Transformed fibroblasts | 291     |
| Esophagus mucosa     | EMC          | Esophagus - Mucosa                   | 276     |
| Esophagus muscularis | EMS          | Esophagus - Muscularis               | 245     |
| Heart left ventricle | HRV          | Heart - Left ventricle               | 212     |
| Lung                 | LNG          | Lung                                 | 290     |
| Skeletal muscle      | SMU          | Muscle - Skeletal                    | 378     |
| Tibial nerve         | TNV          | Nerve - Tibial                       | 278     |
| Skin                 | SKN          | Skin - Not sun exposed (Suprapubic)  | 127     |
|                      |              | Skin - Sun exposed (Lower leg)       | 243     |
|                      |              | Total                                | 370     |
| Thyroid              | THY          | Thyroid                              | 295     |
| Whole blood          | WBL          | Whole blood                          | 365     |

**Table S2:** Tumor suppressor genes and Oncogenes IDs.

**Table S3:** List of cancer-related terms in EBI-GWAS catalog.

**Table S4:** Gene Ontology enrichment for communities.

**Table S5:** Enrichment in trans-eQTLs among cancer-risk SNPs.

| <b>Tissue</b> | <b>Odds ratio</b> | <b>P value</b> |
|---------------|-------------------|----------------|
| <b>ADS</b>    | 1.77              | 4.64E-02       |
| <b>ATA</b>    | 2.09              | 4.56E-02       |
| <b>ATT</b>    | 1.88              | 4.29E-02       |
| <b>FIB</b>    | 2.40              | 1.37E-03       |
| <b>EMC</b>    | 1.59              | 7.81E-02       |
| <b>EMS</b>    | 1.46              | 2.14E-01       |
| <b>HRV</b>    | 0.91              | 1.00E+00       |
| <b>LNG</b>    | 2.11              | 1.35E-02       |
| <b>SMU</b>    | 2.33              | 8.38E-04       |
| <b>TNV</b>    | 1.94              | 1.07E-02       |
| <b>SKN</b>    | 1.40              | 1.79E-01       |
| <b>THY</b>    | 7.84              | 9.51E-41       |
| <b>WBL</b>    | 2.19              | 6.16E-03       |

**Table S6:** Cancer-risk SNPs mapping to communities and corresponding Gene Ontology enrichment.

**Table S7:** Enrichment in cancer-risk SNPs among communities.

**Table S8:** An eQTL example : genes associated with rs72699833

| Ensembl ID         | HGNC           | Chr | Start       | End         | Type  | t.stat | P        | FDR      |
|--------------------|----------------|-----|-------------|-------------|-------|--------|----------|----------|
| ENSG00000092621.7  | <b>PHGDH</b>   | 1   | 120,202,421 | 120,286,838 | cis   | -3.80  | 1.67E-04 | 2.97E-02 |
| ENSG00000159166.9  | LAD1           | 1   | 201,342,372 | 201,368,736 | trans | -5.62  | 3.73E-08 | 1.93E-01 |
| ENSG00000065618.12 | COL17A1        | 10  | 105,791,044 | 105,845,760 | trans | -5.61  | 3.97E-08 | 1.99E-01 |
| ENSG00000186395.6  | <b>KRT10</b>   | 17  | 38,974,369  | 38,978,847  | trans | -6.02  | 4.24E-09 | 4.12E-02 |
| ENSG00000178934.4  | <b>LGALS7B</b> | 19  | 39,279,851  | 39,282,389  | trans | -6.00  | 4.84E-09 | 4.60E-02 |
| ENSG00000101311.11 | FERMT1         | 20  | 6,055,492   | 6,104,191   | trans | -5.70  | 2.54E-08 | 1.53E-01 |