

**Additional File 7:
Ingenuity Pathway Analysis for the CpGs that are
used for calculating DNA methylation age.**

**Horvath S. DNA Methylation age of
human tissues and cell types.**

Top Bio Functions

Diseases and Disorders

| Name | p-value | # Molecules |
|-----------------------------|---------------------|-------------|
| Cancer | 9.20E-05 - 3.17E-02 | 109 |
| Developmental Disorder | 2.55E-04 - 3.17E-02 | 28 |
| Endocrine System Disorders | 2.55E-04 - 3.17E-02 | 22 |
| Hereditary Disorder | 2.55E-04 - 3.17E-02 | 50 |
| Reproductive System Disease | 2.55E-04 - 3.12E-02 | 37 |

Molecular and Cellular Functions

| Name | p-value | # Molecules |
|-----------------------------------|---------------------|-------------|
| Cell Death and Survival | 1.07E-07 - 3.17E-02 | 74 |
| Cellular Growth and Proliferation | 3.65E-05 - 3.17E-02 | 71 |
| Lipid Metabolism | 2.13E-04 - 3.17E-02 | 35 |
| Molecular Transport | 2.13E-04 - 3.17E-02 | 35 |
| Small Molecule Biochemistry | 2.13E-04 - 3.17E-02 | 44 |

Physiological System Development and Function

| Name | p-value | # Molecules |
|---|---------------------|-------------|
| Immune Cell Trafficking | 2.58E-04 - 2.64E-02 | 28 |
| Hematological System Development and Function | 2.90E-04 - 3.17E-02 | 57 |
| Organismal Development | 4.61E-04 - 3.17E-02 | 56 |
| Embryonic Development | 6.06E-04 - 3.17E-02 | 36 |
| Tissue Development | 6.06E-04 - 3.17E-02 | 27 |

Top Canonical Pathways

| Name | p-value | Ratio |
|--|----------|------------------|
| Sertoli Cell-Sertoli Cell Junction Signaling | 7.71E-03 | 8/187 (0.043) |
| Death Receptor Signaling | 1.38E-02 | 4/63 (0.063) |
| Dopamine-DARPP32 Feedback in cAMP Signaling | 1.6E-02 | 7/167 (0.042) |
| D-mannose Degradation | 1.6E-02 | 1/1 (1) |
| Circadian Rhythm Signaling | 1.68E-02 | 3/36 (0.083) |

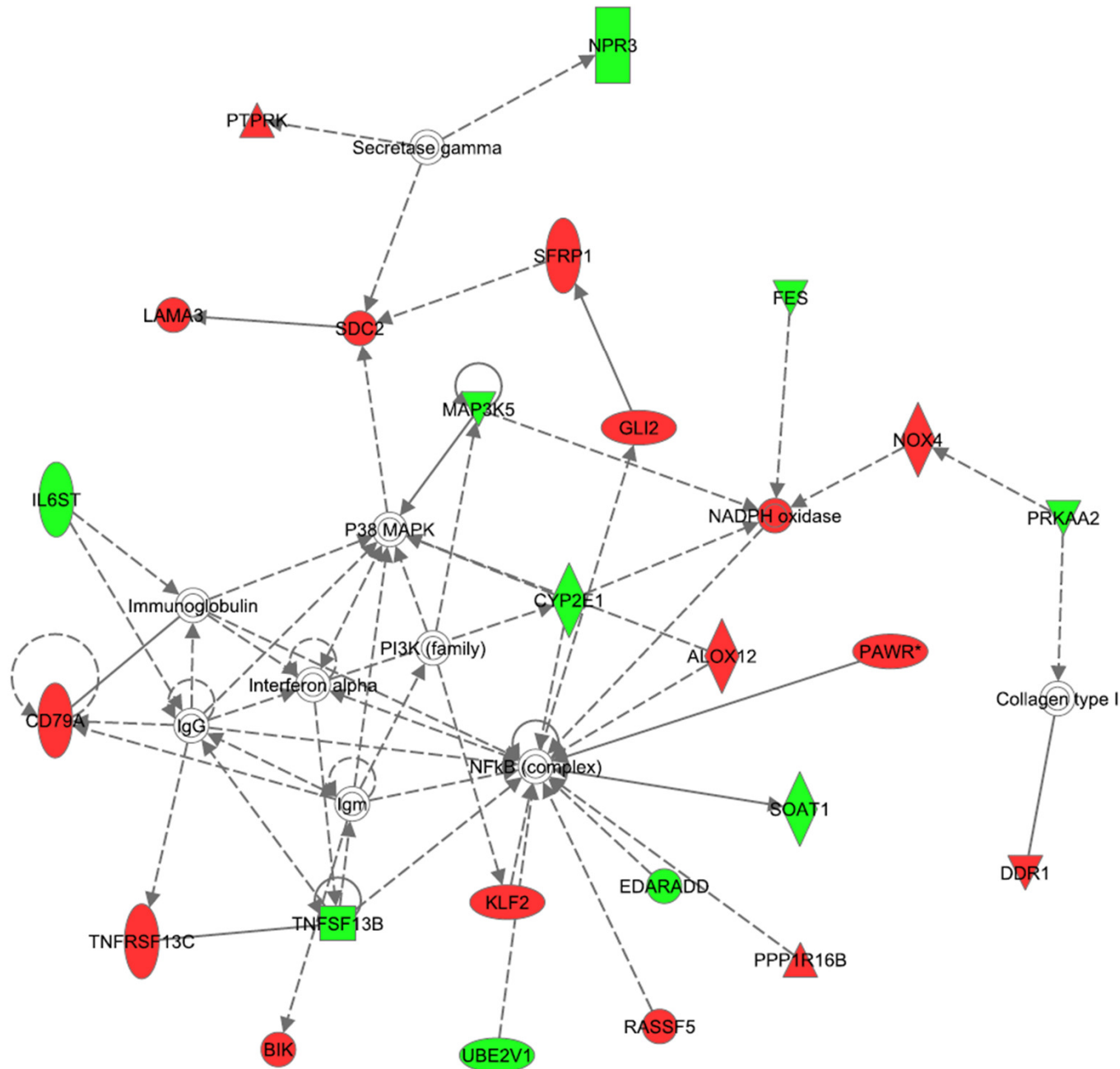
Top Upstream Regulators

| Upstream Regulator | p-value of overlap | Predicted Activation State |
|--------------------|--------------------|----------------------------|
| RHOA | 2.83E-04 | |
| PHC1 | 7.00E-04 | |
| TNF | 9.73E-04 | |
| ZFYVE9 | 1.39E-03 | |
| PI3K (family) | 2.43E-03 | |

Top Networks

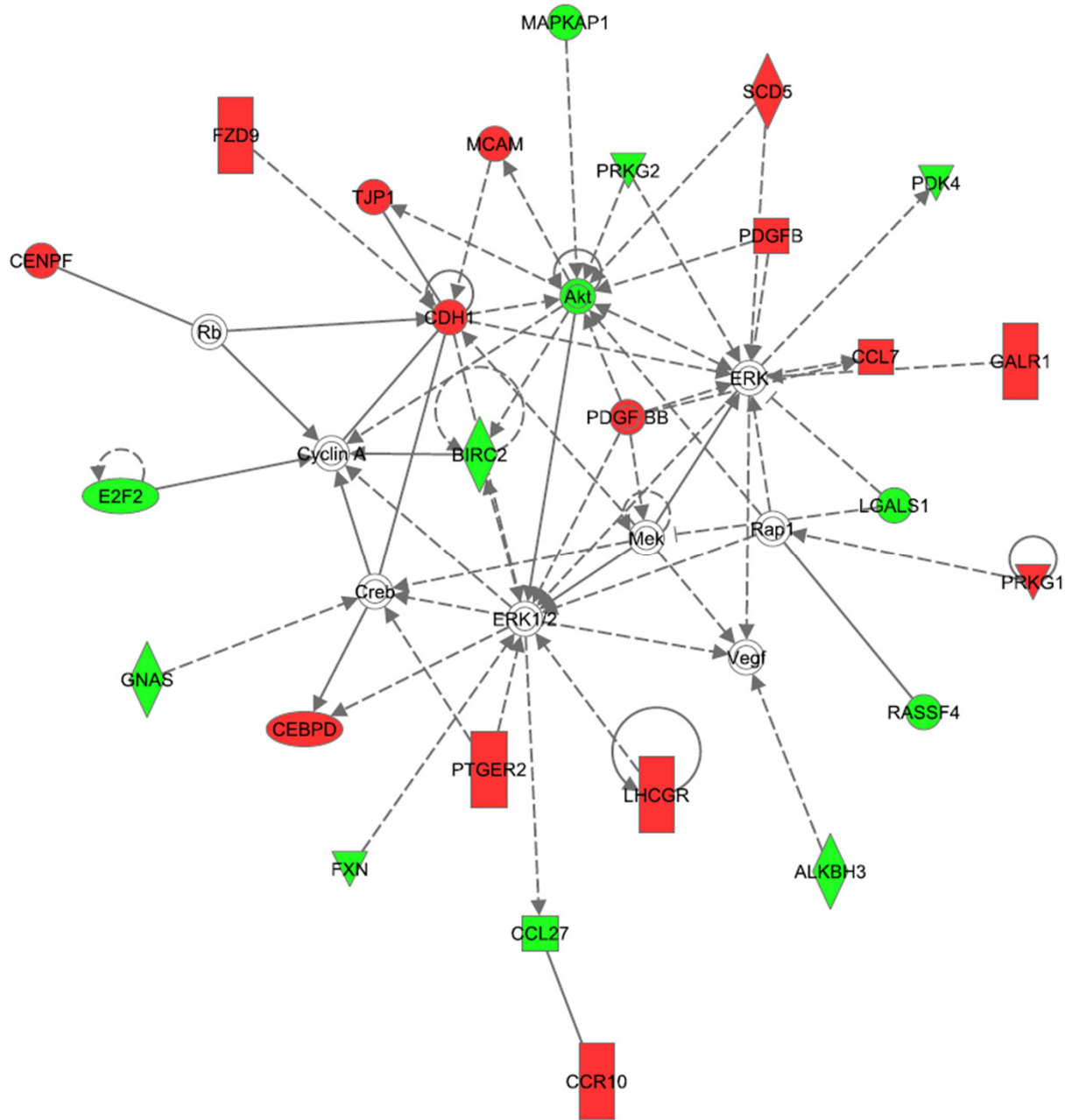
| ID | Associated Network Functions | Score |
|----|---|-------|
| 1 | Hematological System Development and Function, Tissue Morphology, Cell Death and Survival | 37 |
| 2 | Cellular Growth and Proliferation, Cell Signaling, Developmental Disorder | 37 |
| 3 | Hepatocellular Peroxisome Proliferation, Organismal Functions, Cellular Assembly and Organization | 30 |
| 4 | Cellular Development, Hematological System Development and Function, Hematopoiesis | 19 |
| 5 | Cardiovascular Disease, Hematological Disease, Cell-To-Cell Signaling and Interaction | 19 |

Network 1 p=E-37



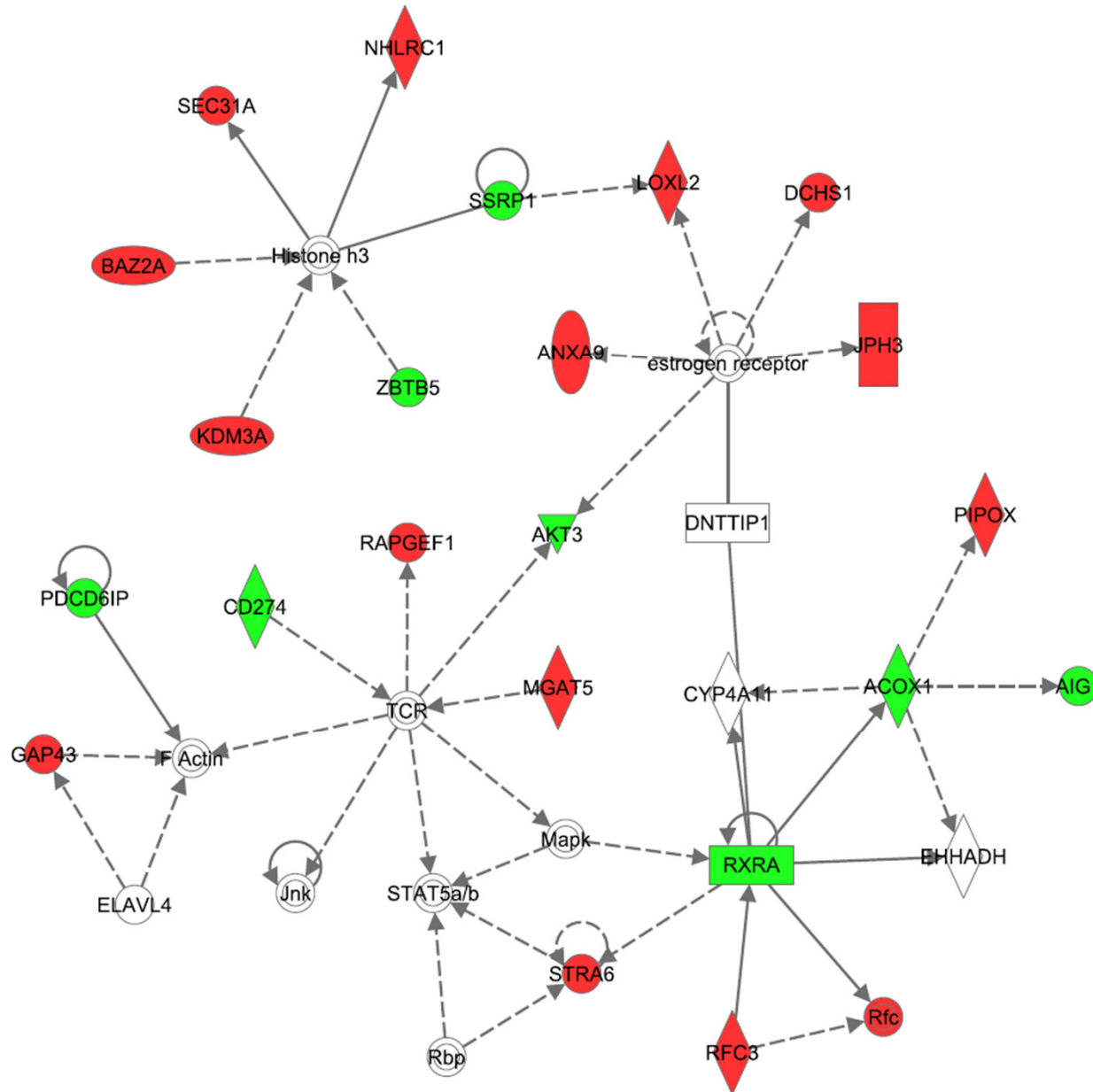
Genes colored in red (green) co-located with a CpG whose DNA methylation level positively (negatively) correlated with chronological age.

Network 2 p=E-37



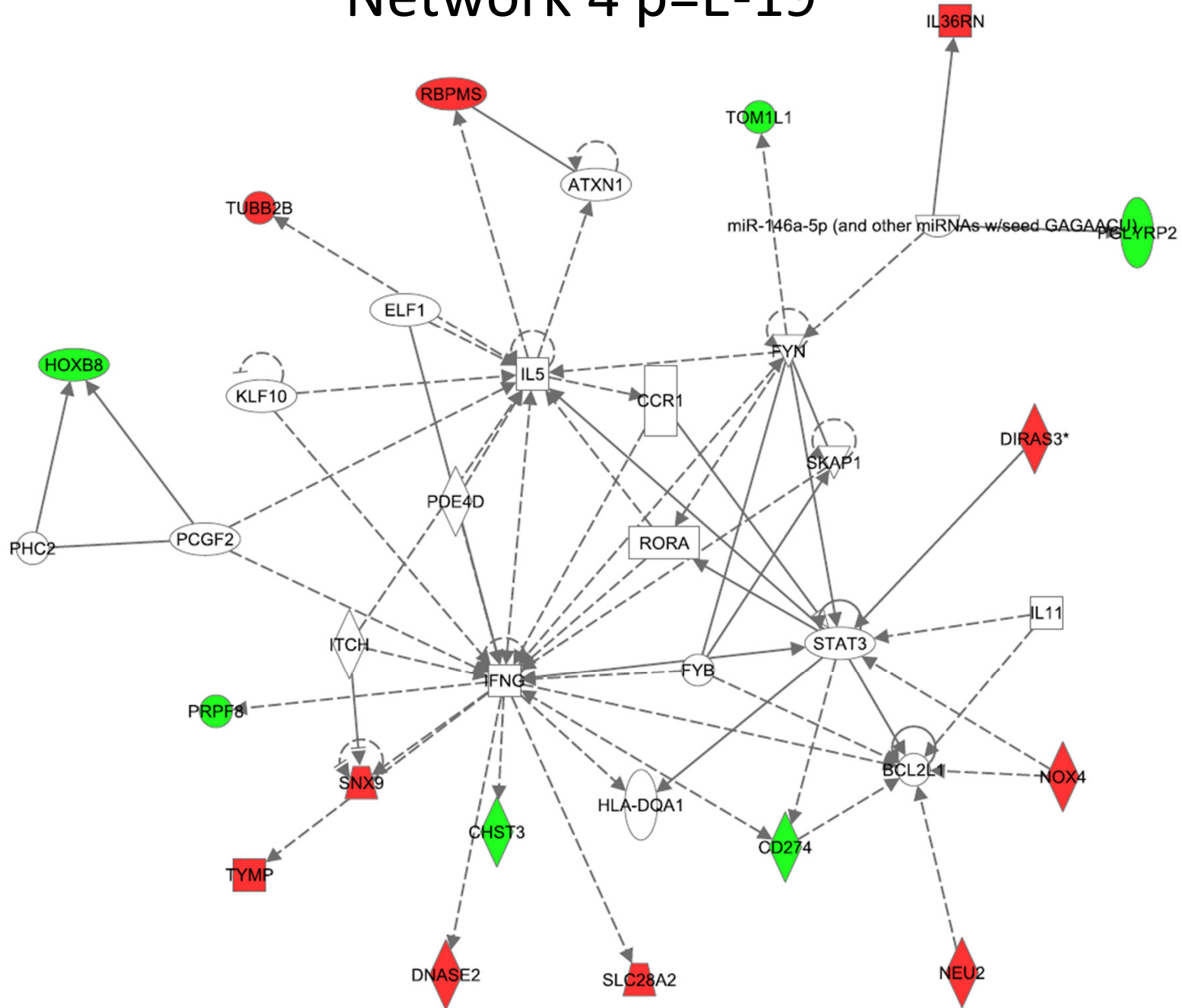
Genes colored in red (green) co-located with a CpG whose DNA methylation level positively (negatively) correlated with chronological age.

Network 3 p=E-30



Genes colored in red (green) co-located with a CpG whose DNA methylation level positively (negatively) correlated with chronological age.

Network 4 p=E-19



Network 5 p=E-19

