

A workflow for the creation of regulatory networks integrating miRNAs and lncRNAs associated with exposure to ionizing radiation using open source data and tools

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Supplementary Material

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1 Supplementary Tables

1.1 Supplementary Table 1

| Probe ID | RefSeq | Gene name |
|-----------------|---------------|------------------|
| A_23_P108751 | NM_001318898 | <i>FHL2</i> |
| A_23_P108751 | NM_001039492 | <i>FHL2</i> |
| A_23_P108751 | NM_001318896 | <i>FHL2</i> |
| A_23_P108751 | NM_201555 | <i>FHL2</i> |
| A_23_P108751 | NM_001318894 | <i>FHL2</i> |
| A_23_P108751 | NM_001450 | <i>FHL2</i> |
| A_23_P108751 | NM_001318899 | <i>FHL2</i> |
| A_23_P108751 | n/a | <i>FHL2</i> |
| A_23_P108751 | NM_001318897 | <i>FHL2</i> |
| A_23_P108751 | NM_001318895 | <i>FHL2</i> |
| A_23_P108751 | NM_201557 | <i>FHL2</i> |
| A_23_P108751 | NM_001374399 | <i>FHL2</i> |
| A_23_P113283 | n/a | n/a |
| A_23_P126836 | NM_001297562 | <i>TNFSF4</i> |
| A_23_P126836 | NM_003326 | <i>TNFSF4</i> |
| A_23_P135248 | n/a | <i>CCL27</i> |
| A_23_P135248 | NM_006664 | <i>CCL27</i> |
| A_23_P135248 | n/a | n/a |
| A_23_P14734 | NM_015920 | <i>RPS27L</i> |
| A_23_P14734 | n/a | <i>RPS27L</i> |
| A_23_P154688 | NM_001174090 | <i>SLC4A11</i> |
| A_23_P154688 | NM_001174089 | <i>SLC4A11</i> |
| A_23_P154688 | n/a | <i>SLC4A11</i> |
| A_23_P154688 | NM_001363745 | <i>SLC4A11</i> |
| A_23_P154688 | NM_032034 | <i>SLC4A11</i> |
| A_23_P23221 | n/a | <i>GADD45A</i> |
| A_23_P23221 | NM_001199742 | <i>GADD45A</i> |
| A_23_P23221 | NM_001924 | <i>GADD45A</i> |
| A_23_P23221 | NM_001199741 | <i>GADD45A</i> |
| A_23_P28886 | NM_182649 | <i>PCNA</i> |
| A_23_P30972 | n/a | <i>ASCC3</i> |
| A_23_P30972 | NM_001284271 | <i>ASCC3</i> |
| A_23_P30972 | NM_022091 | <i>ASCC3</i> |
| A_23_P30972 | NM_006828 | <i>ASCC3</i> |
| A_23_P38154 | NM_001258016 | <i>FDXR</i> |
| A_23_P38154 | NM_001258015 | <i>FDXR</i> |
| A_23_P38154 | n/a | <i>FDXR</i> |
| A_23_P38154 | NM_001258012 | <i>FDXR</i> |
| A_23_P38154 | NM_004110 | <i>FDXR</i> |
| A_23_P38154 | NM_001258014 | <i>FDXR</i> |

| Probe ID | RefSeq | Gene name |
|-----------------|---------------|------------------|
| A_23_P38154 | NM_024417 | <i>FDXR</i> |
| A_23_P38154 | NM_001258013 | <i>FDXR</i> |
| A_23_P39116 | NM_001320970 | <i>LIG1</i> |
| A_23_P39116 | NM_001320971 | <i>LIG1</i> |
| A_23_P39116 | NM_001289063 | <i>LIG1</i> |
| A_23_P39116 | NM_000234 | <i>LIG1</i> |
| A_23_P39116 | NM_001289064 | <i>LIG1</i> |
| A_23_P39116 | n/a | <i>LIG1</i> |
| A_23_P52610 | NM_001300734 | <i>DDB2</i> |
| A_23_P52610 | n/a | <i>DDB2</i> |
| A_23_P52610 | NM_000107 | <i>DDB2</i> |
| A_23_P52986 | n/a | <i>VWCE</i> |
| A_23_P52986 | NM_152718 | <i>VWCE</i> |
| A_23_P83192 | NM_001287343 | <i>PHPT1</i> |
| A_23_P83192 | NM_014172 | <i>PHPT1</i> |
| A_23_P83192 | NM_001135861 | <i>PHPT1</i> |
| A_23_P83192 | n/a | <i>PHPT1</i> |
| A_23_P83192 | NM_001287342 | <i>PHPT1</i> |
| A_23_P83192 | n/a | <i>MAMDC4</i> |
| A_24_P128312 | NM_001322260 | <i>ZNF79</i> |
| A_24_P128312 | NM_001286697 | <i>ZNF79</i> |
| A_24_P128312 | NM_001286696 | <i>ZNF79</i> |
| A_24_P128312 | NM_001286698 | <i>ZNF79</i> |
| A_24_P128312 | NM_007135 | <i>ZNF79</i> |
| A_24_P326739 | NM_001280796 | <i>GLS2</i> |
| A_24_P326739 | NM_001280798 | <i>GLS2</i> |
| A_24_P326739 | n/a | <i>GLS2</i> |
| A_24_P326739 | NM_001280797 | <i>GLS2</i> |
| A_24_P326739 | NM_013267 | <i>GLS2</i> |
| A_24_P88921 | n/a | n/a |
| A_24_P925664 | NM_002392 | <i>MDM2</i> |
| A_24_P925664 | n/a | <i>MDM2</i> |
| A_32_P210202 | n/a | <i>E2F7</i> |
| A_32_P210202 | NM_203394 | <i>E2F7</i> |
| A_32_P347617 | NM_001166003 | <i>APOBEC3H</i> |
| A_32_P347617 | NM_181773 | <i>APOBEC3H</i> |
| A_32_P347617 | NM_001166002 | <i>APOBEC3H</i> |
| A_32_P347617 | n/a | <i>APOBEC3H</i> |
| A_32_P96692 | NM_006502 | <i>POLH</i> |
| A_32_P96692 | NM_001291969 | <i>POLH</i> |
| A_33_P3214501 | n/a | n/a |
| A_33_P3232277 | n/a | n/a |
| A_33_P3248227 | n/a | n/a |
| A_33_P3252834 | n/a | n/a |
| A_33_P3258452 | n/a | n/a |

| Probe ID | RefSeq | Gene name |
|-----------------|---------------|------------------|
| A_33_P3258612 | n/a | n/a |
| A_33_P3267410 | n/a | n/a |
| A_33_P3345031 | n/a | n/a |
| A_33_P3357748 | n/a | n/a |
| A_33_P3361891 | n/a | n/a |
| A_33_P3397763 | n/a | n/a |

Supplementary table 1. Differentially expressed transcripts with their corresponding RefSeq ID and gene name. The first column, Probe ID, corresponds to our uncovered differentially expressed (DE) transcripts with a Bonferroni-adjusted $P < 0.05$ and that were DE in at least 3 of the 4 datasets used in this study. The second column, RefSeq, corresponds to the RefSeq converted names of the DE transcripts. The third column, Gene name, corresponds to the HUGO Gene Nomenclature Committee (HGNC) names of the DE transcripts. n/a implies not available.

1.2 Supplementary Table 2

| Term name | Term ID | Adjusted p-value | Intersections |
|--|---------------|----------------------|---|
| damaged DNA binding | GO:0003684 | 0.00639877920237275 | <i>DDB2, PCNA, POLH</i> |
| cellular response to DNA damage stimulus | GO:0006974 | 2.20046889924381e-05 | <i>ASCC3, DDB2, E2F7, GADD45A, LIG1, MDM2, PCNA, POLH, RPS27L</i> |
| cellular response to radiation | GO:0071478 | 0.000182841554499369 | <i>DDB2, GADD45A, MDM2, PCNA, POLH</i> |
| signal transduction in response to DNA damage | GO:0042770 | 0.0026617093376837 | <i>E2F7, GADD45A, MDM2, RPS27L</i> |
| DNA damage response, signal transduction by p53 class mediator | GO:0030330 | 0.00392268757263919 | <i>E2F7, MDM2, RPS27L</i> |
| response to radiation | GO:0009314 | 0.00392268757263919 | <i>DDB2, GADD45A, MDM2, PCNA, POLH</i> |
| mitotic G1 DNA damage checkpoint signaling | GO:0031571 | 0.0134309632215723 | <i>MDM2, RPS27L</i> |
| regulation of response to DNA damage stimulus | GO:2001020 | 0.019660692919181 | <i>MDM2, PCNA, POLH</i> |
| cellular response to ionizing radiation | GO:0071479 | 0.0273579729138718 | <i>GADD45A, MDM2</i> |
| mitotic DNA damage checkpoint signaling | GO:0044773 | 0.0328077285789804 | <i>MDM2, RPS27L</i> |
| DNA damage checkpoint signaling | GO:0000077 | 0.0489838097428765 | <i>MDM2, RPS27L</i> |
| DNA Damage Bypass | REAC:R-73893 | 0.0162686186167047 | <i>PCNA, POLH</i> |
| ALKBH3 mediated reversal of alkylation damage | REAC:R-112126 | 0.0325554683763622 | <i>ASCC3</i> |
| DNA damage response | WP:WP707 | 0.00121916713799335 | <i>DDB2, GADD45A, MDM2</i> |
| miRNA regulation of DNA damage response | WP:WP1530 | 0.00262868705722079 | <i>DDB2, GADD45A, MDM2</i> |
| Oxidative damage response | WP:WP3941 | 0.00762522359865018 | <i>GADD45A, PCNA</i> |
| DNA IR-damage and cellular response via ATR | WP:WP4016 | 0.0221844497339509 | <i>MDM2, PCNA</i> |

Supplementary table 2. g:Profiler results of overrepresented annotations directly related to DNA damage or radiation using the 20 uncovered differentially expressed genes as an input. g:Profiler was used to perform an overrepresentation analysis (1). Our 20

uncovered differentially expressed genes (DEGs), namely the HUGO Gene Nomenclature Committee (HGNC) names were used as an input. The first column corresponds to the overrepresented term name. The second column corresponds to the term ID, where entries beginning with GO refer to gene ontology terms, entries beginning with REAC refer to Reactome terms, and entries beginning with WP refer to WikiPathways terms. The third column corresponds to false discovery rate (FDR)-adjusted p-values. All adjusted p-values are smaller than 0.05 and may be written in scientific notation E notation. The fourth column, Intersections, corresponds to our DEGs that were associated to the overrepresented term.

1.3 Supplementary Table 3

| MicroRNA | Target gene | Regulation |
|-----------------|--------------------|-------------------|
| miR-148a-3p | <i>GADD45A</i> | Repression |
| miR-148b-3p | <i>GADD45A</i> | Repression |
| miR-152-3p | <i>GADD45A</i> | Repression |
| let-7a-5p | <i>ASCC3</i> | Repression |
| let-7b-5p | <i>ASCC3</i> | Repression |
| let-7f-5p | <i>ASCC3</i> | Repression |
| miR-124-3p | <i>ASCC3</i> | Repression |
| miR-16-5p | <i>ASCC3</i> | Repression |
| miR-30a-5p | <i>ASCC3</i> | Repression |
| miR-98-5p | <i>ASCC3</i> | Repression |
| miR-26b-5p | <i>CCL27</i> | Repression |
| miR-155-5p | <i>DDB2</i> | Repression |
| miR-26b-5p | <i>DDB2</i> | Repression |
| miR-103a-3p | <i>E2F7</i> | Repression |
| miR-10a-5p | <i>E2F7</i> | Repression |
| miR-128-3p | <i>E2F7</i> | Repression |
| miR-15a-5p | <i>E2F7</i> | Repression |
| miR-15b-5p | <i>E2F7</i> | Repression |
| miR-16-5p | <i>E2F7</i> | Repression |
| miR-196a-5p | <i>E2F7</i> | Repression |
| miR-196b-5p | <i>E2F7</i> | Repression |
| miR-26a-5p | <i>E2F7</i> | Repression |
| miR-26b-5p | <i>E2F7</i> | Repression |
| miR-27a-3p | <i>E2F7</i> | Repression |
| miR-27b-3p | <i>E2F7</i> | Repression |
| miR-376a-5p | <i>E2F7</i> | Repression |
| miR-424-5p | <i>E2F7</i> | Repression |
| miR-497-5p | <i>E2F7</i> | Repression |
| miR-548at-5p | <i>E2F7</i> | Repression |
| miR-9-5p | <i>E2F7</i> | Repression |
| miR-16-5p | <i>FDXR</i> | Repression |
| miR-26b-5p | <i>FDXR</i> | Repression |
| miR-124-3p | <i>FHL2</i> | Repression |
| miR-27a-3p | <i>FHL2</i> | Repression |
| miR-26b-5p | <i>GADD45A</i> | Repression |
| miR-331-5p | <i>GADD45A</i> | Repression |
| miR-34a-5p | <i>GADD45A</i> | Repression |
| miR-374a-5p | <i>GADD45A</i> | Repression |
| miR-335-5p | <i>GLS2</i> | Repression |
| miR-26b-5p | <i>LIG1</i> | Repression |
| miR-615-3p | <i>LIG1</i> | Repression |
| miR-106b-5p | <i>MDM2</i> | Repression |
| miR-1270 | <i>MDM2</i> | Repression |

| MicroRNA | Target gene | Regulation |
|-----------------|--------------------|-------------------|
| miR-1305 | <i>MDM2</i> | Repression |
| miR-143-3p | <i>MDM2</i> | Repression |
| miR-145-5p | <i>MDM2</i> | Repression |
| miR-17-5p | <i>MDM2</i> | Repression |
| miR-185-5p | <i>MDM2</i> | Repression |
| miR-18b-5p | <i>MDM2</i> | Repression |
| miR-20a-5p | <i>MDM2</i> | Repression |
| miR-20b-5p | <i>MDM2</i> | Repression |
| miR-218-5p | <i>MDM2</i> | Repression |
| miR-221-3p | <i>MDM2</i> | Repression |
| miR-222-3p | <i>MDM2</i> | Repression |
| miR-224-3p | <i>MDM2</i> | Repression |
| miR-25-3p | <i>MDM2</i> | Repression |
| miR-26a-5p | <i>MDM2</i> | Repression |
| miR-26b-5p | <i>MDM2</i> | Repression |
| miR-29a-3p | <i>MDM2</i> | Repression |
| miR-29b-3p | <i>MDM2</i> | Repression |
| miR-29c-3p | <i>MDM2</i> | Repression |
| miR-32-5p | <i>MDM2</i> | Repression |
| miR-330-3p | <i>MDM2</i> | Repression |
| miR-339-5p | <i>MDM2</i> | Repression |
| miR-340-5p | <i>MDM2</i> | Repression |
| miR-367-3p | <i>MDM2</i> | Repression |
| miR-425-5p | <i>MDM2</i> | Repression |
| miR-484 | <i>MDM2</i> | Repression |
| miR-499a-5p | <i>MDM2</i> | Repression |
| miR-5010-3p | <i>MDM2</i> | Repression |
| miR-504-5p | <i>MDM2</i> | Repression |
| miR-542-3p | <i>MDM2</i> | Repression |
| miR-550a-3p | <i>MDM2</i> | Repression |
| miR-556-5p | <i>MDM2</i> | Repression |
| miR-5680 | <i>MDM2</i> | Repression |
| miR-579-3p | <i>MDM2</i> | Repression |
| miR-590-3p | <i>MDM2</i> | Repression |
| miR-605-5p | <i>MDM2</i> | Repression |
| miR-664b-3p | <i>MDM2</i> | Repression |
| miR-758-3p | <i>MDM2</i> | Repression |
| miR-766-3p | <i>MDM2</i> | Repression |
| miR-92a-3p | <i>MDM2</i> | Repression |
| miR-92b-3p | <i>MDM2</i> | Repression |
| miR-93-5p | <i>MDM2</i> | Repression |
| miR-944 | <i>MDM2</i> | Repression |
| miR-124-3p | <i>PCNA</i> | Repression |
| miR-193b-3p | <i>PCNA</i> | Repression |
| miR-24-3p | <i>PCNA</i> | Repression |

| MicroRNA | Target gene | Regulation |
|-----------------|--------------------|-------------------|
| miR-26b-5p | <i>PCNA</i> | Repression |
| miR-30a-5p | <i>PCNA</i> | Repression |
| miR-542-3p | <i>PCNA</i> | Repression |
| miR-122-5p | <i>PHPT1</i> | Repression |

Supplementary table 3. MicroRNAs, their target genes and regulation uncovered using databases containing validated or predicted microRNA-target interactions. The first column contains the microRNAs, the second column contains their target genes, and the third column contains the type of regulation these microRNAs exert on their target genes. Our 20 uncovered differentially expressed genes in combination with the following databases were used to uncover the 92 listed interaction pairs. The first three rows contain predicted interactions, whereas the following 89 contain validated interactions. The validated interactions were found using a combination of miRTarBase (2), release 8.0, and TarBase, v8 (3). The predicted interactions were found using a combination of TargetScan, release 8.0 (4), miRDB, v6.0 (5), and microT-CDS, v4 (6), with a context score smaller than -0.48, a score greater to 94, and with a miTG score greater than 0.905, respectively.

1.4 Supplementary Table 4

| Molecule | Target | Regulation |
|-----------------|----------------|-------------------|
| <i>ANRIL</i> | <i>GLS2</i> | Repression |
| <i>ANRIL</i> | miR-221-3p | Repression |
| <i>CCAT2</i> | miR-20a-5p | Repression |
| <i>DANCR</i> | miR-1305 | Repression |
| <i>DINO</i> | <i>GADD45A</i> | Repression |
| <i>DINO</i> | <i>DDB2</i> | Repression |
| <i>E2F7</i> | miR-25-5p | Repression |
| <i>E2F7</i> | miR-25-3p | Repression |
| ENST00000414355 | <i>DDB2</i> | Repression |
| <i>H19</i> | let-7a-5p | Repression |
| <i>HOTAIR</i> | let-7a-5p | Repression |
| let-7a-5p | <i>ASCC3</i> | Repression |
| let-7b-5p | <i>ASCC3</i> | Repression |
| let-7f-5p | <i>ASCC3</i> | Repression |
| miR-103a-3p | <i>E2F7</i> | Repression |
| miR-106b-5p | <i>MDM2</i> | Repression |
| miR-10a-5p | <i>E2F7</i> | Repression |
| miR-122-5p | <i>PHPT1</i> | Repression |
| miR-124-3p | <i>ASCC3</i> | Repression |
| miR-124-3p | <i>FHL2</i> | Repression |
| miR-124-3p | <i>PCNA</i> | Repression |
| miR-1270 | <i>MDM2</i> | Repression |
| miR-128-3p | <i>E2F7</i> | Repression |
| miR-1305 | <i>MDM2</i> | Repression |
| miR-143-3p | <i>MDM2</i> | Repression |
| miR-145-5p | <i>MDM2</i> | Repression |
| miR-148a-3p | <i>GADD45A</i> | Repression |
| miR-148b-3p | <i>GADD45A</i> | Repression |
| miR-152-3p | <i>GADD45A</i> | Repression |
| miR-155-5p | <i>DDB2</i> | Repression |
| miR-15a-5p | <i>E2F7</i> | Repression |
| miR-15b-5p | <i>E2F7</i> | Repression |
| miR-16-5p | <i>ASCC3</i> | Repression |
| miR-16-5p | <i>E2F7</i> | Repression |
| miR-16-5p | <i>FDXR</i> | Repression |
| miR-17-5p | <i>MDM2</i> | Repression |
| miR-185-5p | <i>MDM2</i> | Repression |
| miR-18b-5p | <i>MDM2</i> | Repression |
| miR-193b-3p | <i>PCNA</i> | Repression |
| miR-196a-5p | <i>E2F7</i> | Repression |
| miR-196b-5p | <i>E2F7</i> | Repression |
| miR-20a-5p | <i>MDM2</i> | Repression |
| miR-20b-5p | <i>MDM2</i> | Repression |
| miR-218-5p | <i>MDM2</i> | Repression |

| Molecule | Target | Regulation |
|-----------------|----------------|-------------------|
| miR-221-3p | <i>MDM2</i> | Repression |
| miR-222-3p | <i>MDM2</i> | Repression |
| miR-224-3p | <i>MDM2</i> | Repression |
| miR-24-3p | <i>PCNA</i> | Repression |
| miR-25-3p | <i>MDM2</i> | Repression |
| miR-26a-5p | <i>E2F7</i> | Repression |
| miR-26a-5p | <i>MDM2</i> | Repression |
| miR-26b-5p | <i>CCL27</i> | Repression |
| miR-26b-5p | <i>DDB2</i> | Repression |
| miR-26b-5p | <i>E2F7</i> | Repression |
| miR-26b-5p | <i>FDXR</i> | Repression |
| miR-26b-5p | <i>GADD45A</i> | Repression |
| miR-26b-5p | <i>LIG1</i> | Repression |
| miR-26b-5p | <i>MDM2</i> | Repression |
| miR-26b-5p | <i>PCNA</i> | Repression |
| miR-27a-3p | <i>E2F7</i> | Repression |
| miR-27a-3p | <i>FHL2</i> | Repression |
| miR-27b-3p | <i>E2F7</i> | Repression |
| miR-29a-3p | <i>MDM2</i> | Repression |
| miR-29b-3p | <i>MDM2</i> | Repression |
| miR-29c-3p | <i>MDM2</i> | Repression |
| miR-30a-5p | <i>ASCC3</i> | Repression |
| miR-30a-5p | <i>PCNA</i> | Repression |
| miR-32-5p | <i>MDM2</i> | Repression |
| miR-330-3p | <i>MDM2</i> | Repression |
| miR-331-5p | <i>GADD45A</i> | Repression |
| miR-335-5p | <i>GLS2</i> | Repression |
| miR-339-5p | <i>MDM2</i> | Repression |
| miR-340-5p | <i>MDM2</i> | Repression |
| miR-34a-5p | <i>GADD45A</i> | Repression |
| miR-367-3p | <i>MDM2</i> | Repression |
| miR-374a-5p | <i>GADD45A</i> | Repression |
| miR-376a-5p | <i>E2F7</i> | Repression |
| miR-424-5p | <i>E2F7</i> | Repression |
| miR-425-5p | <i>MDM2</i> | Repression |
| miR-484 | <i>MDM2</i> | Repression |
| miR-497-5p | <i>E2F7</i> | Repression |
| miR-499a-5p | <i>MDM2</i> | Repression |
| miR-5010-3p | <i>MDM2</i> | Repression |
| miR-504-5p | <i>MDM2</i> | Repression |
| miR-542-3p | <i>MDM2</i> | Repression |
| miR-542-3p | <i>PCNA</i> | Repression |
| miR-548at-5p | <i>E2F7</i> | Repression |
| miR-550a-3p | <i>MDM2</i> | Repression |
| miR-556-5p | <i>MDM2</i> | Repression |

| Molecule | Target | Regulation |
|-----------------|---------------|-------------------|
| miR-5680 | <i>MDM2</i> | Repression |
| miR-579-3p | <i>MDM2</i> | Repression |
| miR-590-3p | <i>MDM2</i> | Repression |
| miR-605-5p | <i>MDM2</i> | Repression |
| miR-615-3p | <i>LIG1</i> | Repression |
| miR-664b-3p | <i>MDM2</i> | Repression |
| miR-758-3p | <i>MDM2</i> | Repression |
| miR-766-3p | <i>MDM2</i> | Repression |
| miR-9-5p | <i>E2F7</i> | Repression |
| miR-92a-3p | <i>MDM2</i> | Repression |
| miR-92b-3p | <i>MDM2</i> | Repression |
| miR-93-5p | <i>MDM2</i> | Repression |
| miR-944 | <i>MDM2</i> | Repression |
| miR-98-5p | <i>ASCC3</i> | Repression |
| <i>MALAT1</i> | miR-145-5p | Repression |
| <i>PANDAR</i> | <i>PCNA</i> | Repression |
| <i>PVT1</i> | miR-497-5p | Repression |

Supplementary table 4. The complete list of interactions pairs included in the final regulation network. The first column contains the names of the molecules (long non-coding RNAs, microRNAs, or transcription factors) that regulate their targets (either microRNAs or differentially expressed genes) that can be found in the second column. The third column contains the type of regulation these molecules exert on their target. The final network was assembled using these 106 interaction pairs.

1.5 Supplementary Table 5

| Node name | Node degree | Node betweenness centrality |
|------------------|--------------------|------------------------------------|
| <i>ANRIL</i> | 2 | 0 |
| <i>ASCC3</i> | 7 | 0 |
| <i>CCAT2</i> | 1 | 0 |
| <i>CCL27</i> | 1 | 0 |
| <i>DANCR</i> | 1 | 0 |
| <i>DDB2</i> | 4 | 0 |
| <i>DINO</i> | 2 | 0 |
| <i>E2F7</i> | 19 | 0.258591065292096 |
| ENST00000414355 | 1 | 0 |
| <i>FDXR</i> | 2 | 0 |
| <i>FHL2</i> | 2 | 0 |
| <i>GADD45A</i> | 8 | 0 |
| <i>GLS2</i> | 2 | 0 |
| <i>H19</i> | 1 | 0 |
| <i>HOTAIR</i> | 1 | 0 |
| let-7a-5p | 3 | 0.0183634020618557 |
| let-7b-5p | 1 | 0 |
| let-7f-5p | 1 | 0 |
| miR-103a-3p | 1 | 0 |
| miR-106b-5p | 1 | 0 |
| miR-10a-5p | 1 | 0 |
| miR-122-5p | 1 | 0 |
| miR-124-3p | 3 | 0 |
| miR-1270 | 1 | 0 |
| miR-128-3p | 1 | 0 |
| miR-1305 | 2 | 0.00536941580756014 |
| miR-143-3p | 1 | 0 |
| miR-145-5p | 2 | 0.00204037800687285 |
| miR-148a-3p | 1 | 0 |
| miR-148b-3p | 1 | 0 |
| miR-152-3p | 1 | 0 |
| miR-155-5p | 1 | 0 |
| miR-15a-5p | 1 | 0 |
| miR-15b-5p | 1 | 0 |
| miR-16-5p | 3 | 0 |
| miR-17-5p | 1 | 0 |
| miR-185-5p | 1 | 0 |
| miR-18b-5p | 1 | 0 |
| miR-193b-3p | 1 | 0 |
| miR-196a-5p | 1 | 0 |
| miR-196b-5p | 1 | 0 |
| miR-20a-5p | 2 | 0.00579896907216495 |
| miR-20b-5p | 1 | 0 |
| miR-218-5p | 1 | 0 |

| Node name | Node degree | Node betweenness centrality |
|------------------|--------------------|------------------------------------|
| miR-221-3p | 2 | 0.00633591065292096 |
| miR-222-3p | 1 | 0 |
| miR-224-3p | 1 | 0 |
| miR-24-3p | 1 | 0 |
| miR-25-3p | 2 | 0.0849441580756014 |
| miR-25-5p | 1 | 0 |
| miR-26a-5p | 2 | 0 |
| miR-26b-5p | 8 | 0 |
| miR-27a-3p | 2 | 0 |
| miR-27b-3p | 1 | 0 |
| miR-29a-3p | 1 | 0 |
| miR-29b-3p | 1 | 0 |
| miR-29c-3p | 1 | 0 |
| miR-30a-5p | 2 | 0 |
| miR-32-5p | 1 | 0 |
| miR-330-3p | 1 | 0 |
| miR-331-5p | 1 | 0 |
| miR-335-5p | 1 | 0 |
| miR-339-5p | 1 | 0 |
| miR-340-5p | 1 | 0 |
| miR-34a-5p | 1 | 0 |
| miR-367-3p | 1 | 0 |
| miR-374a-5p | 1 | 0 |
| miR-376a-5p | 1 | 0 |
| miR-424-5p | 1 | 0 |
| miR-425-5p | 1 | 0 |
| miR-484 | 1 | 0 |
| miR-497-5p | 2 | 0.00987972508591065 |
| miR-499a-5p | 1 | 0 |
| miR-5010-3p | 1 | 0 |
| miR-504-5p | 1 | 0 |
| miR-542-3p | 2 | 0 |
| miR-548at-5p | 1 | 0 |
| miR-550a-3p | 1 | 0 |
| miR-556-5p | 1 | 0 |
| miR-5680 | 1 | 0 |
| miR-579-3p | 1 | 0 |
| miR-590-3p | 1 | 0 |
| miR-605-5p | 1 | 0 |
| miR-615-3p | 1 | 0 |
| miR-664b-3p | 1 | 0 |
| miR-758-3p | 1 | 0 |
| miR-766-3p | 1 | 0 |
| miR-9-5p | 1 | 0 |
| miR-92a-3p | 1 | 0 |

| Node name | Node degree | Node betweenness centrality |
|------------------|--------------------|------------------------------------|
| miR-92b-3p | 1 | 0 |
| miR-93-5p | 1 | 0 |
| miR-944 | 1 | 0 |
| miR-98-5p | 1 | 0 |
| <i>LIG1</i> | 2 | 0 |
| <i>MALAT1</i> | 1 | 0 |
| <i>MDM2</i> | 44 | 0 |
| <i>PANDAR</i> | 1 | 0 |
| <i>PCNA</i> | 7 | 0 |
| <i>PHPT1</i> | 1 | 0 |
| <i>PVT1</i> | 1 | 0 |

Supplementary table 5. Complete list of nodes and their corresponding degree and betweenness centrality. The first column contains the names of the nodes, the second column contains their degree, the total number of incoming or outgoing edges associated to a node, and the third column contains the betweenness centrality value associated to a node. These network topological parameters were calculated using NetworkAnalyzer, v.4.4.8 (7).

1.6 Supplementary Table 6

| Term name | Term ID | Adjusted p-value | Intersections |
|--|---------------|---------------------|---|
| damaged DNA binding | GO:0003684 | 0.0197730250499389 | <i>DDB2, PCNA</i> |
| cellular response to DNA damage stimulus | GO:0006974 | 0.00200435459058808 | <i>ASCC3, DDB2, E2F7, GADD45A, LIG1, MDM2, PCNA</i> |
| cellular response to radiation | GO:0071478 | 0.00393125068634763 | <i>DDB2, GADD45A, MDM2, PCNA</i> |
| response to radiation | GO:0009314 | 0.0242994368075813 | <i>DDB2, GADD45A, MDM2, PCNA</i> |
| signal transduction in response to DNA damage | GO:0042770 | 0.0242994368075813 | <i>E2F7, GADD45A, MDM2</i> |
| DNA damage response, signal transduction by p53 class mediator | GO:0030330 | 0.0421496887083775 | <i>E2F7, MDM2</i> |
| cellular response to ionizing radiation | GO:0071479 | 0.0421496887083775 | <i>GADD45A, MDM2</i> |
| ALKBH3 mediated reversal of alkylation damage | REAC:R-112126 | 0.0198543626470989 | <i>ASCC3</i> |
| Reversal of alkylation damage by DNA dioxygenases | REAC:R-73943 | 0.0307589365441105 | <i>ASCC3</i> |
| DNA Damage Reversal | REAC:R-73942 | 0.0328404225376314 | <i>ASCC3</i> |
| DNA damage response | WP:WP707 | 0.00276620659702357 | <i>DDB2, GADD45A, MDM2</i> |
| miRNA regulation of DNA damage response | WP:WP1530 | 0.00429040939109052 | <i>DDB2, GADD45A, MDM2</i> |
| Oxidative damage response | WP:WP3941 | 0.0113264458081623 | <i>GADD45A, PCNA</i> |
| DNA IR-damage and cellular response via ATR | WP:WP4016 | 0.0327298442125634 | <i>MDM2, PCNA</i> |

Supplementary table 6. g:Profiler results of overrepresented annotations directly related to DNA damage or radiation using the network nodes as an input. g:Profiler was used to perform an overrepresentation analysis (1). Our 100 network nodes were used as an input. The first column corresponds to the overrepresented term name. The second column corresponds to the term ID, where entries beginning with GO refer to gene ontology terms, entries beginning with REAC refer to Reactome terms, and entries beginning with WP refer to WikiPathways terms. The third column corresponds to false discovery rate (FDR)-adjusted p-values. All adjusted p-values are smaller than 0.05. The fourth column, Intersections, corresponds to our uncovered nodes that were associated to the overrepresented term.

1.7 Supplementary Table 7

| Category | Subcategory | P-adjusted | miRNAs/precursors |
|---|--|-------------------|---|
| Annotations derived over miRTarBase (Gene Ontology) | mitotic DNA damage checkpoint GO0044773 | 0.0049066 | miR-103a-3p, miR-124-3p, miR-128-3p, miR-16-5p, miR-26a-5p, miR-26b-5p, miR-27a-3p, miR-27b-3p |
| Annotations derived over miRTarBase (Gene Ontology) | G1 DNA damage checkpoint GO0044783 | 0.0030387 | miR-106b-5p, miR-15b-5p, miR-17-5p, miR-18b-5p, miR-20a-5p, miR-20b-5p, miR-484, miR-590-3p, miR-93-5p |
| Annotations derived over miRTarBase (Gene Ontology) | positive regulation of DNA damage response, signal transduction by p53 class mediator resulting in transcription of p21 class mediator GO1902164 | 0.0134959 | miR-106b-5p, miR-128-3p, miR-1305, miR-17-5p, miR-185-5p, miR-193b-3p, miR-20a-5p, miR-20b-5p, miR-25-3p, miR-93-5p |
| Annotations derived over miRTarBase (Gene Ontology) | DNA synthesis involved in UV-damage excision repair GO1904161 | 0.0193235 | miR-103a-3p, miR-124-3p, miR-193b-3p, miR-26b-5p, miR-29a-3p, miR-331-5p |
| Annotations derived over miRTarBase (Gene Ontology) | response to G1 DNA damage checkpoint signaling GO0072432 | 0.0243763 | miR-155-5p, miR-221-3p, miR-24-3p, miR-335-5p, miR-34a-5p |
| Annotations derived over miRTarBase (Gene Ontology) | signal transduction involved in mitotic G2 DNA damage checkpoint GO0072434 | 0.0280934 | miR-18b-5p, miR-218-5p, miR-26a-5p, miR-30a-5p, miR-374a-5p, miR-92a-3p |
| Annotations derived over miRTarBase (Gene Ontology) | regulation of DNA damage response, signal transduction by p53 class mediator GO0043516 | 0.0281468 | miR-155-5p, miR-193b-3p, miR-218-5p, miR-26a-5p, miR-26b-5p |
| Annotations derived over miRTarBase (Gene Ontology) | regulation of response to DNA damage checkpoint signaling GO1902153 | 0.0302253 | miR-193b-3p, miR-26b-5p, miR-34a-5p, miR-605-5p, miR-766-3p |

| Category | Subcategory | P-adjusted | miRNAs/precursors |
|---|---|-------------------|---|
| Annotations derived over miRTarBase (Gene Ontology) | signal transduction involved in intra-S DNA damage checkpoint GO0072428 | 0.0392563 | miR-124-3p, miR-128-3p, miR-26a-5p, miR-26b-5p, miR-27a-3p, miR-27b-3p |
| Annotations derived over miRTarBase (Gene Ontology) | response to DNA damage checkpoint signaling GO0072423 | 0.0401586 | let-7a-5p, let-7b-5p, let-7f-5p, miR-339-5p, miR-605-5p, miR-615-3p, miR-92a-3p, miR-98-5p |
| Annotations derived over miRTarBase (Gene Ontology) | negative regulation of DNA damage checkpoint GO2000002 | 0.0408276 | let-7b-5p, let-7f-5p, miR-5680, miR-615-3p, miR-766-3p, miR-93-5p, miR-98-5p |
| Gene Ontology (miRWalk) | GO0071480 cellular response to gamma radiation | 0.0054314 | let-7b-5p, let-7f-5p, miR-122-5p, miR-124-3p, miR-26b-5p, miR-30a-5p, miR-374a-5p, miR-484, miR-92a-3p |
| Gene Ontology (miRWalk) | GO0031573 intra s dna damage checkpoint | 0.0403358 | miR-155-5p, miR-15a-5p, miR-16-5p, miR-484, miR-615-3p |
| GO Biological process (miRPathDB) | response to gamma radiation | 0.0028488 | miR-128-3p, miR-143-3p, miR-148a-3p, miR-185-5p, miR-29b-3p, miR-34a-5p |
| GO Biological process (miRPathDB) | cellular response to radiation | 0.0072316 | miR-124-3p, miR-143-3p, miR-155-5p, miR-25-3p, miR-26a-5p, miR-29b-3p, miR-34a-5p |
| GO Biological process (miRPathDB) | regulation of DNA damage response signal transduction by p53 class mediator | 0.0229285 | miR-128-3p, miR-185-5p, miR-218-5p, miR-26a-5p, miR-34a-5p |
| GO Biological process (miRPathDB) | cellular response to ionizing radiation | 0.0358867 | miR-124-3p, miR-185-5p, miR-218-5p, miR-27a-3p, miR-34a-5p |
| Reactome (miRPathDB) | G1S DNA Damage Checkpoints | 0.0012265 | miR-148a-3p, miR-15a-5p, miR-16-5p, miR-185-5p, miR-24-3p, miR-26a-5p, miR-499a-5p, miR-550a-3p, miR-615-3p, miR-92a-3p |

| Category | Subcategory | P-adjusted | microRNAs |
|--------------------------|---|------------|--|
| Reactome (miRPathDB) | DNA DamageTelomere Stress Induced Senescence | 0.009628 | let-7a-5p, miR-15a-5p, miR-16-5p, miR-185-5p, miR-196a-5p, miR-196b-5p, miR-26a-5p, |
| Reactome (miRPathDB) | p53-Dependent G1S DNA | 0.0210981 | miR-34a-5p, miR-98-5p miR-148a-3p, miR-185-5p, miR-26a-5p, miR-499a-5p, miR-550a-3p, miR-615-3p, miR-92a-3p |
| Reactome (miRPathDB) | p53-Dependent G1 DNA Damage Response | 0.0210981 | miR-148a-3p, miR-185-5p, miR-26a-5p, miR-499a-5p, miR-550a-3p, miR-615-3p, miR-92a-3p |
| WikiPathways (miRPathDB) | Oxidative Damage | 0.0344726 | miR-148a-3p, miR-152-3p, miR-221-3p, miR-34a-5p, miR-499a-5p, miR-542-3p |

Supplementary table 7. The miRNA Enrichment and Annotation tool results of overrepresented annotations directly related to DNA damage or radiation using the network microRNAs as an input. The miRNA Enrichment and Annotation (miEAA) tool was used to perform an overrepresentation analysis (8). Our 78 network microRNAs were used as an input. The first column corresponds to the category to which the overrepresented term belongs to. The second column corresponds to the overrepresented term name. The third column corresponds to false discovery rate (FDR)-adjusted p-values. All adjusted p-values are smaller than 0.05. The fourth column corresponds to our uncovered microRNAs that were associated to the overrepresented term.

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