**Supplemental Table 1. Experimental groups and drug dose (rats)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Groups** | **DMH (mg/kg)** | **VD3(IU/kg)** | **Met (mg/kg)** |
| 1. Normal  | 0 | - | - |
| 2. DMH control  | 30 | - | - |
| 3. VD3-L dose | 30 | 30 | - |
| 4. VD3-M dose  | 30 | 100 | - |
| 5. VD3-H dose  | 30 | 300 | - |
| 6. Met-L dose  | 30 | - | 40 |
| 7. Met-M dose  | 30 | - | 120 |
| 8. Met-H dose  | 30 | - | 360 |
| 9. VD3-M + Met-L dose | 30 | 100 | 40 |
| 10. VD3-L + Met-M dose  | 30 | 30 | 120 |
| 11. VD3-M + Met-M dose  | 30 | 100 | 120 |

1. DMH, 1,2-dimethyl-hydrazine; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 2. Experimental groups and drug dose (mice)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Groups** | **DMH(mg/kg)** | **DSS** | **VD3(IU/kg)** | **Met (mg/kg)** |
| 1. Normal  | 0 | 0 | - | - |
| 2. DMH+DSS control  | 20 | 2% | - | - |
| 3. VD3-M dose  | 20 | 2% | 200 | - |
| 4. Met-M dose | 20 | 2% | - | 240 |
| 5. VD3-M + Met-M dose  | 20 | 2% | 200 | 240 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.
2. DSS was dissolved in drinking water.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Groups** | **Week 0** | **Week 18** | **Body weight gains** | **Tumor incidence (n/N)** |
| 1. Normal  | 101.3±3.6 | 377.5±27.5 | 272.16±25.36 | 0/10 |
| 2. DMH control  | 99.0±5.4 | 294.3±22.1### | 195.33±19.37### | 10/10 |
| 3. VD3-L dose | 100.3±4.1 | 328.8±23.6\*\* | 228.45±21.80\*\* | 10/10 |
| 4. VD3-M dose  | 102.9±5.8 | 345.5±25.9\*\*\* | 242.58±21.57\*\*\* | 10/10 |
| 5. VD3-H dose  | 101.5±5.2 | 330.6±24.6\*\* | 229.13±20.44\*\* | 8/10 |
| 6. Met-L dose  | 102.3±6.4 | 305.7±33.9 | 203.45±28.39 | 10/10 |
| 7. Met-M dose  | 102.1±6.6 | 303.7±30.1 | 201.61±25.75 | 10/10 |
| 8. Met-H dose  | 102.7±5.5 | 276.0±12.3\* | 173.27±7.22\*\* | 10/10 |
| 9. VD3-M + Met-L dose | 99.4±4.0 | 276.8±25.8 | 177.35±22.50 | 10/10 |
| 10. VD3-L + Met-M dose  | 101.6±4.6 | 292.2±14.7 | 190.63±13.51 | 10/10 |
| 11. VD3-M + Met-M dose  | 102.8±4.2 | 295.2±15.5 | 192.35±13.69 | 7/10 |

 **Supplemental Table 3. Body weight changes and tumor incidence of rats**

1. DMH, 1,2-dimethyl-hydrazine; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.
2. All data were expressed as mean± SD, n=10 per group.
3. ###*P*<0.001 *vs.* Normal group; \**P*＜0.05, \*\**P*＜0.01, \*\*\**P*＜0.001 *vs*. DMH control group.
4. N: total number of rats; n: number of rats having tumor.

**Supplemental Table 4. Body weight changes and tumor incidence of mice**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Groups** | **Week 0** | **Week 20** | **Body weight gains** | **Tumor incidence (n/N)** |
| 1. Normal  | 29.02±2.06 | 41.01±4.15 | 12.00±3.25 | 0/25 |
| 2. DMH+DSS control  | 28.59±2.11 | 40.04±3.34 | 11.44±2.34 | 22/22 |
| 3. VD3-M dose  | 28.35±1.98 | 38.78±3.80 | 10.43±3.35 | 20/20 |
| 4. Met-M dose | 28.64±1.74 | 40.24±4.54 | 11.60±4.05 | 18/20 |
| 5. VD3-M + Met-M dose  | 28.97±1.60 | 39.37±3.42 | 10.40±2.85 | 22/24 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.
2. All data were expressed as mean± SD, n =20-25 pre group.
3. N: total number of mice; n: number of mice having tumor.

**Supplemental Table 5. The tumor numbers and volumes in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |  |
| --- | --- | --- |
| **Animal Number** | **DHM+DSS group** | **VD3-M+MET-M group** |
| **Tumor numbers** | **Tumor volumes/mm3** | **Tumor numbers** | **Tumor volumes/mm3** |
| 1 | 8 | 112.35 | 2 | 5.79 |
| 2 | 2 | 41.1 | 7 | 63.39 |
| 3 | 11 | 144.71 | 0 | 0 |
| 4 | 10 | 77.86 | 2 | 50.09 |
| 5 | 5 | 48.58 | 2 | 24.26 |
| 6 | 11 | 368.13 | 0 | 0 |
| 7 | 3 | 42.95 | 1 | 7.97 |
| 8 | 1 | 43.71 | 2 | 14.56 |
| 9 | 2 | 10.05 | 1 | 6.91 |
| 10 | 3 | 10.11 | 3 | 10.57 |
| 11 | 5 | 50.49 | 1 | 0.89 |
| 12 | 8 | 252.52 | 4 | 38.12 |
| 13 | 2 | 13.3 | 3 | 15.39 |
| 14 | 5 | 81.21 | 3 | 53.67 |
| 15 | 5 | 37.64 | 3 | 18.85 |
| 16 | 2 | 9.98 | 3 | 9.99 |
| 17 | 6 | 39.84 | 2 | 4.82 |
| 18 | 2 | 15.27 | 2 | 17.54 |
| 19 | 3 | 38.82 | 2 | 4.95 |
| 20 | 3 | 162.75 | 1 | 1.05 |
| 21 | 6 | 112.65 | 2 | 2.04 |
| 22 | 6 | 35.07 | 1 | 1.6 |
| 23 |  |  | 1 | 1.82 |
| 24 |  |  | 2 | 3.39 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 6. The number of ACs and ACFs in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |  |
| --- | --- | --- |
| **Animal Number** | **DHM+DSS group** | **VD3-M+MET-M group** |
| **ACs** | **ACFs** | **ACs** | **ACFs** |
| 1 | 1 | 1 | 6 | 3 |
| 2 | 2 | 1 | 0 | 0 |
| 3 | 3 | 2 | 0 | 0 |
| 4 | 10 | 7 | 3 | 1 |
| 5 | 4 | 2 | 0 | 0 |
| 6 | 0 | 0 | 0 | 0 |
| 7 | 7 | 3 | 0 | 0 |
| 8 | 1 | 1 | 0 | 0 |
| 9 | 5 | 3 | 4 | 1 |
| 10 | 7 | 3 | 0 | 0 |
| 11 | 5 | 3 | 0 | 0 |
| 12 | 9 | 5 | 3 | 1 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 7. Fasting blood glucose concentration in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |
| --- | --- |
| **Animal Number** | **Fasting blood glucose concentration (mmoL/L)** |
| **DHM+DSS group** | **VD3-M+MET-M group** |
| 1 | 4.6 | 5.7 |
| 2 | 7.9 | 10.1 |
| 3 | 7.4 | 11.2 |
| 4 | 6.8 | 6.2 |
| 5 | 8.4 | 8 |
| 6 | 6 | 6.6 |
| 7 | 6.1 | 6.8 |
| 8 | 5.7 | 8 |
| 9 | 8.9 | 6.7 |
| 10 | 9 | 6.7 |
| 11 | 8.7 | 3.6 |
| 12 | 6.8 |  |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 8. Serum Insulin concentration in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |
| --- | --- |
| **Animal Number** | **Serum insulin (ug/ml)** |
| **DHM+DSS group** | **VD3-M+MET-M group** |
| 1 | 0.235589 | 1.003838 |
| 2 | 0.331524 | 0.276369 |
| 3 | 0.317031 | 0.449795 |
| 4 | 0.258906 | 0.279278 |
| 5 | 0.400879 | 0.235589 |
| 6 | 0.773281 | 0.276369 |
| 7 | 0.3778 | 0.218075 |
| 8 | 0.223915 | 0.397997 |
| 9 | 0.255994 | 1.840781 |
| 10 | 0.212232 | 2.662397 |
| 11 | 1.337814 | 0.688918 |
| 12 | 0.604009 | 6.171937 |
| 13 | 0.354681 | 0.26473 |
| 14 | 0.229753 | 0.215154 |
| 15 | 1.113456 | 0.360464 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 9. Serum IGF-1 concentration in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |
| --- | --- |
| **Animal Number**  | **Serum IGF-1 (ug/ml)** |
| **DHM+DSS group** | **VD3-M+MET-M group** |
| 1 | 0.793288 | 0.683925 |
| 2 | 0.72831 | 0.724619 |
| 3 | 0.493031 | 0.717233 |
| 4 | 1.091515 | 0.800616 |
| 5 | 1.082045 | 0.996361 |
| 6 | 0.869956 | 0.840822 |
| 7 | 0.747972 | 0.162866 |
| 8 | 0.549555 | 0.630644 |
| 9 | 0.431124 | 0.839606 |
| 10 | 0.557068 | 1.063074 |
| 11 | 1.014278 | 0.993969 |
| 12 |  | 1.314662 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 10. Serum IGFBP-1 concentration in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |
| --- | --- |
| **Animal Number**  | **Serum IGFBP-1 (ng/ml)** |
| **DHM+DSS group** | **VD3-M+MET-M group** |
| 1 | 4.904687 | 1.949411 |
| 2 | 2.441957 | 3.235504 |
| 3 | 1.224274 | 0.540183 |
| 4 | 4.713142 | 0.909592 |
| 5 | 4.193232 | 0.567546 |
| 6 | 11.77297 | 13.62001 |
| 7 | 4.959415 | 6.272871 |
| 8 | 5.287779 | 10.07642 |
| 9 | 5.999234 | 6.081325 |
| 10 | 8.899783 | 5.835052 |
| 11 | 2.031502 | 6.573871 |
| 12 |  | 15.41234 |

a. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 11. Serum IGFBP-3 concentration in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |
| --- | --- |
| **Animal Number**  | **Serum IGFBP-3 (ug/ml)** |
| **DHM+DSS group** | **VD3-M+MET-M group** |
| 1 | 17.76663 | 20.31511 |
| 2 | 12.08822 | 33.92283 |
| 3 | 14.72648 | 23.41468 |
| 4 | 6.336913 | 17.56793 |
| 5 | 10.6914 | 10.79913 |
| 6 | 16.79799 | 14.7074 |
| 7 | 13.74139 | 12.80754 |
| 8 | 15.91949 | 19.80286 |
| 9 | 19.09119 | 17.68709 |
| 10 | 13.53482 | 22.75596 |
| 11 | 9.466057 | 20.78928 |
| 12 |  | 18.00576 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.

**Supplemental Table 12. The relative IOD of p-AKT, p-AMPK, p-mTOR, p-P70S6K and p-PS6 normalized to β-actin in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Time** | **DHM+DSS** | **VD3-M+MET-M** |
| **IOD (p-Akt/β-actin)** |  |  |  |
|  | 1 | 0.356689 | 0.17522 |
|  | 2 | 0.499656 | 0.16977 |
|  | 3 | 0.316862 | 0.100585 |
| **IOD (p-AMPK/β-actin)** |  |  |  |
|  | 1 | 0.537706 | 0.723362 |
|  | 2 | 0.541541 | 0.710216 |
|  | 3 | 0.521271 | 0.673362 |
| **IOD (p-mTOR/β-actin)**  |  |  |  |
|  | 1 | 0.292464 | 0.175032 |
|  | 2 | 0.294187 | 0.183169 |
|  | 3 | 0.38864 | 0.236588 |
| **IOD(p-P70S6K/β-actin)**  |  |  |  |
|  | 1 | 1.54 | 1.008 |
|  | 2 | 1.3 | 0.765 |
|  | 3 | 1.253 | 0.96035 |
| **IOD (p-PS6/β-actin)**  |  |  |  |
|  | 1 | 1.609633 | 0.308527 |
|  | 2 | 2.17437 | 0.603037 |
|  | 3 | 1.696623 | 0.781571 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.
2. IOD = integral optical density

**Supplemental Table 13. The relative IOD of CYP27B1, VDR, β-catenin, c-Myc and Cyclin- D1 normalized to β-actin in DMH+DSS and Met-M+VD3-M group of mice model (raw data)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Time** | **DHM+DSS** | **VD3-M+MET-M** |
| **IOD(CYP27B1/β-actin)** |  |  |  |
|  | 1 | 0.619742 | 1.423429 |
|  | 2 | 1.037331 | 1.718415 |
|  | 3 | 0.5563 | 1.488446 |
| **IOD(VDR/β-actin)**  |  |  |  |
|  | 1 | 0.481778 | 0.804654 |
|  | 2 | 0.375673 | 0.767548 |
|  | 3 | 0.391556 | 0.777578 |
| **IOD(β-catenin/β-actin)** |  |  |  |
|  | 1 | 0.857306 | 0.481761 |
|  | 2 | 0.648523 | 0.309125 |
|  | 3 | 0.919371 | 0.352829 |
| **IOD(c-Myc/β-actin)**  |  |  |  |
|  | 1 | 1.595695 | 0.722049 |
|  | 2 | 1.543911 | 0.746971 |
|  | 3 | 1.337169 | 0.669617 |
| **IOD(Cyclin D1/β-actin)**  |  |  |  |
|  | 1 | 0.264603 | 0.034331 |
|  | 2 | 0.238554 | 0.052133 |
|  | 3 | 0.228082 | 0.081441 |

1. DMH, 1,2-dimethyl-hydrazine; DSS, dextran sodium sulfate; VD3, vitamin D3; Met, metformin; L, low; M, medium; H, high.
2. IOD = integral optical density