

# Appendix

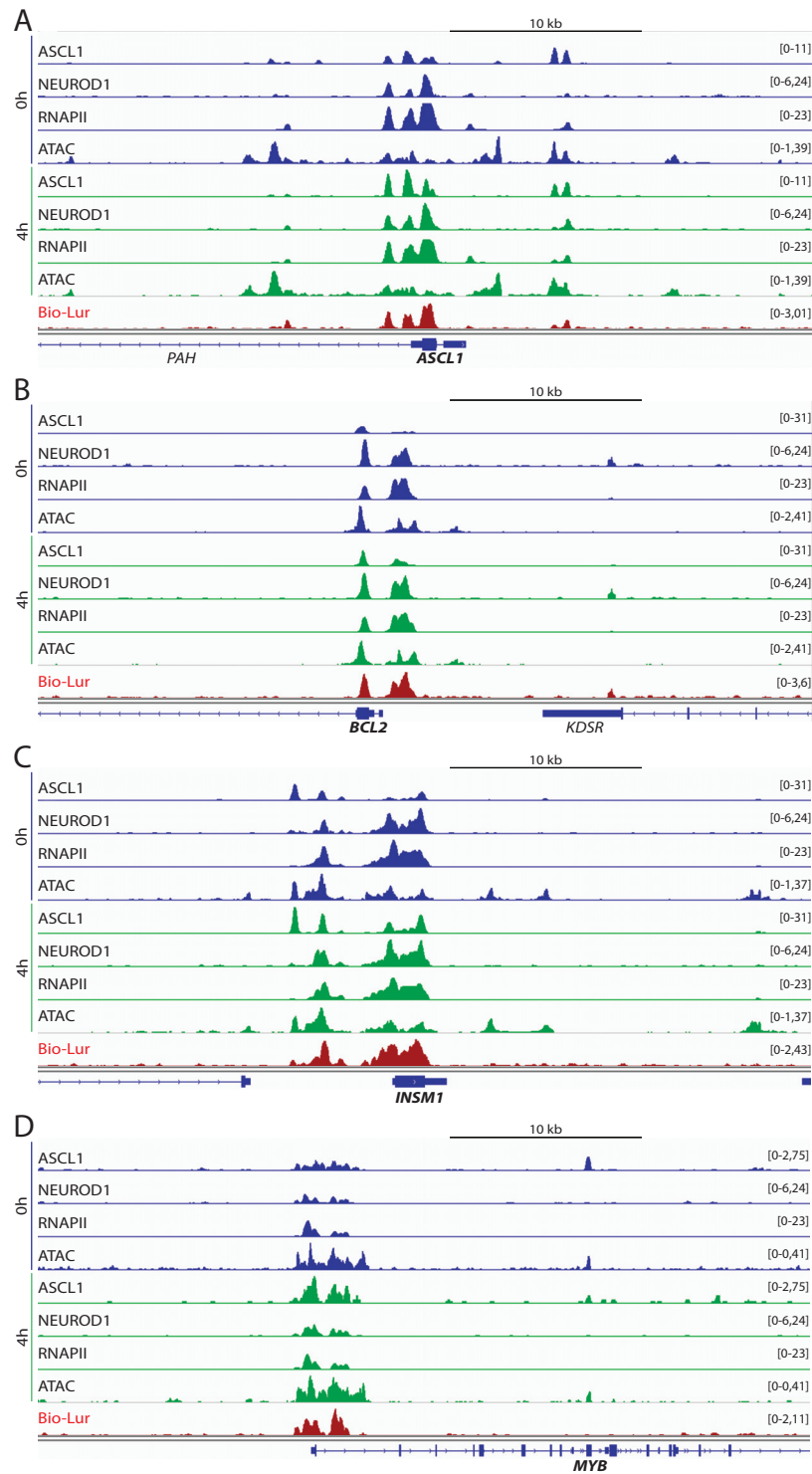
## Promoters of ASCL1- and NEUROD1-dependent genes are specific targets of lurbinectedin in SCLC cells.

Federico Costanzo et al.,

### Table of content:

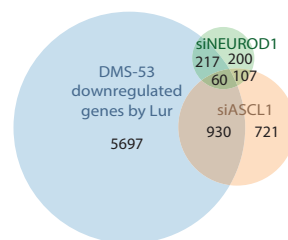
- **Appendix Figure S1: (A-D)** ATAC-seq and Chip-seq genome track of ASCL1/NEUROD1, RNAPII and Bio-Lur on *ASCL1*, *BCL2*; *INSM1* and *MYB*, in untreated (dark blue) and in lurbinectedin treated (green) conditions, respectively.
- **Appendix Figure S2:** Venn diagram of downregulated genes in DMS-53 after lurbinectedin, siNEUROD1 and siASCL1 treatments.
- **Appendix Figure S3:** (A)Venn diagram of genes expression in DMS-53, NCI-H510A and NCI-H82 cells. (B-C) Venn diagram of genes targeted by ASCL1 (B) and NEUROD1 (C) in DMS-53, NCI-H510A and NCI-H82 cells.
- **Appendix Figure S4:** ASCL1 and NEUROD1-dependent genes in DMS-53, NCI-H510A and NCI-H82 cells.
- **Appendix Figure S5:** Statistical analyses for Figure 4A, 4C, 5A-E, EV5B and EV5D

Appendix Figure S1



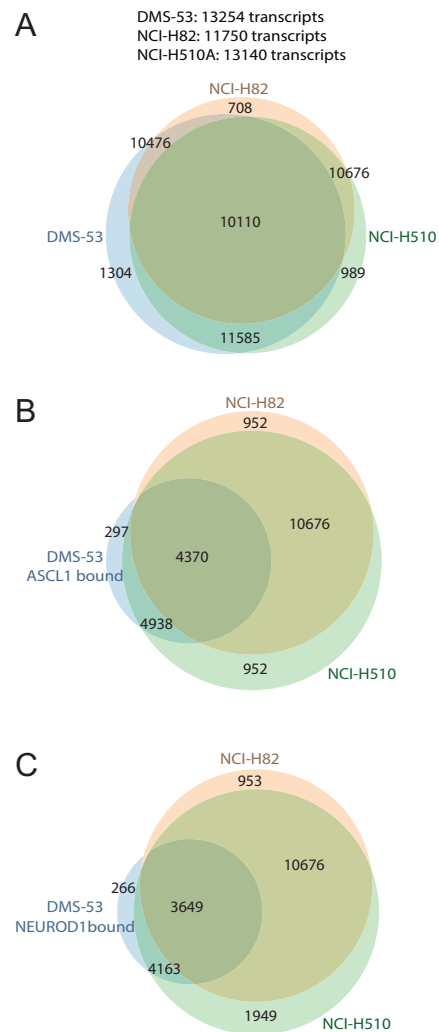
Chip-seq genome track of a second set of experiment showing ASCL1/NEUROD1, RNAPII, ATAC and H3K27Ac on *ASCL1* (A), *BCL2* (B), *INSM1*(C) and *MYB* (D) loci in untreated (dark blue) and in lurbinectedin treated (green) conditions, respectively. The presence of lurbinectedin (Bio-Lur, red) is also shown.

## Appendix Figure S2



Venn diagrams showing the overlap between genes downregulated after 50nM treatment with lurbinectedin (Blue circle) and genes downregulated after silencing either ASCL1 (orange circle) or Neurod1 (green Circle).

## Appendix Figure S3



Expressed genes shared between DMS53, NCI-H82, and NCI H510A in untreated conditions (A) and targeted either by ASCL1 (B) or NEUROD1 (C). The number of transcripts from NCI-H82 and NCI-H510A cell lines was defined with the same parameters used for DMS-53 in Figure 1 (i.e. coverage equal to or higher than 1 and a TPM cut off value of 4).

### Appendix Figure S4

|   |                                             |      |
|---|---------------------------------------------|------|
| A | DMS-53 down + NCI-H82 down                  | 3701 |
| B | NCI-H82 down + NCI-H510A down               | 4053 |
| C | DMS-53 down + NCI-H510A down                | 4399 |
| D | DMS-53 down + NCI-H510A down + NCI-H82 down | 3374 |
| E | ASCL1 ChIPseq                               | 8131 |
| F | NEUROD1 ChIPseq                             | 7329 |

|           |      |
|-----------|------|
| A + E     | 1671 |
| A + F     | 1408 |
| A + E + F | 1096 |

|           |      |
|-----------|------|
| B + E     | 1853 |
| B + F     | 1607 |
| B + E + F | 1244 |

|           |      |
|-----------|------|
| C + E     | 1957 |
| C + F     | 1612 |
| C + E + F | 1241 |

|           |      |
|-----------|------|
| D + E     | 1523 |
| D + F     | 1289 |
| D + E + F | 998  |

Overlapping and comparison of the ASCL1 and NEUROD1 targeted genes and downregulated genes between the DMS53, NCI-H82, and NCI H510A cell lines after 50nM lurbinectedin treatment. Promoter-TSS annotated ChIPseq datasets. Letters corresponding to respective conditions are shown in the left. Overlap between different conditions are shown as additional tables below.

## Appendix Figure S5

Statistical analyses for Figure 4A, 4C, 5A-E, EV5B and EV5D.

**Figure 4A**

**Two-way RM ANOVA**

| ANOVA table                | SS     | DF | MS      | F (DFn, DFd)       | P value  |
|----------------------------|--------|----|---------|--------------------|----------|
| Row Factor x Column Factor | 0,1778 | 8  | 0,02223 | F (8, 18) = 0,4541 | P=0,8721 |
| Row Factor                 | 3,295  | 8  | 0,4119  | F (8, 18) = 1,143  | P=0,3832 |
| Column Factor              | 4,261  | 1  | 4,261   | F (1, 18) = 87,05  | P<0,0001 |
| Subject                    | 6,489  | 18 | 0,3605  | F (18, 18) = 7,365 | P<0,0001 |
| Residual                   | 0,881  | 18 | 0,04895 |                    |          |

| Šidák's multiple comparisons test | Mean Diff, | 95,00% CI of diff, | Below threshold? | Summary | Adjusted P Value |
|-----------------------------------|------------|--------------------|------------------|---------|------------------|
|                                   |            |                    |                  |         |                  |
| <b>Ctrl - Lur</b>                 |            |                    |                  |         |                  |
| A549                              | 0,6837     | 0,1168 to 1,251    | Yes              | *       | 0,0121           |
| NCI-H460                          | 0,7192     | 0,1523 to 1,286    | Yes              | **      | 0,0078           |
| IMR90                             | 0,3182     | -0,2487 to 0,8851  | No               | ns      | 0,5932           |
| NCI-H146                          | 0,6456     | 0,07872 to 1,212   | Yes              | *       | 0,0194           |
| NCI-H82                           | 0,6042     | 0,03734 to 1,171   | Yes              | *       | 0,032            |
| DMS-53                            | 0,5056     | -0,06130 to 1,072  | No               | ns      | 0,1019           |
| NCI-H510                          | 0,5268     | -0,04006 to 1,094  | No               | ns      | 0,0799           |
| NCI-H526                          | 0,4825     | -0,08440 to 1,049  | No               | ns      | 0,1318           |
| SHP-77                            | 0,5703     | 0,003372 to 1,137  | Yes              | *       | 0,048            |

**Figure 4C**

| Unpaired t test                     |                 |                                        |                  |
|-------------------------------------|-----------------|----------------------------------------|------------------|
| P value                             | <0,0001         | Mean of column A                       | 46,15            |
| P value summary                     | ****            | Mean of column B                       | 18,55            |
| Significantly different (P < 0.05)? | Yes             | Difference between means (B - A) ± SEM | -27,60 ± 1,514   |
| One- or two-tailed P value?         | Two-tailed      | 95% confidence interval                | -30,58 to -24,63 |
| t, df                               | t=18,23, df=719 | R squared (eta squared)                | 0,3161           |

|                          |     |       |     |     |
|--------------------------|-----|-------|-----|-----|
| Sample size, column Ctrl | 508 | F     | Dfn | Dfd |
| Sample size, column Lur  | 213 | 4,495 | 507 | 212 |

Figure 5A

| Carboplatin                                                          | A549             | NCIH460        | DMS53               | NCIH82             | NCIH510A       |
|----------------------------------------------------------------------|------------------|----------------|---------------------|--------------------|----------------|
| log(inhibitor) vs. response -<br>Variable slope (four<br>parameters) |                  |                |                     |                    |                |
| <b>Best-fit values</b>                                               |                  |                |                     |                    |                |
| Bottom                                                               | ~ -25871         | ~ -68331       | -316,9              | ~ -1371            | ~ -62140       |
| Top                                                                  | 87,62            | 100,3          | 109,5               | 102,3              | 122,7          |
| LogIC50                                                              | ~ -1,736         | ~ 4,694        | -2,578              | ~ -2,300           | ~ 6,884        |
| HillSlope                                                            | -1,395           | ~ -0,3490      | -0,5551             | -1,108             | ~ -0,2607      |
| IC50                                                                 | ~ 0,01838        | ~ 49428        | 0,002645            | ~ 0,005009         | ~ 7653588      |
| Span                                                                 | ~ 25959          | ~ 68431        | 426,4               | ~ 1473             | ~ 62262        |
| <b>Std. Error</b>                                                    |                  |                |                     |                    |                |
| Bottom                                                               | ~ 11367900       | ~ 36267963     | 667,2               | ~ 31783            | ~ 44500781     |
| Top                                                                  | 1,462            | 7,46           | 2,882               | 1,206              | 28,37          |
| LogIC50                                                              | ~ 137,9          | ~ 665,0        | 1,815               | ~ 9,387            | ~ 1206         |
| HillSlope                                                            | 0,9096           | ~ 0,1991       | 0,1586              | 0,5395             | ~ 0,3307       |
| Span                                                                 | ~ 11367901       | ~ 36267969     | 669,3               | ~ 31784            | ~ 44500807     |
| <b>95% CI (asymptotic)</b>                                           |                  |                |                     |                    |                |
| Bottom                                                               | (Very wide)      | (Very wide)    | -1634 to 1000       | (Very wide)        | (Very wide)    |
| Top                                                                  | 84,73 to 90,50   | 85,00 to 115,7 | 103,8 to 115,2      | 99,86 to 104,7     | 65,85 to 179,5 |
| LogIC50                                                              | (Very wide)      | (Very wide)    | -6,161 to 1,006     | (Very wide)        | (Very wide)    |
| HillSlope                                                            | -3,192 to 0,4031 | (Very wide)    | -0,8682 to -0,2419  | -2,180 to -0,03503 | (Very wide)    |
| IC50                                                                 | ???              | ???            | 6,900e-007 to 10,14 | ???                | ???            |
| Span                                                                 | (Very wide)      | (Very wide)    | -895,1 to 1748      | (Very wide)        | (Very wide)    |
| <b>Goodness of Fit</b>                                               |                  |                |                     |                    |                |
| Degrees of Freedom                                                   | 146              | 26             | 165                 | 86                 | 56             |
| R squared                                                            | 0,7368           | 0,9633         | 0,8571              | 0,8362             | 0,8463         |
| Sum of Squares                                                       | 24740            | 808,1          | 24158               | 4986               | 11712          |
| Sy.x                                                                 | 13,02            | 5,575          | 12,1                | 7,614              | 14,46          |
| <b>Number of points</b>                                              |                  |                |                     |                    |                |
| # of X values                                                        | 240              | 240            | 240                 | 240                | 240            |
| # Y values analyzed                                                  | 150              | 30             | 169                 | 90                 | 60             |

Figure 5B

| Etoposide                                                            | A549         | NCIH460         | DMS53                    | NCIH82     | NCIH510A                 |
|----------------------------------------------------------------------|--------------|-----------------|--------------------------|------------|--------------------------|
| log(inhibitor) vs. response -<br>Variable slope (four<br>parameters) |              |                 |                          |            |                          |
| <b>Best-fit values</b>                                               |              |                 |                          |            |                          |
| Bottom                                                               | ~ -151,3     | -1,219          | 53,42                    | -745146    | -1,767                   |
| Top                                                                  | ~ 3857       | ~ 55020         | 117,1                    | 97,05      | 130,7                    |
| LogIC50                                                              | ~ -30,52     | ~ -20,96        | -5,927                   | 9,099      | -6,004                   |
| HillSlope                                                            | ~ -0,05055   | ~ -0,2044       | -0,7447                  | -0,3436    | -0,7475                  |
| IC50                                                                 | ~ 3,037e-031 | ~ 1,102e-021    | 0,000001184              | 1255131688 | 9,904E-07                |
| Span                                                                 | ~ 4008       | ~ 55022         | 63,67                    | 745243     | 132,4                    |
| <b>Std. Error</b>                                                    |              |                 |                          |            |                          |
| Bottom                                                               | ~ 1668       | 34              | 4,997                    |            | 3,338                    |
| Top                                                                  | ~ 547880     | ~ 51203074      | 9,076                    |            | 6,902                    |
| LogIC50                                                              | ~ 1548       | ~ 2002          | 0,2059                   |            | 0,07373                  |
| HillSlope                                                            | ~ 0,7659     | ~ 0,3319        | 0,2716                   |            | 0,09339                  |
| Span                                                                 | ~ 549543     | ~ 51203106      | 12,59                    |            | 9,2                      |
| <b>95% CI (asymptotic)</b>                                           |              |                 |                          |            |                          |
| Bottom                                                               | (Very wide)  | -71,10 to 68,67 | 43,55 to 63,28           |            | -8,454 to 4,920          |
| Top                                                                  | (Very wide)  | (Very wide)     | 99,16 to 135,0           |            | 116,8 to 144,5           |
| LogIC50                                                              | (Very wide)  | (Very wide)     | -6,333 to -5,520         |            | -6,152 to -5,856         |
| HillSlope                                                            | (Very wide)  | (Very wide)     | -1,281 to -0,2085        |            | -0,9346 to -0,5604       |
| IC50                                                                 | ???          | ???             | 4,644e-007 to 3,019e-006 |            | 7,049e-007 to 1,392e-006 |
| Span                                                                 | (Very wide)  | (Very wide)     | 38,82 to 88,52           |            | 114,0 to 150,9           |
| <b>Goodness of Fit</b>                                               |              |                 |                          |            |                          |
| Degrees of Freedom                                                   | 146          | 26              | 166                      |            | 56                       |
| R squared                                                            | 0,864        | 0,9406          | 0,5616                   |            | 0,9702                   |
| Sum of Squares                                                       | 16427        | 1050            | 57539                    |            | 3389                     |
| Sy.x                                                                 | 10,61        | 6,353           | 18,62                    |            | 7,779                    |
|                                                                      |              |                 |                          |            |                          |
| <b>Number of points</b>                                              |              |                 |                          |            |                          |
| # of X values                                                        | 240          | 240             | 240                      | 240        | 240                      |
| # Y values analyzed                                                  | 150          | 30              | 170                      | 90         | 60                       |

Figure 5C

| Topotecan                                                            | A549           | NCIH460                  | DMS53        | NCIH82         | NCIH510A                 |
|----------------------------------------------------------------------|----------------|--------------------------|--------------|----------------|--------------------------|
| log(inhibitor) vs. response -<br>Variable slope (four<br>parameters) |                |                          |              |                |                          |
| <b>Best-fit values</b>                                               |                |                          |              |                |                          |
| Bottom                                                               | ~ -121383      | 19,36                    | ~ -3,169     | ~ -7031        | 34,69                    |
| Top                                                                  | 107,5          | 102,7                    | ~ 1297       | ~ 133,1        | 105,6                    |
| LogIC50                                                              | ~ 8,848        | -7,048                   | ~ -16,24     | ~ 11,89        | -6,573                   |
| HillSlope                                                            | ~ -0,2332      | -2,071                   | ~ -0,1317    | ~ -0,1166      | -0,6135                  |
| IC50                                                                 | ~ 704494874    | 8,945E-08                | ~ 5,745e-017 | ~ 780328278226 | 2,675E-07                |
| Span                                                                 | ~ 121491       | 83,37                    | ~ 1301       | ~ 7164         | 70,96                    |
| <b>Std. Error</b>                                                    |                |                          |              |                |                          |
| Bottom                                                               | ~ 191885000    | 1,419                    | ~ 105,1      | ~ 4165887      | 11,14                    |
| Top                                                                  | 19,86          | 2,405                    | ~ 35917      | ~ 239,7        | 13,58                    |
| LogIC50                                                              | ~ 2958         | 0,03187                  | ~ 120,4      | ~ 2330         | 0,2972                   |
| HillSlope                                                            | ~ 0,2585       | 0,2889                   | ~ 0,4054     | ~ 1,053        | 0,3293                   |
| Span                                                                 | ~ 191885018    | 2,958                    | ~ 36020      | ~ 4166123      | 22,62                    |
| <b>95% CI (asymptotic)</b>                                           |                |                          |              |                |                          |
| Bottom                                                               | (Very wide)    | 16,54 to 22,18           | (Very wide)  | (Very wide)    | 12,38 to 57,00           |
| Top                                                                  | 68,05 to 147,0 | 97,94 to 107,5           | (Very wide)  | (Very wide)    | 78,45 to 132,8           |
| LogIC50                                                              | (Very wide)    | -7,112 to -6,985         | (Very wide)  | (Very wide)    | -7,168 to -5,977         |
| HillSlope                                                            | (Very wide)    | -2,646 to -1,497         | (Very wide)  | (Very wide)    | -1,273 to 0,04615        |
| IC50                                                                 | ???            | 7,731e-008 to 1,035e-007 | ???          | ???            | 6,794e-008 to 1,054e-006 |
| Span                                                                 | (Very wide)    | 77,49 to 89,25           | (Very wide)  | (Very wide)    | 25,65 to 116,3           |
| Goodness of Fit                                                      |                |                          |              |                |                          |
| <b>Degrees of Freedom</b>                                            | 86             | 86                       | 86           | 86             | 56                       |
| R squared                                                            | 0,8694         | 0,9402                   | 0,8635       | 0,5399         | 0,6994                   |
| Sum of Squares                                                       | 7317           | 6956                     | 6696         | 20382          | 11893                    |
| Sy.x                                                                 | 9,224          | 8,994                    | 8,824        | 15,39          | 14,57                    |
| <b>Number of points</b>                                              |                |                          |              |                |                          |
| # of X values                                                        | 240            | 240                      | 240          | 240            | 240                      |
| # Y values analyzed                                                  | 90             | 90                       | 90           | 90             | 60                       |

Figure 5D

| Lurbinectedin                                                        | A549                        | NCIH460                     | DMS53                       | NCIH82                      | NCIH510A                    |
|----------------------------------------------------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| log(inhibitor) vs. response -<br>Variable slope (four<br>parameters) |                             |                             |                             |                             |                             |
| <b>Best-fit values</b>                                               |                             |                             |                             |                             |                             |
| Bottom                                                               | 19,41                       | 8,215                       | 1,52                        | 16,25                       | 9,723                       |
| Top                                                                  | 93,15                       | 97,41                       | 105,1                       | 101,4                       | 94,69                       |
| LogIC50                                                              | -8,822                      | -8,975                      | -8,674                      | -8,879                      | -9,786                      |
| HillSlope                                                            | -1,752                      | -1,447                      | -0,9883                     | -1,66                       | -1,212                      |
| IC50                                                                 | 1,506E-09                   | 1,059E-09                   | 2,116E-09                   | 1,322E-09                   | 1,637E-10                   |
| Span                                                                 | 73,75                       | 89,19                       | 103,6                       | 85,1                        | 84,97                       |
| <b>Std. Error</b>                                                    |                             |                             |                             |                             |                             |
| Bottom                                                               | 3,12                        | 5,991                       | 15,18                       | 5,221                       | 3,113                       |
| Top                                                                  | 1,222                       | 2,579                       | 2,863                       | 2,138                       | 3,516                       |
| LogIC50                                                              | 0,04165                     | 0,07574                     | 0,1637                      | 0,06351                     | 0,06836                     |
| HillSlope                                                            | 0,2474                      | 0,3141                      | 0,2434                      | 0,3402                      | 0,2177                      |
| Span                                                                 | 3,549                       | 7,051                       | 16,58                       | 6,007                       | 5,312                       |
| <b>95% CI (asymptotic)</b>                                           |                             |                             |                             |                             |                             |
| Bottom                                                               | 13,26 to 25,55              | -3,651 to 20,08             | -28,54 to 31,58             | 5,791 to 26,71              | 3,571 to 15,88              |
| Top                                                                  | 90,74 to 95,56              | 92,30 to 102,5              | 99,47 to 110,8              | 97,07 to 105,6              | 87,74 to 101,6              |
| LogIC50                                                              | -8,904 to -<br>8,740        | -9,125 to -<br>8,825        | -8,999 to -<br>8,350        | -9,006 to -<br>8,752        | -9,921 to -<br>9,651        |
| HillSlope                                                            | -2,240 to -<br>1,265        | -2,069 to -<br>0,8249       | -1,470 to -<br>0,5063       | -2,341 to -<br>0,9785       | -1,642 to -<br>0,7818       |
| IC50                                                                 | 1,247e-009 to<br>1,820e-009 | 7,499e-010 to<br>1,496e-009 | 1,003e-009 to<br>4,464e-009 | 9,860e-010 to<br>1,772e-009 | 1,200e-010 to<br>2,235e-010 |
| Span                                                                 | 66,76 to 80,74              | 75,23 to 103,2              | 70,77 to 136,5              | 73,07 to 97,14              | 74,47 to 95,47              |
| <b>Goodness of Fit</b>                                               |                             |                             |                             |                             |                             |
| Degrees of Freedom                                                   | 236                         | 116                         | 116                         | 56                          | 146                         |
| R squared                                                            | 0,8221                      | 0,7959                      | 0,7846                      | 0,9015                      | 0,8122                      |
| Sum of Squares                                                       | 39963                       | 35262                       | 32194                       | 6838                        | 40072                       |
| Sy.x                                                                 | 13,01                       | 17,44                       | 16,66                       | 11,05                       | 16,57                       |
| <b>Number of points</b>                                              |                             |                             |                             |                             |                             |
| # of X values                                                        | 240                         | 240                         | 240                         | 240                         | 240                         |
| # Y values analyzed                                                  | 240                         | 120                         | 120                         | 60                          | 150                         |

Figure 5E

| Cisplatin                                                            | A549                     | NCIH460                  | DMS53                    | NCIH82                   | NCIH510A                |
|----------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-------------------------|
| log(inhibitor) vs. response -<br>Variable slope (four<br>parameters) |                          |                          |                          |                          |                         |
| <b>Best-fit values</b>                                               |                          |                          |                          |                          |                         |
| Bottom                                                               | 6,276                    | -0,4616                  | 9,243                    | 0,5795                   | 0,932                   |
| Top                                                                  | 94,5                     | 102,6                    | 100,1                    | 99,89                    | 94,87                   |
| LogIC50                                                              | -4,791                   | -5,226                   | -4,125                   | -4,755                   | -4,076                  |
| HillSlope                                                            | -1,942                   | -1,416                   | -2,248                   | -2,788                   | -3,063                  |
| IC50                                                                 | 0,00001618               | 0,000005938              | 0,00007501               | 0,00001757               | 0,00008404              |
| Span                                                                 | 88,22                    | 103                      | 90,86                    | 99,31                    | 93,94                   |
| <b>Std. Error</b>                                                    |                          |                          |                          |                          |                         |
| Bottom                                                               | 1,931                    | 1,098                    | 1,561                    | 0,901                    | 5,403                   |
| Top                                                                  | 1,272                    | 1,05                     | 0,4401                   | 0,6378                   | 1,765                   |
| LogIC50                                                              | 0,02686                  | 0,01768                  | 0,01304                  | 0,009778                 | 0,04206                 |
| HillSlope                                                            | 0,2023                   | 0,07424                  | 0,1172                   | 0,1603                   | 0,5719                  |
| Span                                                                 | 2,448                    | 1,674                    | 1,68                     | 1,147                    | 5,774                   |
| <b>95% CI (asymptotic)</b>                                           |                          |                          |                          |                          |                         |
| Bottom                                                               | 2,437 to 10,11           | -2,644 to 1,721          | 6,139 to 12,35           | -1,212 to 2,371          | -9,808 to 11,67         |
| Top                                                                  | 91,97 to 97,03           | 100,5 to 104,7           | 99,23 to 101,0           | 98,62 to 101,2           | 91,36 to 98,38          |
| LogIC50                                                              | -4,844 to -4,738         | -5,262 to -5,191         | -4,151 to -4,099         | -4,775 to -4,736         | -4,159 to -3,992        |
| HillSlope                                                            | -2,345 to -1,540         | -1,563 to -1,268         | -2,481 to -2,015         | -3,106 to -2,469         | -4,200 to -1,926        |
| IC50                                                                 | 1,431e-005 to 1,830e-005 | 5,476e-006 to 6,438e-006 | 7,066e-005 to 7,962e-005 | 1,680e-005 to 1,837e-005 | 6,932e-005 to 0,0001019 |
| Span                                                                 | 83,36 to 93,09           | 99,71 to 106,4           | 87,52 to 94,20           | 97,03 to 101,6           | 82,46 to 105,4          |
| <b>Goodness of Fit</b>                                               |                          |                          |                          |                          |                         |
| Degrees of Freedom                                                   | 86                       | 86                       | 86                       | 86                       | 86                      |
| R squared                                                            | 0,9612                   | 0,9887                   | 0,99                     | 0,9915                   | 0,8614                  |
| Sum of Squares                                                       | 5079                     | 1891                     | 902,4                    | 1474                     | 16048                   |
| Sy.x                                                                 | 7,685                    | 4,689                    | 3,239                    | 4,14                     | 13,66                   |
| <b>Number of points</b>                                              |                          |                          |                          |                          |                         |
| # of X values                                                        | 240                      | 240                      | 240                      | 240                      | 240                     |
| # Y values analyzed                                                  | 90                       | 90                       | 90                       | 90                       | 90                      |

Figure EV5B

ASCL1 (a.u.)

| Unpaired t test                     |                  |
|-------------------------------------|------------------|
| P value                             | <0,0001          |
| P value summary                     | ****             |
| Significantly different (P < 0.05)? | Yes              |
| One- or two-tailed P value?         | Two-tailed       |
| t, df                               | t=54,11, df=2205 |

|                          |      |
|--------------------------|------|
| Sample size, column Ctrl | 994  |
| Sample size, column Lur  | 1213 |

|                                        |                |
|----------------------------------------|----------------|
| Mean of column A                       | 44,34          |
| Mean of column B                       | 21,94          |
| Difference between means (B - A) ± SEM | 22,40 ± 0,4140 |
| 95% confidence interval                | 21,59 to 23,21 |
| R squared (eta squared)                | 0,5704         |

|       |     |      |
|-------|-----|------|
| F     | Dfn | Dfd  |
| 2,197 | 993 | 1212 |

**Figure EV5D**

**Viabale Cells**

**Unpaired t test**

|                                     |                  |
|-------------------------------------|------------------|
| P value                             | 0,0034           |
| P value summary                     | **               |
| Significantly different (P < 0.05)? | Yes              |
| One- or two-tailed P value?         | Two-tailed       |
| t, df                               | t=6,237,<br>df=4 |

|                                        |                  |
|----------------------------------------|------------------|
| Mean of column A                       | 62,9             |
| Mean of column B                       | 48               |
| Difference between means (B - A) ± SEM | -14,90 ± 2,389   |
| 95% confidence interval                | -21,53 to -8,267 |
| R squared (eta squared)                | 0,9068           |

|                                 |   |
|---------------------------------|---|
| <b>Sample size, column Ctrl</b> | 3 |
| <b>Sample size, column Lur</b>  | 3 |

|      |     |     |
|------|-----|-----|
| F    | Dfn | Dfd |
| 4,47 | 2   | 2   |

**Early Apoptotic Cells**

**Unpaired t test**

|                                     |                  |
|-------------------------------------|------------------|
| P value                             | 0,0906           |
| P value summary                     | ns               |
| Significantly different (P < 0.05)? | No               |
| One- or two-tailed P value?         | Two-tailed       |
| t, df                               | t=2,220,<br>df=4 |

|                                        |                  |
|----------------------------------------|------------------|
| Mean of column A                       | 0,1933           |
| Mean of column B                       | 1,177            |
| Difference between means (B - A) ± SEM | 0,9833 ± 0,4429  |
| 95% confidence interval                | -0,2463 to 2,213 |
| R squared (eta squared)                | 0,552            |

|                                 |   |
|---------------------------------|---|
| <b>Sample size, column Ctrl</b> | 3 |
| <b>Sample size, column Lur</b>  | 3 |

|     |     |     |
|-----|-----|-----|
| F   | Dfn | Dfd |
| 193 | 2   | 2   |

**Late Apoptotic Cells**

**Unpaired t test**

|                                     |                   |
|-------------------------------------|-------------------|
| P value                             | 0,5865            |
| P value summary                     | ns                |
| Significantly different (P < 0.05)? | No                |
| One- or two-tailed P value?         | Two-tailed        |
| t, df                               | t=0,5906,<br>df=4 |

|                                        |                 |
|----------------------------------------|-----------------|
| Mean of column A                       | 7,49            |
| Mean of column B                       | 9,19            |
| Difference between means (B - A) ± SEM | 1,700 ± 2,878   |
| 95% confidence interval                | -6,291 to 9,691 |
| R squared (eta squared)                | 0,08021         |

|                                 |   |
|---------------------------------|---|
| <b>Sample size, column Ctrl</b> | 3 |
| <b>Sample size, column Lur</b>  | 3 |

|       |     |     |
|-------|-----|-----|
| F     | Dfn | Dfd |
| 3,839 | 2   | 2   |