
B.

D.


Figure S1. Effect of 17 -aminogeldanamycin (AG) at $0.4 \mu \mathrm{M}$ on viability of DMBC11 cells. A. DMBC11 melanoma cells were exposed to AG at $0.4 \mu \mathrm{M}$. Acid phosphatase activity (APA) was determined colorimetrically at indicated time points. Data presented are mean $\pm \mathrm{SD}$ of a representative experiment performed in triplicate. B. The percentages of Annexin-V-positive cells were determined by flow cytometry after 24 and 48 hours. $\mathrm{n}=3(* \mathrm{p} \leq 0.05$ vs. control). C. Activation of caspase- $3 / 7$ was assessed over the course of 72 hours by time-lapse imaging system IncuCyte ZOOM. Data presented are mean $\pm$ SD of a representative experiment performed in duplicate. D. Level of cleaved PARP (cPARP) was determined by Western Blotting after 24 hours. $\beta$-actin was used as a loading control. The relative level of cPARP versus $\beta$-actin is shown below the blot.

DMBC21
DMBC29


Figure S2. Effect of $0.4 \mu \mathrm{M}$ geldanamycin on mRNA levels of NF-кB-dependent genes, CXCL8 (IL-8), CCND1 (cyclin D1) and BCL2L1 (BCL- $\mathrm{X}_{\mathrm{L}}$ ) in melanoma cells. The transcript levels were assessed by qRT-PCR after 22 h , and shown relative to the control.

Table S1. PCR array layout corresponding to Figure 1B.

|  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| A | ADM | AGT | AKT1 | ALDH3A2 | BCL2A1 | BCL2L1 | BIRC2 | BIRC3 | C3 | CCL11 | CCL2 | CCL22 |
| B | CCL5 | CCND1 | CCR5 | CD40 | CD69 | CD80 | CD83 | CDKN1A | $C F B$ | CSF1 | CSF2 | CSF2RB |
| C | CSF3 | CXCL1 | CXCL10 | CXCL2 | CXCL9 | EGFR | EGR2 | F3 | F8 | $F A S$ | FASLG | GADD458 |
| D | ICAM1 | IFNB1 | IFNG | ILI2B | IL15 | IL1A | IL1B | IL1R2 | IL1RN | IL2 | IL2RA | ILA |
| E | IL6 | CXCL8 | INS | IRF1 | LTA | LTB | MAP2K6 | MMP9 | MYC | MYD88 | NCOA3 | NFKB1 |
| F | NFKB2 | NFKBIA | NQO1 | NR4A2 | PDGFB | PLAU | PTGS2 | REL | RELA | RELB | SELE | SELP |
| G | SNAP25 | SOD2 | STAT1 | STAT3 | STAT5B | TNF | TNFRSF1B | TNFSF10 | TP53 | TRAF2 | VCAM1 | XIAP |

Table S2. Mutation status of genes associated with NF-кB signaling pathway. Only non-synonymous mutations and indels are included. Mutations are marked as homozygous ( $+/+$ ) or heterozygous ( $+/-$ ). Nonsense mutation is marked as X. Prediction of functional effects of amino acid substitutions were assessed by using Polyphen-2 software. Polyphen-2 predictions were classified based on the Polyphen-2 scores as benign (scores 0.000-0.449), possibly damaging (scores $0.450-0.959$ ) and probably damaging (scores $0.960-1.000$ ). Names of proteins are given in the brackets if they differ from gene names

| gene | DMBC11 | DMBC12 | DMBC21 | DMBC28 | DMBC29 | DMBC22 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| BCL10 |  |  |  |  |  |  |
| BIRC2 (cIAP1) |  |  |  |  |  |  |
| BIRC3 (cIAP2) |  |  |  |  |  |  |
| BLNK |  |  |  |  |  |  |
| BTK |  |  |  |  |  |  |
| CARD11 (CARMA1) |  |  |  |  |  |  |
| CD14 |  |  |  |  |  |  |
| CD40 |  |  |  |  |  |  |
| CD40LG |  |  |  |  |  |  |
| CHUK (IKK $\alpha$ ) |  |  | V268I +/- <br> benign 0.000 | V268I +/- <br> benign 0.000 | V268I +/- $\text { benign } 0.000$ | V268I +/+ <br> benign 0.000 <br> P364S +/- <br> probably damaging 1.000 |
| CSNK2A1 (CK2) |  |  |  |  |  |  |
| CSNK2A2 (CK2) |  |  | N63T +/- <br> benign 0.029 |  |  |  |
| CSNK2A3 (CK2) |  |  |  |  |  |  |
| CSNK2B (CK2) |  |  |  |  |  |  |
| DDX58 (RIG-1) | R7C +/+ <br> probably damaging 0.997 | R7C $+/+$ probably damaging 0.997 $\mathrm{~N} 495 \mathrm{~K}+/-$ benign 0.025 |  |  | Q498K +/- $\text { benign } 0.078$ |  |
| ERCl (ELKS) | $\begin{gathered} \mathrm{T} 1032 \mathrm{~A}+/- \\ \text { benign } 0.000 \end{gathered}$ | $\begin{gathered} \mathrm{T} 1032 \mathrm{~A}+/- \\ \text { benign } 0.000 \end{gathered}$ |  |  |  |  |
| $I K B K B(\mathrm{IKK} \beta)$ |  |  |  |  |  |  |


| $I K B K G$ (NEMO) |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ILIB |  | $\begin{gathered} \mathrm{Y} 206 \mathrm{~N}+/- \\ \text { probably damaging } 0.999 \\ \mathrm{P} 203 \mathrm{H}+/ \\ \text { probably damaging } 1.000 \end{gathered}$ | Y206N +/- <br> probably damaging 0.999 |  | Y206N $+/-$ probably yamaging 0.999 P203 probably damaging 1.000 M2111I +- probably damaging 1.000 K209 possibly damaging 0.454 K208N $+/-$ probably damaging 0.999 | P203H + <br> probably damaging 1.000 <br> K209N +- <br> possibly damaging 0.454 |
| ILIR1 |  |  |  |  |  |  |
| IL1R2 |  |  |  |  |  |  |
| IRAKI | F196S +/+ benigng 0.002 S532 benign 0.000 | $\begin{aligned} & \hline \text { F196S +/+ } \\ & \text { benign } 0.02 \\ & \text { S532 } \\ & \text { benign } 0.000 \end{aligned}$ | $\begin{aligned} & \hline \text { F196S +/- } \\ & \text { bening } 0.002 \\ & \text { S532. } \\ & \text { benign } 0.000 \end{aligned}$ | $\begin{aligned} & \hline \text { F196S +/+ } \\ & \text { benigng } 0.02 \\ & \text { S532. } \\ & \text { benign } 0.000 \end{aligned}$ | F196S +/+ S532L +/+ benign 0.000 | $\begin{aligned} & \text { F196S +/+ } \\ & \text { benign } 0.002 \end{aligned}$ |
| IRAK4 |  |  |  |  |  |  |
| LAT |  |  |  |  |  |  |
| LBP |  |  |  |  |  |  |
| LCK |  |  |  |  |  |  |
| LTA |  |  |  |  |  |  |
| LTB |  |  |  |  |  |  |
| LTBR |  |  |  |  |  |  |
| LY96 (MD-2) | $\begin{aligned} & \hline \text { R56G +/+ } \\ & \text { benign } 0.000 \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline \text { R56G +/+ } \\ & \text { benign } 0.000 \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline \text { R56G +/+ } \\ & \text { benign } 0.000 \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline \text { R56G +/+ } \\ & \text { benign } 0.000 \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline \text { R56G +/+ } \\ & \text { benign } 0.000 \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline \text { R56G +/+ } \\ & \text { benign } 0.000 \\ & \hline \end{aligned}$ |
| LYN |  |  |  |  |  |  |
| MALT1 |  |  |  |  |  |  |
| MAP3K7 (TAK1) |  |  |  |  |  |  |
| MAP3K14 (NIK) | $\underset{\substack{\text { frameshift variant }+/+ \\ \text { (insertion) }}}{\text { R219P/X }}$ | $\underset{\substack{\text { frameshift variant }+/+ \\ \text { (insertion) }}}{\text { R21P/X }}$ | $\underset{\substack{\text { frameshift variant }+/+ \\ \text { (insertion) }}}{\mathrm{R} 219 \mathrm{X}}$ | $\underset{\substack{\text { Rrameshift variant }+/+ \\ \text { (insertion) }}}{\text { R219P/X }}$ | $\underset{\substack{\text { frameshift variant }+/+ \\ \text { (insertion) }}}{\text { R219P/X }}$ | $\underset{\substack{\text { frameshift variant }+/+ \\ \text { (insertion) }}}{\text { R219P/X }}$ |
| MYD88 |  |  |  |  |  |  |
| NFKB1 (p50) |  |  |  |  |  |  |
| NFKB2 (p100) |  |  |  |  |  |  |


| NFKBIA ( $\mathrm{I} \kappa \mathrm{B} \alpha$ ) |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| NFKBIE ( $\mathrm{I} \kappa \mathrm{B} \varepsilon$ ) | $\begin{gathered} \text { G34E +/- } \\ \text { probably damaging } 0.978 \end{gathered}$ | G34E +/- <br> probably damaging 0.978 | $\begin{aligned} & \text { S33F +/- } \\ & \text { possibly damaging } 0.940 \\ & \text { V194A +/- } \\ & \text { benign } 0.000 \\ & \text { P175L }+/- \\ & \text { benign } 0.000 \\ & \hline \end{aligned}$ | $\mathrm{S} 33 \mathrm{~F}+/$ <br> possibly damaging 0.940 <br> V194A +/- <br> benign 0.000 <br> P175L +/- <br> benign 0.000 | S33F +/- <br> possibly damaging 0.940 <br> V194A +/ <br> benign 0.000 <br> P175L +/- <br> benign 0.000 |  |
| PLCG1 (PLC l 1 ) | S279G +/- <br> benign 0.000 <br> I813T +/- <br> benign 0.000 | S279G +/- <br> benign 0.000 I813T +/ <br> benign 0.000 |  |  |  | $\begin{aligned} & \text { I813T +/- } \\ & \text { benign } 0.000 \end{aligned}$ |
| PLCG2 (PLC 2 2) |  |  |  |  |  |  |
| PRKCA (PKC) | V568I +/+ <br> benign 0.000 | V568I +/+ <br> benign 0.000 | V568I +/+ <br> benign 0.000 | V568I +/+ <br> benign 0.000 | V568I +/+ <br> benign 0.000 | V568I +/+ <br> benign 0.000 |
| PRKCB (PKC) |  |  |  |  |  |  |
| PRKCZ (PKC) |  |  | S148R +/- <br> benign 0.002 | S148R +/- <br> benign 0.002 | S148R +/- <br> benign 0.002 |  |
| PRKCG (PKC) |  |  |  |  |  |  |
| PRKCE (PKC) |  |  |  |  |  |  |
| PRKCD (PKC) |  |  |  |  |  |  |
| PRKCH (PKC) |  |  |  |  |  |  |
| PRKCI (PKC) |  |  |  |  |  |  |
| RELA (p65) |  |  |  |  |  |  |
| RELB |  |  |  |  |  |  |
| RIPK1 (RIP1) |  |  | A569V +/- <br> possibly damaging 0.617 | A569V +/- <br> possibly damaging 0.617 | A569V +/- <br> possibly damaging 0.617 |  |
| SYK |  |  |  |  |  |  |
| TAB1 |  |  |  |  |  |  |
| TAB2 |  |  |  |  |  |  |
| TAB3 | $\begin{gathered} \text { W394R +/+ } \\ \text { benign } 0.000 \\ \hline \end{gathered}$ | $\begin{gathered} \text { W394R +/+ } \\ \text { benign } 0.000 \\ \hline \end{gathered}$ | $\begin{gathered} \text { W394R +/+ } \\ \text { benign } 0.000 \\ \hline \end{gathered}$ | W394R +/+ <br> benign 0.000 | $\begin{gathered} \text { W394R +/+ } \\ \text { benign } 0.000 \\ \hline \end{gathered}$ | $\begin{gathered} \text { W394R +/+ } \\ \text { benign } 0.000 \\ \hline \end{gathered}$ |
| TICAM1 (TRIF) |  |  |  |  |  |  |
| TIRAP |  |  | $\begin{gathered} \text { S180L +/+ } \\ \text { possibly damaging } 0.456 \end{gathered}$ | S180L +/+ <br> possibly damaging 0.456 | S180L +/+ <br> possibly damaging 0.456 | S180L +/- <br> possibly damaging 0.456 |


| TLR4 |  |  | $\begin{aligned} & \mathrm{D} 299 \mathrm{G}+/- \\ & \text { benign } 0.026 \\ & \text { T399I +/- } \\ & \text { benign } 0.177 \\ & \hline \end{aligned}$ | $\begin{gathered} \mathrm{D} 299 \mathrm{G}+/- \\ \text { benign } 0.026 \\ \mathrm{~T} 399 \mathrm{I}+/- \\ \text { benign } 0.177 \\ \hline \end{gathered}$ | $\begin{gathered} \mathrm{D} 299 \mathrm{G}+/- \\ \text { benign } 0.026 \\ \text { T399I +/- } \\ \text { benign } 0.177 \\ \hline \end{gathered}$ | P202T +/- <br> possibly damaging 0.488 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| TNF |  |  |  |  |  |  |
| TNFRSF1A (TNFR1) |  |  |  |  |  |  |
| TNFRSF11A (RANK) | $\begin{aligned} & \mathrm{A} 192 \mathrm{~V}+/- \\ & \text { benign } 0.051 \end{aligned}$ | $\begin{aligned} & \mathrm{A} 192 \mathrm{~V}+/- \\ & \text { benign } 0.051 \end{aligned}$ |  |  |  | $\mathrm{A} 192 \mathrm{~V}+/$ $\text { benign } 0.051$ |
| TNFRSF13B (BAFFR) |  |  |  |  |  |  |
| TNFSF11 (RANKL) |  |  |  |  |  |  |
| TNFSF13B (BAFF) |  |  |  |  |  |  |
| TRADD |  |  |  |  |  |  |
| TRAF2 |  |  |  |  |  |  |
| TRAF3 |  |  |  |  |  | $\begin{gathered} \mathrm{M} 129 \mathrm{~T}+/- \\ \text { benign } 0.000 \end{gathered}$ |
| TRAF5 |  |  |  |  |  |  |
| TRAF6 |  |  |  |  |  |  |
| TRAM |  |  |  |  |  |  |
| TRIM25 | P358L +/+ <br> benign 0.050 | P358L +/+ $\text { benign } 0.050$ |  |  |  | P358L +/- <br> benign 0.050 |
| ZAP70 |  |  |  |  |  |  |

