Hematopoietic niche drives FLT3-ITD acute myeloid leukemia resistance to quizartinib via STAT5- and hypoxia-dependent upregulation of AXL

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Received: September 12, 2018.
Accepted: March 21, 2019.
Pre-published: March 28, 2019.
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SUPPLEMENTAL TABLES

Table S1. shRNA sequences

|          | AXL             | STAT5           | GAS6             |
|----------|-----------------|-----------------|------------------|
|          | AGAACAGCGAGATTTATGACTA | GTACTACACTCTGTGTG | GCTGTAATGAAGATCGCCTCGTA |
|          | GGTACCCTGCGCTATCA    | GCAACAGGCCCATGACCTA | CCGGCACTGATGGAAATCAA |

Table S2. Clinical and biological features of primary AML samples

| Num | Gender | Age  | WBC  | FAB | Status       | Blasts | Karyotype      | NPM1   | FLT3 |
|-----|--------|------|------|-----|--------------|--------|----------------|--------|------|
| #1  | F      | 75   | 51   | 2   | de novo      | 68     | 46,XY [20]    | No     | ITD  |
| #2  | F      | 74   | 150  | 4   | de novo      | 83     | 46,XY [25]    | Yes    | ITD  |
| #3  | F      | 53   | 58   | 2   | de novo      | 97     | 46,XX [25]    | Yes    | ITD  |
| #4  | F      | 46   | 260  | 1   | de novo      | 70     | 46,XX [25]    | No     | ITD  |
| #5  | M      | 71   | 150  | 2   | de novo      | 97     | 46,XY [25]    | Yes    | ITD  |
| #6  | F      | 50   | 36   | 1   | de novo      | 96     | 46,XX [25]    | No     | ITD  |
| #7  | M      | 27   | 114  | 2   | de novo      | 95     | 46,XY [25]    | No     | ITD  |
| #8  | M      | 37   | 95   | 5   | de novo      | 78     | 46,XY [25]    | Yes    | ITD  |
| #9  | F      | 49   | 118  | 5   | de novo      | 89     | 46,XY [25]    | Yes    | ITD  |
| #10 | M      | 82   | 15   | 5   | Post MDS     | 60     | 46,XY [25]    | No     | ITD  |
| #11 | M      | 54   | 47   | 4   | Post MPN     | 30     | NA             | Yes    | ITD  |
| #12 | F      | 87   | 1.5  | 1   | de novo      | 82     | 46,XX [25]    | Yes    | negative |
| #13 | F      | 73   | 3.2  | 5   | Post MDS     | 66     | 46,XX [25]    | Yes    | ITD  |
| #14 | F      | 57   | 280  | 4   | de novo      | 43     | 46,XX [25]    | No     | negative |
| #15 | F      | 74   | 17   | 1   | de novo      | 96     | 46,XX [25]    | Yes    | ITD  |
| #16 | M      | 78   | 118  | 5   | de novo      | 57     | 46,XX [25]    | Yes    | ITD  |
| #17 | F      | 57   | 60   | 4   | de novo      | 98     | 46,XX [25]    | Yes    | ITD  |
| #18 | M      | 68   | 7.3  | 2   | de novo      | 58     | 46,XX [25]    | No     | negative |
| #19 | F      | 20   | 21.5 | 6   | de novo      | 21     | 46,XY [25]    | No     | negative |
| #20 | M      | 57   | 19.2 | 5   | de novo      | 70     | 46,XY [25]    | Yes    | negative |

Age: in years, M: male, F: female, WBC: white blood cell count (G/L), FAB: French American British classification, Status: de novo or secondary AML, MDS: Myelodysplastic syndrome, MPN:
myeloproliferative neoplasm, ITD: internal tandem duplication, blasts: medullar blasts (%), NPM1: mutation yes/no, NA: not available.

Table S3. Gene expression change in human CD34⁺ CD38⁻ HSPC upon STAT5 knockdown

Sorted CD34⁺ CD38⁻ cells were transduced with STAT5A or control luciferase shRNA and GFP co-encoding lentiviral vectors as previously described (1). Total RNA was isolated from sorted cord blood (CB) CD34⁺GFP⁺ cells at day 5 post transduction, using Trizol reagent following manufacturer’s instructions. Genome wide expression analysis was performed on Affymetrix IVT3' Human Gene U133 plus 2.0 arrays. Two independent transduction experiments with two independent lots of CD34⁺CD38⁻ HSPC were performed and used for microarray screening. Data were analyzed using expression console software and common targets in the two independent experiments were selected considering targets with a p value below 0.1. The whole list of genes was ordered according to fold change (FC) of expression in shSTAT5- compared to shCtrl-expressing cell (Gene Expression Omnibus (GEO) number GSE97552). Then, transmembrane containing protein encoding genes were selected for and listed up to AXL expression FC. Dimly highlighted rows focus on the two regulated tyrosine kinase receptors; darker row indicates STAT5A down-regulation.
| p-value     | FC   | Symbol | Gene Name                                                                 |
|------------|------|--------|---------------------------------------------------------------------------|
| 5.53E-02   | -1.707 | AXL    | AXL receptor tyrosine kinase                                               |
| 1.13E-01   | 1.717  | KLRB1  | killer cell lectin like receptor B1                                       |
| 5.11E-01   | 1.721  | TAS2R50 | taste 2 receptor member 50                                                |
| 4.37E-01   | 1.725  | LPAR4  | lysophosphatidic acid receptor 4                                           |
| 4.83E-01   | 1.730  | TRPC3  | transient receptor potential cation channel subfamily C member 3           |
| 2.53E-01   | 1.742  | KCNV2  | potassium voltage-gated channel modifier subfamily V member 2             |
| 2.14E-01   | 1.743  | PCDH19 | protocadherin 19                                                          |
| 1.33E-01   | -1.746 | CD1C   | CD1c molecule                                                             |
| 5.83E-01   | 1.771  | TMC1   | transmembrane channel like 1                                              |
| 4.28E-01   | 1.773  | RSPO3  | R-spondin3                                                                |
| 2.27E-01   | -1.781 | CD36   | CD36 molecule                                                              |
| 3.37E-01   | 1.785  | CMTM5  | CKLF like MARVEL transmembrane domain containing 5                         |
| 8.52E-04   | -1.794 | GPNMB  | glycoprotein nmb                                                          |
| 4.55E-01   | 1.800  | PTPRG  | protein tyrosine phosphatase, receptor type G                              |
| 1.68E-01   | -1.807 | LILRA4 | leukocyte immunoglobulin like receptor A4                                  |
| 5.00E-01   | 1.824  | SLC47A1| solute carrier family 47 member 1                                         |
| 2.96E-01   | 1.830  | DCSTAMP| dendrocyte expressed seven transmembrane protein                           |
| 1.57E-01   | -1.832 | TMEM31 | transmembrane protein 31                                                  |
| 7.51E-02   | -1.838 | SIT1   | signaling threshold regulating transmembrane adaptor 1                    |
| 1.54E-01   | 1.845  | ADRB2  | adrenoceptor beta 2                                                        |
| 1.24E-01   | -1.860 | BTLA   | B and T lymphocyte associated                                               |
| 2.73E-01   | -1.863 | RHAG   | Rh-associated glycoprotein                                                 |
| 6.26E-01   | 1.870  | ERBB4  | erb-b2 receptor tyrosine kinase 4                                          |
| 4.82E-01   | -1.908 | KEL    | Kell blood group, metallo-endopeptidase                                    |
| 3.80E-01   | -1.913 | KCNH2  | potassium voltage-gated channel subfamily H member 2                       |
| 5.05E-01   | -1.918 | XK     | X-linked Kx blood group                                                    |
| 3.84E-01   | 1.945  | KLRC4  | killer cell lectin like receptor C4                                        |
| 1.73E-01   | -2.033 | CD24   | CD24 molecule                                                              |
| 6.40E-01   | 2.084  | LRFN5  | leucine rich repeat and fibronectin type III domain containing 5           |
| 2.29E-02   | -2.089 | CLEC4C | C-type lectin domain family 4 member C                                    |
| 5.72E-01   | 2.104  | SCN2A  | sodium voltage-gated channel alpha subunit 2                              |
| 4.57E-01   | 2.274  | ADGRL4 | adhesion G protein-coupled receptor L4                                     |
| 6.27E-01   | 2.435  | GABRB2 | gamma-aminobutyric acid type A receptor beta2 subunit                      |
| 5.45E-01   | -2.469 | GYPB   | glycophorin B (MNS blood group)                                            |
| 3.74E-01   | -2.495 | DEFA4  | defensin alpha 4                                                           |
| 3.39E-03   | -2.509 | STAT5A | signal transducer and activator of transcription 5A                       |
| 4.55E-01   | 2.775  | ADAMDEC1| ADAM like decysin 1                                                        |
| 5.47E-01   | 3.319  | TPTE   | transmembrane phosphatase with tensin homology                             |
| 1.45E-01   | -3.693 | LY6G5B | lymphocyte antigen 6 family member G5B                                     |
Table S4. Antibodies for Western Blot analysis

| Primary antibody | Clone      | Company                              |
|------------------|------------|--------------------------------------|
| AXL              | C44G1      | Cell Signaling Technologies          |
| pY_{779}AXL      | 713610     | R&D                                  |
| STAT5            | sc-835     | Santa Cruz Biotech                   |
| pY_{694}STAT5    | 9351       | Cell Signaling Technologies          |
| β actin          | AC-15      | Sigma                                |
| HSP60            | SMC-110A   | Stressmarq                           |
| pY_{593}FLT3     | 33G6       | Cell Signaling Technologies          |
| FLT3             | 8F2        | Cell Signaling Technologies          |
| pTyr             | 4G10       | Millipore                            |
| ERK              | L34F12     | Cell Signaling Technologies          |
| pT_{202}/Y_{204}ERK | D13.14.4E | Cell Signaling Technologies          |
| AKT              | 9272       | Cell Signaling Technologies          |
| pSer_{473}AKT    | D9E        | Cell Signaling Technologies          |
| GAS6             | A-9        | Santa Cruz Biotech                   |

| Secondary antibody | Clone | Company                              |
|--------------------|-------|--------------------------------------|
| Rabbit IgG-HRP     | 7074  | Cell Signaling Technologies          |
| Mouse IgG-HRP      | 7076  | Cell Signaling Technologies          |
| Goat IgG-HRP       | sc-2020 | Santa Cruz Biotech                |

| Immunoprecipitation | Clone | Company                              |
|---------------------|-------|--------------------------------------|
| AXL                 | C44G1 | Cell Signaling Technologies          |
| RNA polymerase II   | N-20, sc-899 | Santa Cruz Biotech          |
| STAT5               | C-17, sc-835 | Santa Cruz Biotech            |
| Rabbit IgG          | sc-2027 | Santa Cruz Biotech                |
| Goat IgG            | 0109-01 | Southern Biotech                   |

Table S5. Primer sequences for qPCR

|          | Forward Primer sequences | Reverse Primer sequences |
|----------|--------------------------|--------------------------|
| CHIP     | AXL-P1       | CCTAGTCTCCCTCA6GCTTGG   | GCCCTCCTTCTCACTACCC |
|          | AXL-P2       | GGGCAGATTTCAAGGGTTCTCA | TGTTTCCAGCAGAGTTCCTCA |
| Other    | AXL          | TTCAACTCCTCGCTTCTCGT   | AAGGTGGAGTTTCTCCCCAGT |
|          | GUS          | GTTTACCAGGATCCACCTC   | CTCGTCGGTGACTGAGGCTAGT |
Supplementary Methods

Animal models for *in vivo* studies

NOD Cg-Prkdcsid Il2rg<sup>(tm1Wjl)/SzJ</sup> immunodeficient mice (NSG) were bred at the University of Bordeaux’s animal facility for experiments validated by the French ministry (N°00048.2 authorization). Animals were included in protocols at eight weeks old and were monitored weekly for body weight. For subcutaneous xenografts, prior to implantation, cells were resuspended in 25% Matrigel (BD Biosciences) and 75% culture medium without FCS. Female NSG mice received injections into their hind flanks with 1.75x10<sup>6</sup> cells. Tumor growth was measured three times a week. When tumors reached 400-500mm<sup>3</sup>, treatments began. At the indicated times, the mice were euthanized by cervical dislocation and tumors weighed. For hematopoietic engraftment, female NSG mice were conditioned with intraperitoneal injections of busulfan (Fabre) 20 mg/kg/day for two days, and then injected intravenously with 10<sup>6</sup> shCtrl (MV4-11 shCtrl) or shAXL (MV4-11 shAXL) luciferase-transduced cells (10<sup>6</sup> cells/100μL) at day 0. At day 7, engraftment was analyzed by whole bioluminescent imaging (BLI) before treating mice with vehicle or AC220 (5 mg/kg/day body weight) by daily oral gavage until the times indicated. At day 14, mice were injected intraperitoneally with firefly luciferase substrate D-luciferin (150 mg/kg) before imaging using a photon bioimager and M3Vision software (BIOSPACE LAB). Bones, spleen and liver were collected at sacrifice and analyzed by BLI *ex vivo* or fixed in 10% formalin and processed for hematoxylin, eosin and immunohistochemical labeling.
Immunoblotting, immunoprecipitation, chromatin immunoprecipitation assay, ELISA and quantitative PCR

The antibodies are listed in Supplemental Table S4. Total cell lysates were prepared by incubating cells for 30min at 4°C in a lysis buffer (50 mM Tris-HCl pH 7.4, 150 mM NaCl, 1 mM EDTA, 1% NP-40, 0.25% sodium deoxycholate, 10% Glycerol) supplemented with a protease inhibitor cocktail (Roche), sodium orthovanadate (1 mM) and NaF (10 mM) phosphatase inhibitors. Immunoprecipitations (IP) were performed with 500 µg proteins and 5µg of antibody or 20-50 µg of whole cell lysates were loaded onto SDS-PAGE gels and transferred onto nitrocellulose or PVDF membranes (Amersham-Biosciences). Detection was performed using ECL (Amersham-Biosciences). Images were captured using a CCD camera, Fuji-LAS4000 (Fujifilm). ELISA experiments were performed according to manufacturer’s instructions for mouse GAS6 (Duoset®, R&D system) and human GAS6 (Duoset®, R&D system). For chromatin immunoprecipitation (IP) assays, cells were processed as previously described (Supplementary reference 1). Briefly, cells (5×10^6) were stimulated for 30min with or without TPO (20 nM), washed and cross-linked with 1% formaldehyde (10^6 cells/ml) at room temperature for 5 min before adding glycine (0.125 M). IP of cell lysates were performed overnight with the indicated antibodies before adding salmon-sperm DNA pre-saturated protein G-dynabeads (Invitrogen) for 1h at 4°C. Immunoprecipitates were eluted with 1% SDS in 0.1 M NaHCO3. Formaldehyde cross-linking was reversed by heating for 1 at 45°C with proteinase K (40 µg/ml). DNA was extracted and analyzed by real-time quantitative PCR experiments. Two independent pairs of primers that encompassed the conserved STAT-responsive element (SRE) TTCN3GAA of human AXL intron 16 were used (Supplemental Table SS). All PCR assays were performed in triplicate, and the average value obtained for each sample was normalized to the amount of AXL chromatin DNA added to the IP reaction ("input DNA"). 1:10 of beads/immunoprecipitated complexes were removed to conduct an immunoblotting analysis. For AXL mRNA quantification, complementary DNA (cDNAs) were
synthesized from 1 μg of RNA, using the First Strand cDNA synthesis kit (Roche®, Meylan, France) according to manufacturer’s instructions. The real time quantitative PCR (qRT-PCR) was performed using Brilliant SYBR® Green QPCR kit as previously described with primers in Supplemental Table S5 (13).
**Figure S1A. Stromal cells protect FLT3-ITD AML cells from apoptosis upon AC220 treatment**

MOLM-13 or MOLM-14 FLT3-ITD AML cells were cultured for 48 hours in the absence (Vehicle) or presence of AC220 (3 nM) and in the absence (None) or presence of stromal cell lines (OP9 or MS5), as indicated. Apoptosis was assessed by Annexin V/DAPI labeling and flow cytometry analysis. Data are expressed as mean ± SEM, n ≥ 3; *, p < 0.05; **, p < 0.01; ***, p < 0.001; NS, non-significant.
Figure S1B. Human stromal cells protect FLT3-ITD AML cells from apoptosis upon AC220 treatment

MOLM-13 or MOLM-14 FLT3-ITD AML cells were cultured for 48 hours in the absence (Vehicle) or presence of AC220 (3 nM) and in the absence (No stroma) or presence of HS27a stromal cell lines, as indicated. Apoptosis was assessed by Annexin V/DAPI labeling and flow cytometry analysis. Data are expressed as mean ± SEM, n ≥ 3; *, p < 0.05; **, p < 0.01; ***, p < 0.001; NS, non-significant.
Figure S1C. Stromal cells protect FLT3-ITD AML cells from apoptosis upon AC220 treatment

MV4-11 or MOLM-14 FLT3-ITD AML cells were cultured for 48 hours in the absence (Vehicle) or presence of AC220 (10 and 20 nM) and in the absence (None) or presence of stromal cell lines (OP9, MS5 or HS27a), as indicated. Apoptosis was assessed by Annexin V/DAPI labeling and flow cytometry.
analysis. Data are expressed as mean ± SEM, n ≥ 3; *, p < 0.05; **, p < 0.01; ***, p < 0.001; NS, non-significant.

**Figure S1D. Stromal cells protection is not correlated to AC220 degradation**

Stromal cells (OP9, MS5 and HS27) were incubated with the indicated concentrations of AC220 for 48 h. Then, MV4-11 or Molm14 were incubated either with the culture media from these stromal cells as indicated, or with fresh medium (no stroma) supplemented with the indicated concentrations of AC220. After 48h, MV4-11 and Molm14 were labeled with annexin V and the
percent of annexin V positive cells was quantified by flow cytometry. Results are from one experiment representative of 3

| MOLM-  | Non  | MS5  |
|--------|------|------|
|        | Vehcl| AC22 |
|        | Vehcl| AC22 |

**Figure S1E. Stromal cells protection of MOLM-14 against AC220 correlates with enhanced STAT5 activation**

MOLM-14 cells were incubated in the absence (Vehicle) or presence of AC220 (1 nM), without (none) or with MS5 stromal cells (Stroma) for 48 hrs. Immunoblot analysis of the indicated protein, each of protein-dedicated immunoblot without (none) or with stroma (MS5) have been performed on the same membrane. Results shown are representative of 4 experiments.
**Figure S1F. Stromal cells protection of MV4-11 and MOLM-14 cells against AC220 correlates with enhanced STAT5 activation**

MV4-11 and MOLM-14 cells were incubated in the absence or in the presence of AC220 (10 or 20 nM), without (none) or with MS5 or HS27 stromal cells for 48 hrs. Immunoblot analysis of the indicated protein, each of protein-dedicated immunoblot has been performed on the same membrane. Results shown are representative of 3 experiments.
Figure S2A. Knock down of STAT5 inhibits AXL expression in human HSPCs

CD34+ CB cells were transduced without (Untransduced) or with control luciferase (shCtrl) or STAT5 (shSTAT5) shRNA encoding lentiviral vectors and were collected 5 days later. (A) RT-qPCR analysis of AXL mRNA in the indicated cells. Results are normalized to GAPDH expression and expressed relative to untransduced cells (n=3). (B) Immunoblot analysis of the indicated proteins in the indicated cells. β-actin is used as a loading control. Data are expressed as mean ± SEM, n ≥ 3; *, p < 0.05; **, p < 0.01; ***, p < 0.001; NS, non-significant.
Figure S2B. Both STAT5A and STAT5B regulate AXL expression of myeloid cells.

UT7 AML cells were first transduced with inducible HA-tagged murine STAT5A (5A) or Flag-tagged murine STAT5B (5B) encoding vectors and cultured in absence of inducer for a few days before transducing them with or without shSTAT5A-encoding vector. Cells were then cultured in absence (-) or presence of increasing concentration (++) of doxycycline to induce transgene (tg) expression and incubated for 8hrs before cell lysis. Expression of the indicated proteins was analyzed by immunoblotting. GAPDH served as a loading control; mol.wt (kDa) of appropriate markers is indicated on the left. Arrow points at slower migrating HA-tagged pYSTAT5A transgene compared to whole endogenous pYSTAT5, as revealed by anti-pY694STAT5A/pY699STAT5B antibodies (pYSTAT5).
Figure S2C. Inhibition of STAT5 prevent stroma-induced AXL expression and activation (pTyr\textsubscript{779} phosphorylation)

MV4-11 and MOLM-14 cells were incubated without (−) or with HS27 stromal cells (+) in the absence or in the presence of AC-4-130 1 or 5 µM for 48 hrs. Immunoblot analysis of the indicated protein, each of protein-dedicated immunoblot has been performed on the same membrane. Results shown are representative of 2 experiments.
Figure S2D. AXL activity contributes to FLT3-ITD AML cell survival

FLT3-ITD AML cell lines MV4-11, MOLM-13 and MOLM-14 were treated in the absence or presence of AC220 (top panel) or R428 (bottom panel) at increasing doses for 48 hours. Apoptosis was then assessed by Annexin V/DAPI labeling and flow cytometry analysis. Data are expressed as mean ± SEM, n ≥ 3; *, p < 0.05; **, p < 0.01; ***, p < 0.001; NS, non-significant.
Figure S2E. Species-specific ELISA assay of GAS6

Human MV4-11 AML cells and murine OP9 and MS5 stromal cells were cultured for 24h. GAS6 was quantified in the supernatant by ELISA upon 24h of culture.
Figure S2F. Transduction of stromal cells with GAS6 shRNA-encoding lentiviral vectors inhibits GAS6 expression

Human stromal OP9 cells were either untransduced (UT) or transduced with GAS6 (shGAS6-1, shGAS6-2) or scramble (shCtrl) shRNA encoding lentiviral vector and collected 14 days later. Protein expression was assessed by immunoblot analysis. β-actin serves as a loading control.
**Figure S3.** STAT5 activation enhances AXL expression through STAT5 binding to AXL gene sequence

(A) Human cord blood (CB) CD34⁺ cells were incubated in absence of the four-exogenous cytokines/growth factors cocktail for 18h before being incubated for 8 hr in the absence (-) or presence of TPO (20 nM), IL-3 (50 ng/ml) or FLT3 ligand (FLT3L, 100 ng/ml) and lysed. Immunoblot analysis of the indicated proteins; HSP60 serves as a loading control. (B) UT7-mpl cells were growth-factor deprived for 18h before being incubated in the absence (-) or presence of TPO (20 nM) for 1 hr (T₁h). Cells were lysed and oligonucleotide (ON) pulldown assays were performed with biotinylated-AXL (ONAXL) or -consensus (ONc) SRE from IRF1 promoter sequence. ON-bound and -unbound (flowthrough) proteins were analyzed by immunoblotting using the indicated antibodies. β actin is used as a loading control.
Figure S4. Low O$_2$ enhanced apoptotic response to AXL inhibition in presence of stroma

MV4-11 cells were incubated in the presence of R428 (1 µM) for 48 hrs, without (no stroma) or with MS5 (stroma) at 20% or 1% O$_2$. Apoptosis was assessed by Annexin V/DAPI labeling and flow cytometry analysis. Results are expressed as the ratio of the apoptotic response at 1% on the apoptotic response at 20%. Graphs show the mean ± SEM of results of at least three independent experiments with *, p < 0.05; **, p < 0.01; ***, p < 0.001; NS, non-significant.
Figure S5. Loss of AXL does not impair leukemia cell growth upon sub-cutaneous injection

(A) MV4-11 were transduced with shCtrl or shAXL encoding lentiviral vector. Cells were maintained in culture for 7 days before being sorted for GFP expression and lysed. Proteins were analyzed by immunoblotting with the indicated antibodies. β-actin serves as a loading control.

(B) Quantification of photon flux bioluminescent signals from the whole body of the indicated
mice (n=40) at day 7 post injection of luciferase-labelled MV4-11 shCtrl or MV4-11 shAXL cells.

Ph stands for photon, s for second and sr for steradian. *, p < 0.05; **, p < 0.01; ***, p < 0.001;
NS, non-significant. (C) Control (MV4-11 shCtrl) or shAXL expressing (MV4-11 shAXL) MV4-11
cells were subcutaneously injected into the limbs of NSG mice at day 0 and treated or not with
AC220 (5 mg/kg/day), as indicated. Tumor volume was measured at the indicated days (mean ±
SEM, n=20). (D) Weights of collected tumors from NSG mice injected subcutaneously with the
indicated shRNA transduced MV4-11 cells. Upon leukemia cell injection, tumors grew and when
tumor volume were about 400-500 mm³, half of mice were treated with AC220 (5 mg/kg/day)
for 14 days. Relapse tumors reappeared upon AC220 discontinuation. For primary tumors,
animals were maintained until ~2 cm³ tumor volume before necropsy (n=10). Relapse tumors
were collected at day 35 post AC220 withdrawal (n=10). Data reported are the mean ± SEM
(n=40); *, p < 0.05; **, p < 0.01; ***, p < 0.001; NS, non-significant.
1. Rouyez MC, Lestingi M, Charon M, Fichelson S, Buzyn A, Dusanter-Fourt I. IFN regulatory factor-2 cooperates with STAT1 to regulate transporter associated with antigen processing-1 promoter activity. J Immunol. 2005;3948-3958.