



# **Corrigendum: RUNX2 Phosphorylation by Tyrosine Kinase ABL Promotes Breast Cancer Invasion**

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#### A Corrigendum on

### RUNX2 Phosphorylation by Tyrosine Kinase ABL Promotes Breast Cancer Invasion

*By He F, Matsumoto Y, Asano Y, Yamamura Y, Katsuyama T, Rose JL, Tomonobu N, Komalasari NLGY, Sakaguchi M, Rottapel R and Wada J (2021). Front. Oncol. 11:665273. doi: 10.3389/fonc.2021.665273* 

In the original article, there was a mistake in **Figures 1A, B, D, F, 2D, 3B–D, F, 4D, S5A** as published. We noticed that several qPCR data were not correctly normalized since the calculation program of the  $\Delta$ Ct method did not work. The corrected **Figures 1A, B, D, F, 2D, 3B–D, F, 4D, S5A** and the equivalent raw data in **Figures S1–S4** and **S5A** appears below.

The authors apologize for these errors and state that this does not change the scientific conclusions of the article in any way. The original article has been updated.



**FIGURE 1** | ABL kinase activity is required for RUNX2-mediated MMP13 expression. (A) Quantitative PCR analysis of *MMP2, 9, and 13* mRNA expression in HEK293T cells transfected with RUNX2. n = 3. (B) Quantitative PCR analysis of *MMP13* mRNA expression in HEK293T cells co-transfected with RUNX2 with or without TAZ or ABL (PP). n = 3. (C) HEK293T cells were co-transfected with RUNX2 with or without TAZ or ABL (PP). N = 3. (C) HEK293T cells were co-transfected with RUNX2 with or without TAZ or ABL (PP). Whole cell lysates were probed with the indicated antibodies for Western blot analysis. (D) Quantitative PCR analysis of *MMP13* mRNA expression in HEK293T cells co-transfected with RUNX2 with or without ABL (WT, PP or KD). n = 3. (E) HEK293T cells were co-transfected with RUNX2 with or without ABL (WT, PP or KD). n = 3. (E) HEK293T cells were co-transfected with RUNX2 with or without ABL (WT, PP or KD). n = 3. (F) Quantitative PCR analysis of *MMP13* mRNA expression in HEK293T cells co-transfected with RUNX2 with or without ABL (WT, PP or KD). n = 3. (F) Quantitative PCR analysis of *MMP13* mRNA expression in HEK293T cells co-transfected with RUNX2 with or without ABL (PP) and cultured in the presence or absence of 10  $\mu$ M imatinib for 24 hours. n = 3. P values were determined by the unpaired t-test (A) or ANOVA with Tukey–Kramer's *post hoc* test (B–F). Data are presented as means ± SEM. \*P < 0.05.



**FIGURE 2** | ABL binds to, phosphorylates, and activates RUNX2 through its SH2 domain. (A-C) HEK2931 cells were co-transfected with wild-type (W1) or all tyrosine to phenylalanine mutant (YF) RUNX2 with or without ABL (PP). RUNX2 immune complexes were probed with an anti-phosphotyrosine (4G10), anti-pY245ABL, anti-ABL or anti-RUNX2 antibody. Whole cell lysates (WCL) were probed with the indicated antibodies for Western blot analysis. (**D**) Quantitative PCR analysis of *MMP13* mRNA expression in HEK293T cells co-transfected with RUNX2 (WT or YF) with or without ABL (PP). n = 3. (**E**) HEK293T cells were co-transfected with RUNX2 with or without GFP-ABL (SH2). GFP-ABL (SH2) immune complexes were probed with an anti-RUNX2 or anti-GFP antibody. P values were determined by ANOVA with Tukey–Kramer's *post hoc* test. Data are presented as means  $\pm$  SEM. \*P < 0.05.



FIGURE 3 | RUNX2 transcriptional activity is dependent on the number of its tyrosine residues phosphorylated by ABL. (A) Schematic models of RUNX2 (W1) and RUNX2 (YF). (**B–D, F**) Quantitative PCR analysis of *MMP13* mRNA expression in HEK293T cells co-transfected with the indicated constructs. n = 3. (**E**) HEK293T cells were co-transfected with the indicated constructs and RUNX2 immune complexes were probed with an anti-4G10 or anti-RUNX2 antibody. P values were determined by ANOVA with Tukey–Kramer's *post hoc* test. Data are presented as means  $\pm$  SEM. \*P < 0.05. ns, no significance.



**FIGURE 4** | ABL regulates RUNX2 expression through control of the BMP-SMAD pathway. (**A**, **B**) Saos-2 cells were infected with an empty vector control or an FKBP-ABL- or FKBP-expressing retroviral vector. Whole cell lysates were probed with the indicated antibodies for Western blot analysis. (**C**) Saos-2 cells were infected with an empty vector control or an FKBP-ABL-expressing retroviral vector in the presence of shGFP or sh*BMPR1A*. Whole cell lysates were probed with the indicated antibodies for Western blot analysis. (**D**) Quantitative PCR analysis of *MMP13* mRNA expression in cells in (**C**). n = 3. (**E**) MDA-MB231 cells were infected with an shGFP-, sh*ABL*- or sh*RUNX2*-expressing vector. Whole cell lysates were probed with the indicated antibodies for Western blot analysis. P values were determined by ANOVA with Tukey–Kramer's *post hoc* test. Data are presented as means  $\pm$  SEM. \*P < 0.05.

# SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2021.729192/full#supplementary-material

Supplementary Figure 1 | ABL kinase activity is required for RUNX2-mediated MMP13 expression. (A–D) Independent raw data of the panels shown in Figures 1A (A), 1B (B), 1D (C) and 1F (D).

Supplementary Figure 2 | ABL binds to, phosphorylates, and activates RUNX2 through its SH2 domain. (A) Independent raw data of the panel shown in Figure 2D.

Supplementary Figure 3 | RUNX2 transcriptional activity is dependent on the number of its tyrosine residues phosphorylated by ABL. (A–D) Independent raw data of the panels shown in Figures 3B (A), 3C (B), 3D (C) and 3F (D).

Supplementary Figure 4 | ABL regulates RUNX2 expression through control of the BMP-SMAD pathway. (A) Independent raw data of the panel shown in Figure 4D.

Supplementary Figure 5 | ABL-mediated RUNX2 expression and phosphorylation regulate breast cancer invasion. (A) Quantitative PCR analysis of *MMP13* mRNA expression in MDA-MB231 cells infected with an shGFP-, sh*ABL*- or sh*RUNX2*-expressing vector and the independent raw data. n = 3. (B) MDA-MB231 cells infected with an shGFP-, sh*ABL*- or sh*RUNX2*-expressing vector were subjected to a Matrigel invasion assay, and invading cells in five independent regions were counted. Representative photographs were taken at 10 × magnification. (C) MDA-MB231 cells stably expressing luciferase were infected with an shGFP- or sh*ABL*-expressing vector and injected into the lateral tail veins of BALB/c-nu/nu female mice as described in the methods section. After 4 weeks, the presence of metastases was detected by IVIS, and regions of interest from displayed images were identified and quantified as total photon counts or photons/ s. n = 6-7. (D) A representative image of H&E staining of the lungs from mice in (C). P values were determined by the unpaired t-test (C) or ANOVA with Tukey–Kramer's post hoc test (A, B). Data are presented as means ± SEM. \*P < 0.05.

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