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**Supplementary Data**

**FOLR1-induced folate deficiency reduces viral replication via modulating APOBEC3 family expression**

**Jing Wua, Yajing Hane, Ruining Lyua, Fang Zhangb, Na Jianga, Hongji Taoa, Qiao Youa, Rui Zhanga, Meng Yuana, Waqas Nawazf, Deyan Chena,\*, Zhiwei Wua, c, d,\***

*a Center for Public Health Research, Medical School of Nanjing University, Nanjing, 210093, China.*

*b Department of Burn and Plastic Surgery, Affiliated Hospital of Zunyi Medical University, Zunyi, 563099, China.*

*c Medical School and Jiangsu Key Laboratory of Molecular Medicine, Nanjing University, Nanjing, 210093, China.*

*d State Key Lab of Analytical Chemistry for Life Science, Nanjing University, Nanjing, 210093, China.*

*e Environmental Protection Key Laboratory of Environmental Pollution Health Risk Assessment, South China Institute of Environmental Sciences, Ministry of Ecology and Environment, Guangzhou, 510535, China.*

*f Hȏpital Maisonneuve-Rosemont, School of medicine, University of Montreal, Quebec, 999040, Canada.*

Corresponding authors.

E-mail: wzhw@nju.edu.cn (Z.W.), chendeyan@nju.edu.cn (D.C.)

ORCID: 0000-0002-0672-948X (Z.W.), 0000-0001-7351-4617 (D.C.)



Figure S1. Bap inhibits the replication of VSV *in vitro* and *in vivo*. **A** HeLa cells were stimulated with Bap at 5 μmol/L and 10 μmol/L from 1 d to 3 d, and cell viability was detected by CCK-8. **B** HeLa cells were pre-exposed to Bap at 10 μmol/L for 2 days, and then they were infected with VSV (MOI = 1) in the presence of Bap for 24 h. The expression of virus-related protein and mRNA were detected by Western blot and qPCR, respectively. **C** An inverted fluorescence microscope was used to observe the effect of different concentrations of Bap on the expression of VSV-GFP, scale bar: 100 μm. **D** VSV-G mRNA levels in C57BL/6J mice lung tissues were detected by qPCR. GAPDH was shown as a loading control. Data expressed as Means ± SD (n=3, “ns” means no significant differences, \*\**P*<0.01, \*\*\**P*<0.001).



Figure S2. **A** Volcano map showed DEGs between Bap group and mock group. Red represents up-regulated genes and blue represents down-regulated genes. **B** Heat map of DEGs associated with RNA viral replication in RNA-seq results. **C** HeLa cell was transfected with siNC or siAPOBEC3A-H for 36 h. qPCR was performed to detect the mRNA expression of APOBEC3s. **D** HeLa cell was stimulated with MTX for 24 h at different concentrations, and cell viability was detected by CCK-8. **E** HeLa cells were pretreated with MTX at 1 μmol/L for 2 h, and then they were infected with VSV (MOI=1), RSV (MOI=1), EV71 (MOI=1), CA16 (MOI=1), and SFTSV (TCID50=1) for 24 h, respectively. The expression of virus-related mRNAs was measured by qPCR analysis. Data expressed as Means ± SD (n= 3, “ns” means no significant differences, \**P*<0.05, \*\**P*<0.01, \*\*\**P*<0.001).



Figure S3. IFN-β and AhR were not involved in Bap-mediated inhibition of VSV replication. **A–C** HeLa cells were pre-exposed with Bap for 2 days, then they were infected with VSV and RSV or stimulated with poly (I:C) (2 μg/mL) in the presence of Bap for 24 h, and then ELISA and qPCR were performed to measure IFN-β expression. The pink lines and Y axis in the right side showed the expression of IFN-β protein levels in the supernatant, green chart and Y axis in the left side represented the copies of IFN-β mRNA levels in A and C. **D–F** HeLa cells were pre-exposed to Bap, FICZ (AhR’s natural agonist, 50 nmol/L) or SR1 (AhR's antagonist, 50 nmol/L) for 2 d, and then they were infected with VSV (MOI = 1) in presence of Bap, FICZ or SR1 for another 24 h. The expression of VSV-G mRNA was detected by qPCR analysis. The expression of VSV-G and GAPDH were measured by Western blot analysis. Data expressed as means ± SD (n = 3, \*\**P*<0.01, \*\*\**P*<0.001).

Supplementary Table S1 siRNA sequences of APOBEC3 protein family used in the study.

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| Name | Target sequence |
| siAPOBEC3A | GCTT TCTA CACA ACCA GGCT A |
| siAPOBEC3B | CCAG GTGT ATTT CAAG CCTC A |
| siAPOBEC3C | CGCT GTGG AGAT CATG GACT A |
| siAPOBEC3D | TTTG AGAA CCAC GCAG AAAT |
| siAPOBEC3F | CGCG TGAA GATT ATGG ACGA T |
| siAPOBEC3G | GCCA GGTG TATT CCGA ACTT A |
| siAPOBEC3H | GCCA TGCA GAAA TTTG CTTT A |

Supplementary Table S2 Primer sequences used for qPCR detection in this study.

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| Primer name | Forward and Reverse | (5’-3’) |
| VSV-G | Forward | ACGGCGTACTTCCAGATGG |
| Reverse | CTCGGTTCAAGATCCAGGT |
| VSV viral RNA | Forward | ACGAAGACAAACAAACCA  |
| Reverse | GTTTCTCCTGAGCCTTTTA |
| RSV-G | Forward | AGGATTGTTTATGAATGCCTATGG |
| Reverse | GCTTTTGGGTTGTTCAATATATGGTAG |
| EV71 and CA16  | Forward | TCCGGCCCCTGAATGCGGCTAATCC |
| Reverse | ACACGGACACCCAAAGTAGTCGGTC |
| SFTSV | Forward | GGGTCCCTGAAGGAGTTGTAAA |
| Reverse | TGCCTTCACCAAGACTATCAATGT |
| FOLR1 (Human) | Forward | CCACTTCATCCAGGACACCTGT |
| Reverse | CATCCAGGAAGCGTTCTTTGCG |
| FOLR1 (Mouse) | Forward | GGACTGAACTTCTCAATGTCTGC |
| Reverse | CTTCCTGGCTTGTGTTCGTGGA |
| APOBEC3A (Human) | Forward | GACAATGGCACCTCGGTCAAGA |
| Reverse | CCAACTGCAAAGAAGGAACCAGG |
| APOBEC3B (Human) | Forward | CCTCTATGGTCGGAGCTACACT  |
| Reverse | GAGGAAGCACATTTCTGCGTGG |
| APOBEC3C (Human) | Forward | CGGAACGAAACTTGGCTGTGCT |
| Reverse | CCAAGAGAGGAAGCACCTTTCTG |
| APOBEC3D (Human) | Forward | ACGTCAGTCGAATCACAGGCAG |
| Reverse | CAAACCAGGTGATCTGGAAGCG |
| APOBEC3F (Human) | Forward | GGAATACCGTCTGGCTGTGCTA |
| Reverse | GAGGAAGCACATTTCTGCGTGG |
| APOBEC3G (Human) | Forward | ATGACACCTGGGTCCTGCTGAA |
| Reverse | GAATCACGTCCAGGAAGCACAG |
| APOBEC3H (Human) | Forward | GCCTGTACTACCACTGGTGCAA |
| Reverse | CGGTTTCTCGTGGTCCACAAAG |
| APOBEC3 (Mouse) | Forward | GACAATGGTGGCAGGCGATTCA |
| Reverse | GCAGAGATGCTTGACTCGTTGG |
| GAPDH (Human) | Forward | GTCTCCTCTGACTTCAACAGCG |
| Reverse | ACCACCCTGTTGCTGTAGCCAA |
| GAPDH (Mouse) | Forward | CATCACTGCCACCCAGAAGACTG |
| Reverse | ATGCCAGTGAGCTTCCCGTTCAG |