Cite this as: Yuliang GUO, Siyu SONG, Xiaoxiao DU, Li TIAN, Man ZHANG, Hongmin ZHOU, Zhonghua Klaus CHEN, Sheng CHANG. Romidepsin (FK228) improves the survival of allogeneic skin grafts through downregulating the production of donor-specific antibody via suppressing the IRE1α-XBP1 pathway[J]. Journal of Zhejiang University Science B, 2022, 23(5): 392-406.
http://doi.org/10.1631/jzus.B2100780

Romidepsin (FK228) improves the survival of allogeneic skin grafts through downregulating the production of donor-specific antibody via suppressing the IRE1α-XBP1 pathway

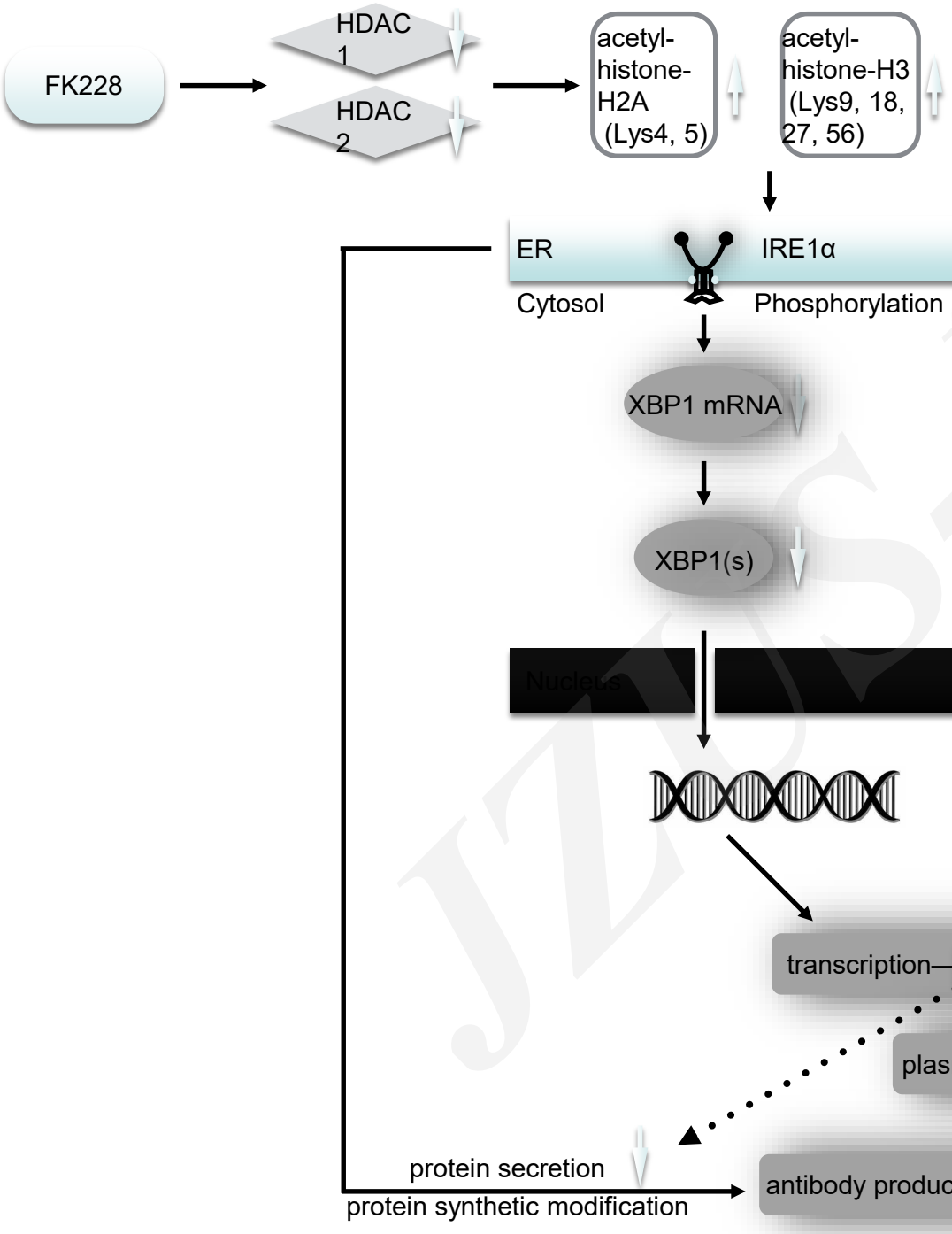
Key words: Histone acetylation; FK228; Romidepsin; Skin transplantation; Donor-specific antibody; Unfolded protein

Research Summary

This study aimed to evaluate the effects of FK228 on antibody production by using cultured B cells in vitro and DSA in vivo. In addition, to investigate the mechanism of FK228 in antibody production, we investigated the effect of acetylated histones on the pathway of IRE1α/XBP1.

- **Regulation of gene transcription**
- **Cell growth and differentiation**
- **The survival of allogeneic skin grafts**
- **The IRE1α/XBP1 signaling pathways**

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Innovation points

- **Introduction** of FK228 significantly improved the survival of allogeneic skin grafts

- **Summary** of the effect of the IRE1α/XBP1 signaling pathways in the production of antibody

- **Emphasis** of the newly identified interplay among HDACI family members in various of transplantation

ER-UPR pathway

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Innovation points

A series of comprehensive figures were generated that FK228 is considered as a promising therapeutic agent for the clinical treatment of AMR.

Figure 1 | FK228 reduced the DSA levels in mice with allogeneic skin grafts and improved the survival of skin grafts

Figure 2 | Effects of FK228 on the differentiation of Tfh and plasma cells

Figure 3 | FK228 suppresses IRE1α-XBP1 pathway activity in the ER UPR and class switch recombination in vivo

Figure 4 | FK228 upregulates the acetylation levels of histone H2A and H3 by inhibiting the expression of HDAC1 and 2 in the spleens of skin-transplanted mice

Figure 5 | FK228 promotes apoptosis and suppresses the proliferation of B cells in vitro

Figure 6 | FK228 inhibits plasma cell differentiation and reduces IgG and IgM levels in vitro

Figure 7 | FK228 inhibits AID and the IRE1α-XBP1 pathway in the ER UPR in vitro

Figure 8 | FK228 promotes histone acetylation by suppressing HDAC1 and HDAC2 activity in B cells in vitro

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