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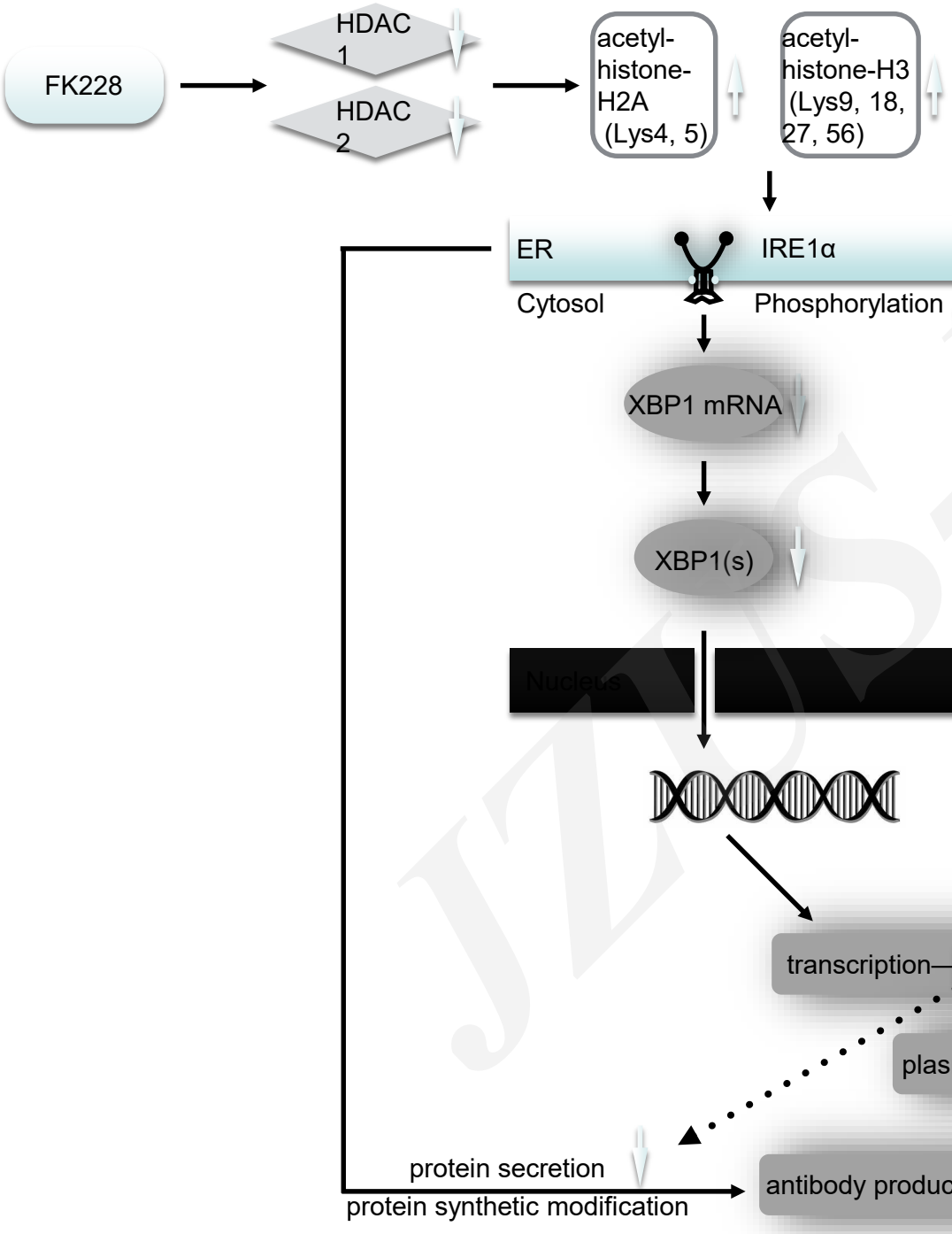
Romidepsin (FK228) improves the survival of allogeneic skin grafts through downregulating the production of donor-specific antibody via suppressing the IRE1α-XBP1 pathway

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**



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

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