Hyperoside alleviates endometrial stromal cell senescence in unexplained recurrent spontaneous abortion via DHX9-mediated R-loop resolution

Yuepeng Jiang[1, 2#], Hongli Zhao[1#], Xinyi Ding[2#], Haoling Zhang[3#], Yadong Guo[4#], Yiming Ma[5], Lingyi Cai[6], Qingnan Fan[6], Ruisi Peng[6], Fuyuan Yang[6], Doblin Sandai[3], Xianling Cao[7], Jiali Yao8, Wenyi Wang[9], Zhiheng Lin[10*], Wangzheqi Zhang[11*], Jialin He[1*], Aihua Zhang[12*], Xiaoxuan Zhao[1*]

[1] Department of Traditional Chinese Medicine (TCM) Gynecology, Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medical University, Hangzhou 310007, China.
[2]College of Basic Medical Sciences, Zhejiang Chinese Medical University, Hangzhou 310053, China.
[3] Department of Biomedical Sciences, Pusat Kanser Tun Abdullah Ahmad Badawi, University Sains Malaysia, Kepala Batas Pulau Pinang 13200, Malaysia.
[4] Shanghai Tenth People's Hospital, Tongji University. 301 Yanchang Road, Jing'an District, Shanghai 200040, China.
[5] Faculty of Chinese Medicine, Macau University of Science and Technology, Macau 999078, China.
[6] The Third Clinical Medical College, Zhejiang Chinese Medical University, Hangzhou 310053, China.
[7] Harvard University Joslin diabetes center, Department of Medicine Harvard Medical School (HMS), Boston 02215, USA.
[8]Clinical Cancer Institute, Center for Translational Medicine, Naval Medical University, Shanghai 200433, China.
[9] Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan.
[10] Department of Gynecology, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200032, China.
[11] Naval Medical University, Shanghai 200433, China.
[12] Hainan Medical University, Haikou 571199, China.

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Overview

CLINICAL CONTEXT

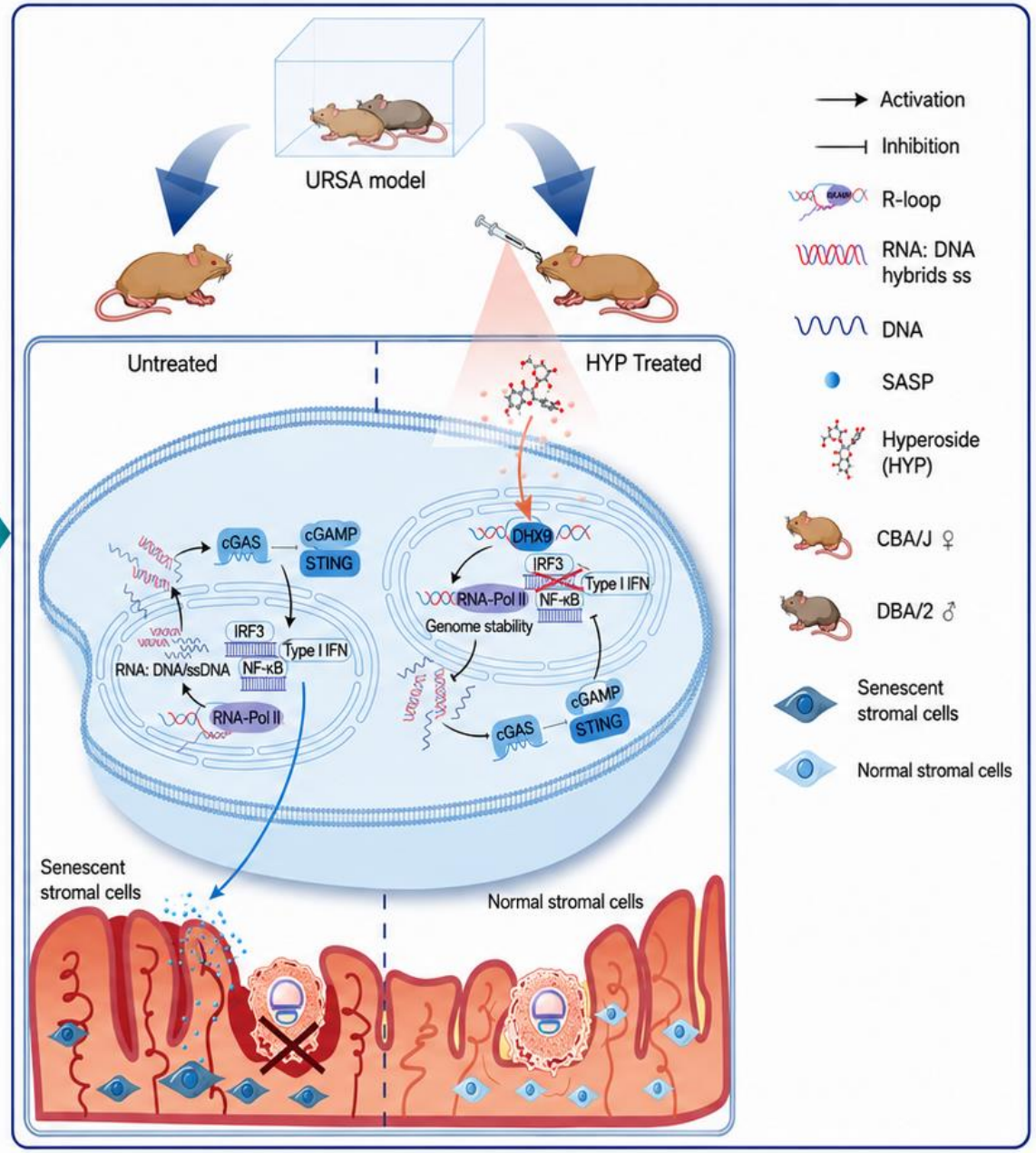
1. URSA
2. Decidualization deficiency

IDENTIFYING THE MOLECULAR DEFECT

3. Stromal cell senescence
4. Unknown upstream mechanism?

MULTI-DIMENSIONAL RESEARCH DESIGN

1. Clinical URSA samples
2. URSA mouse model
3. T-HESC senescence model
4. Multi-omics + Lip-MS + molecular docking



HYP restores decidualization dysfunction in URSA mice

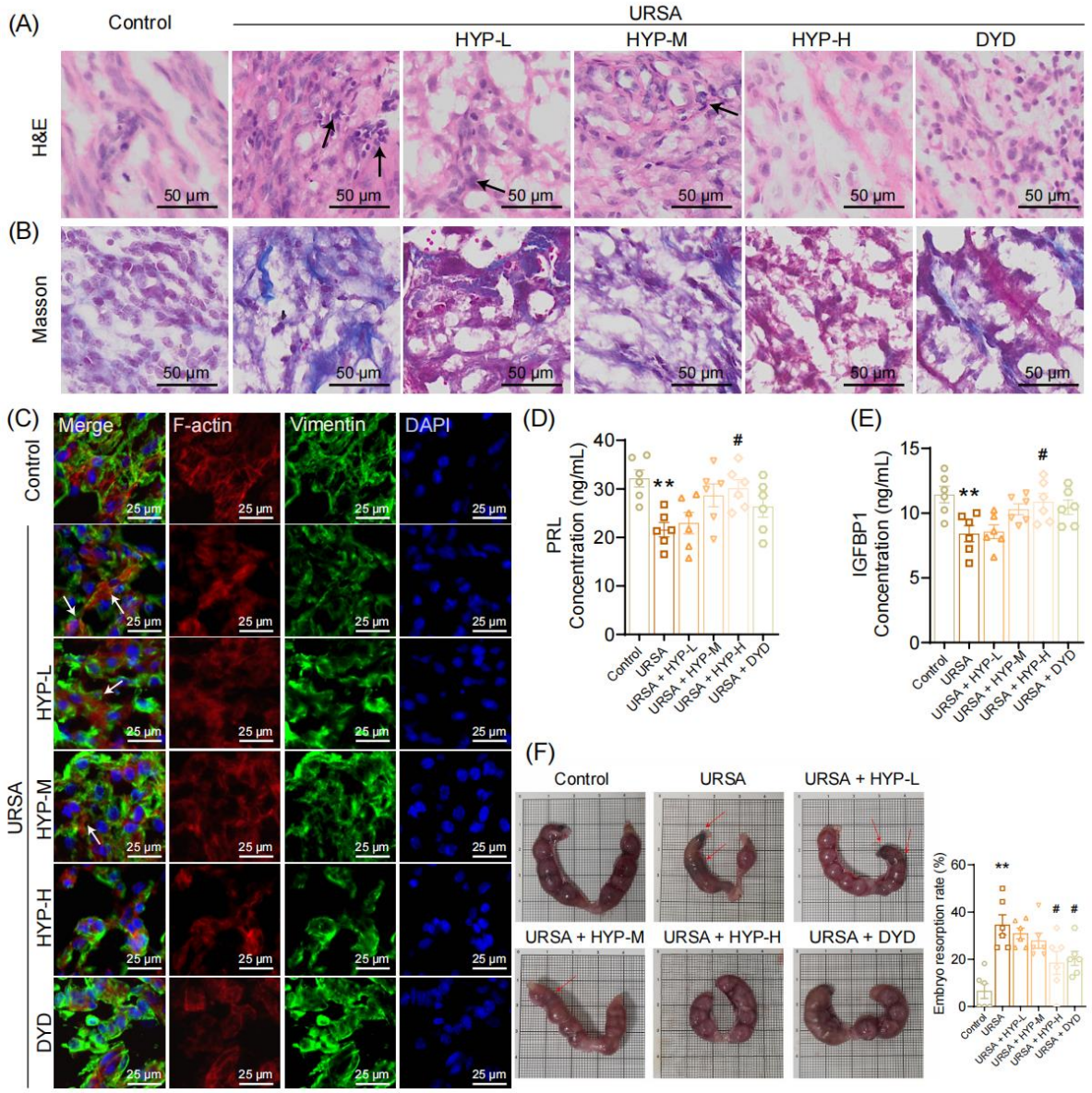


Figure 1. HYP alleviated decidualization dysfunction and decreased embryo resorption rate in URSA mice.

Hyperoside reduces stromal cell senescence in URSA

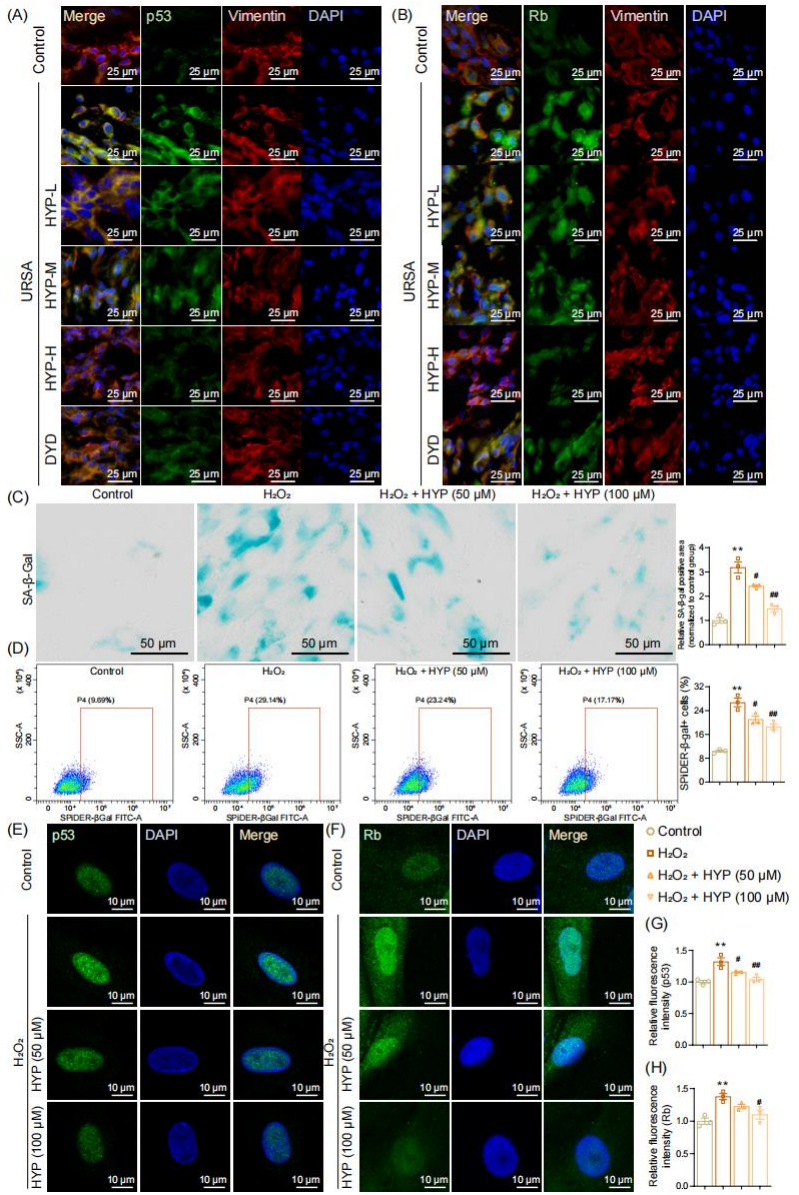


Figure 2. Hyperoside ameliorated stromal cell senescence in URSA mice and T-hESCs.

HYP restores R-loop homeostasis in stromal cell

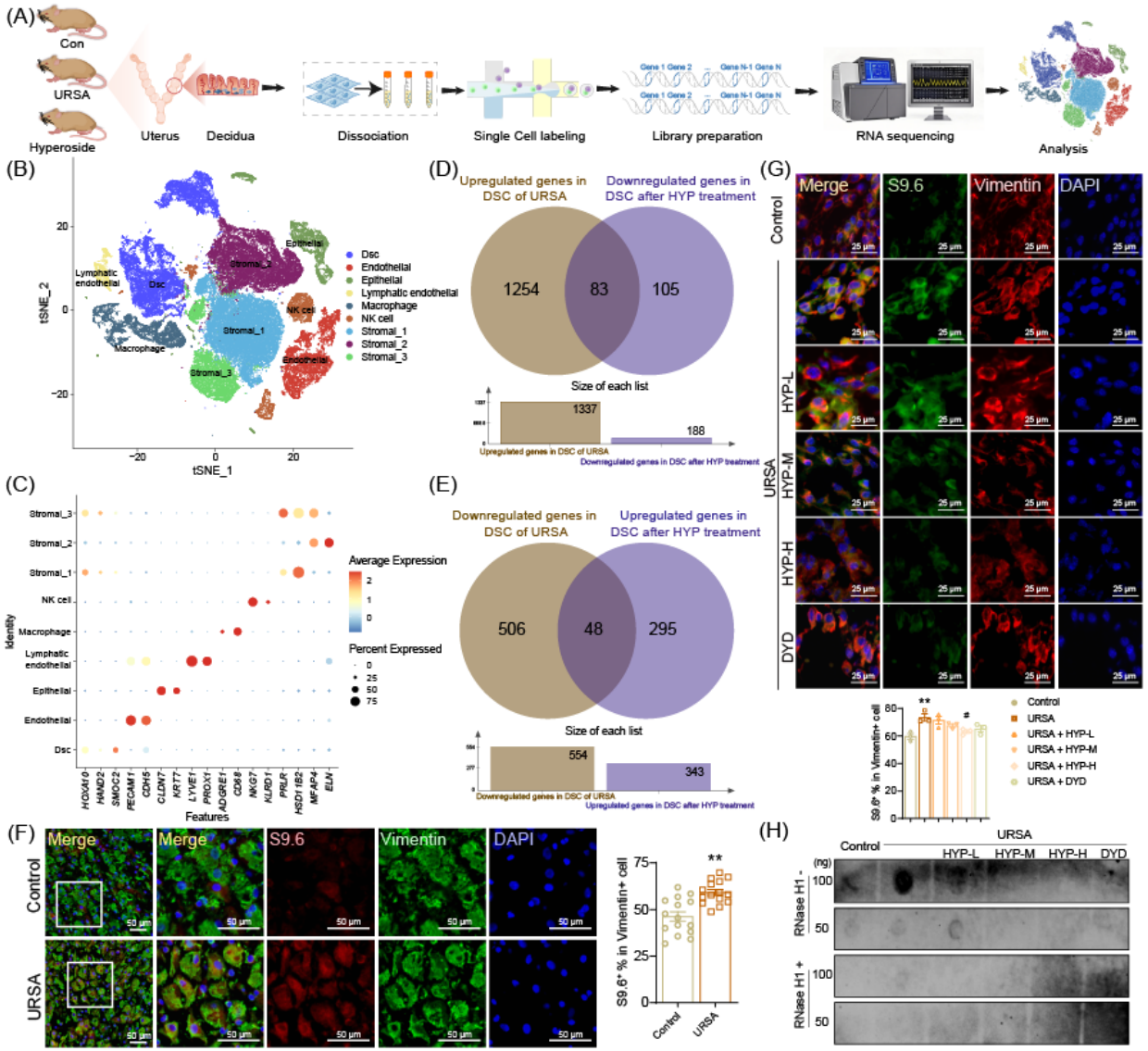


Figure 3. Hyperoside rescues stromal cell senescence in URSA by restoring R-loop homeostasis.

HYP anti-cell senescence via R-loop dysregulation

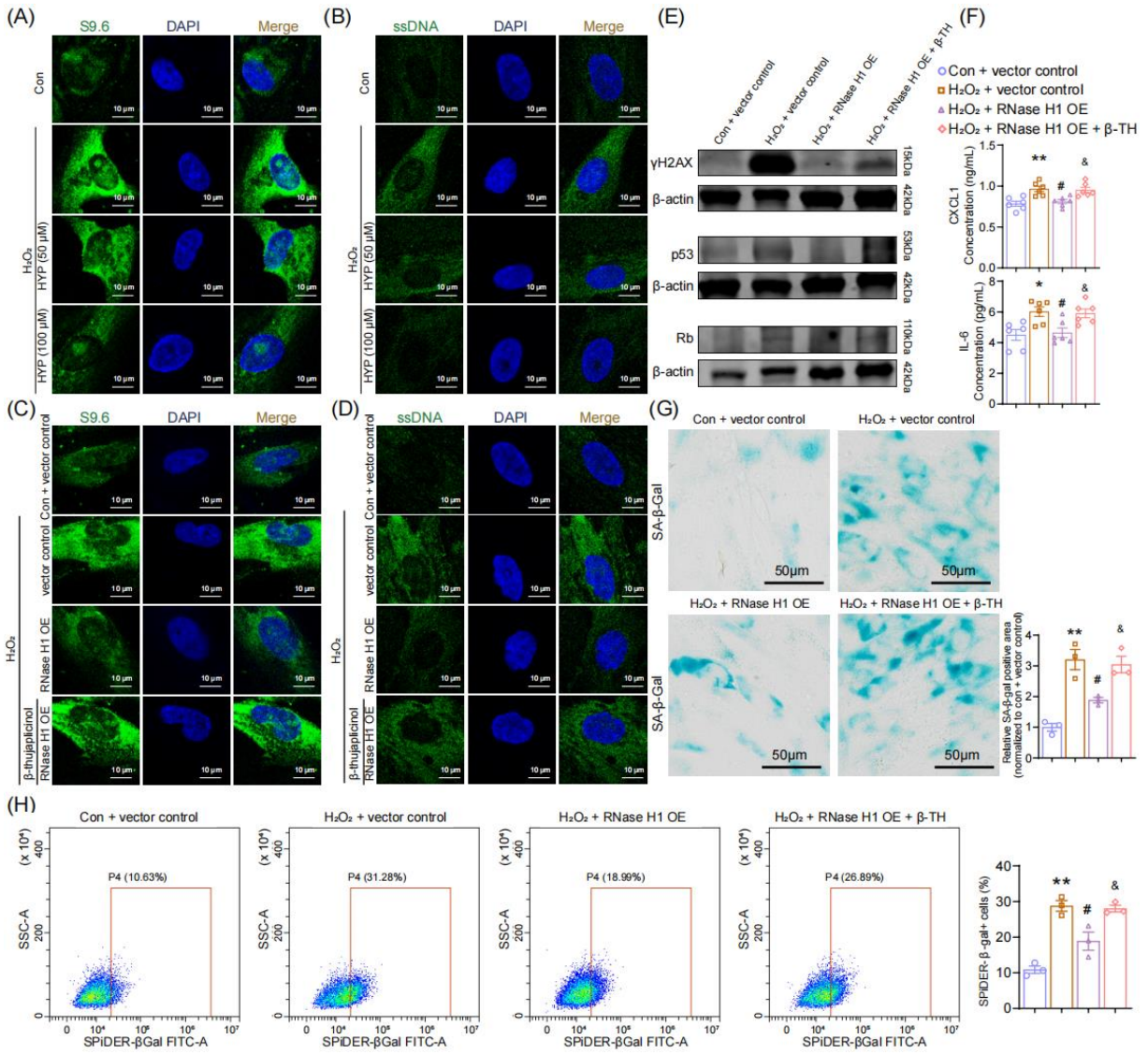


Figure 4. HYP anti-cell senescence via R-loop dysregulation.

HYP targets DHX9 to resolve R-loop accumulation

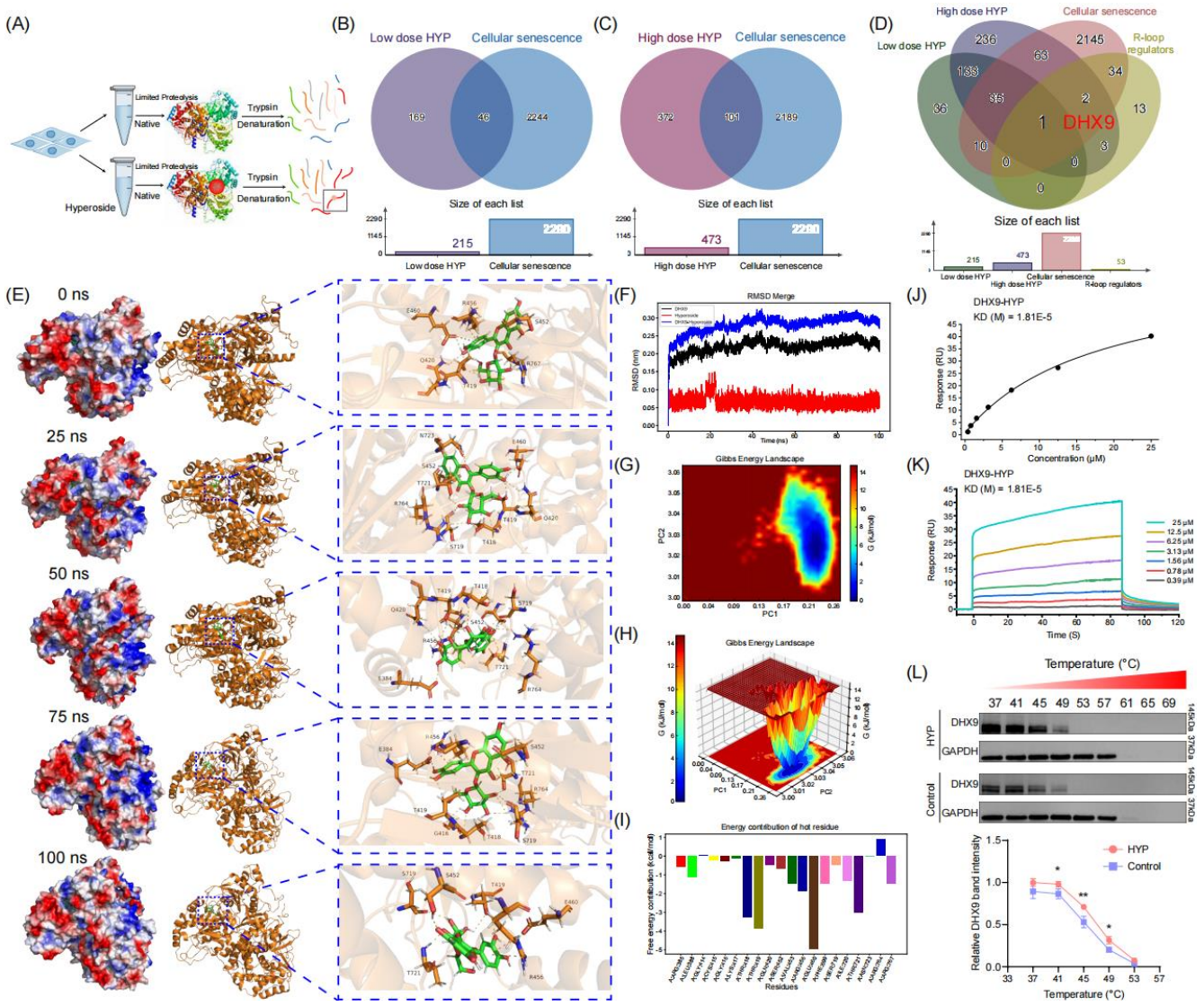


Figure 5. Hyperoside targets DHX9 to resolve R-loops and attenuate senescence in endometrial stromal cells via interaction at key residues.

HYP suppresses R-loop-cGAS-STING via targeting DHX9

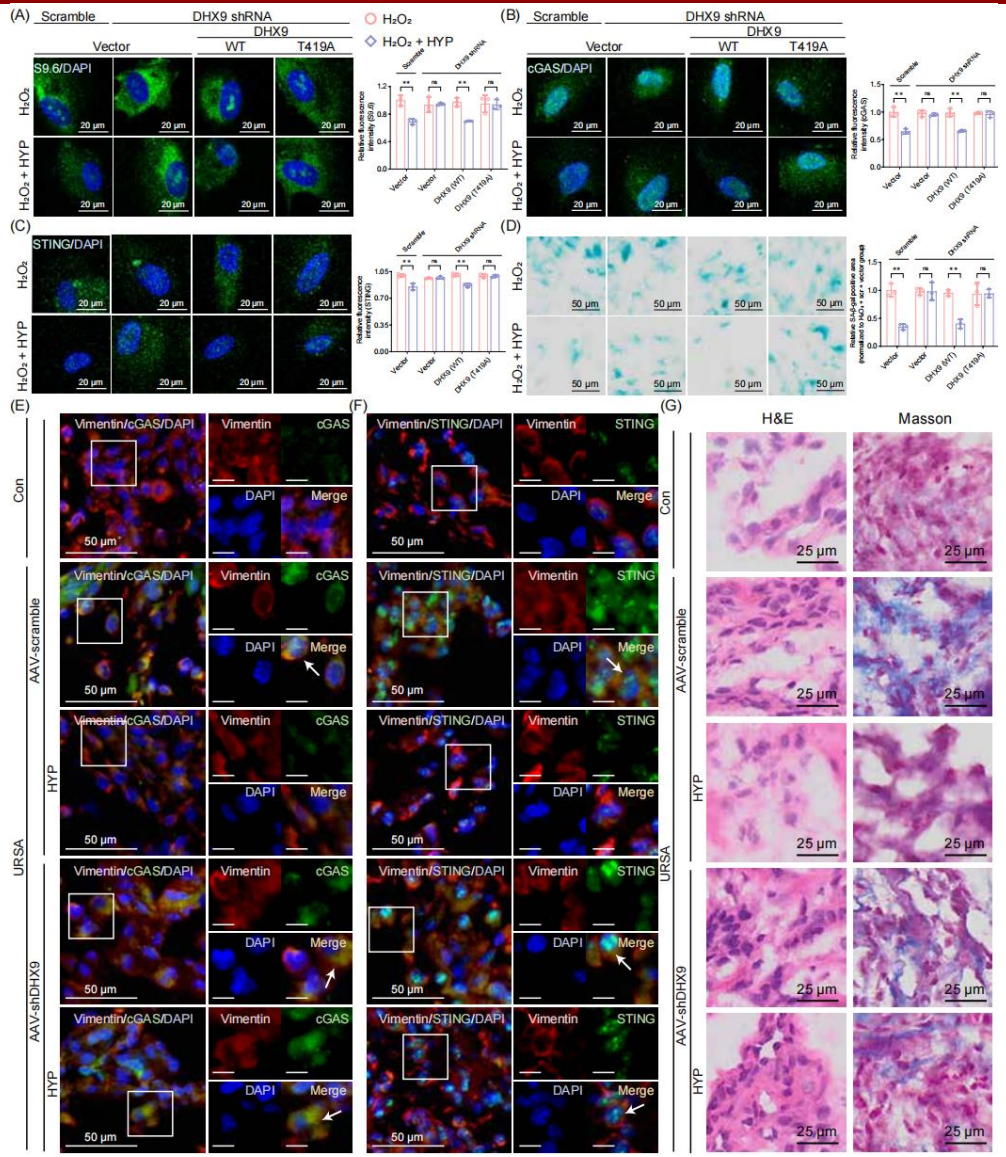


Figure 6. Hyperoside suppresses R-loop-driven cGAS-STING activation via functional modulation of DHX9 both in vitro and in vivo.

HYP targets a specific DHX9 residue to treat mice

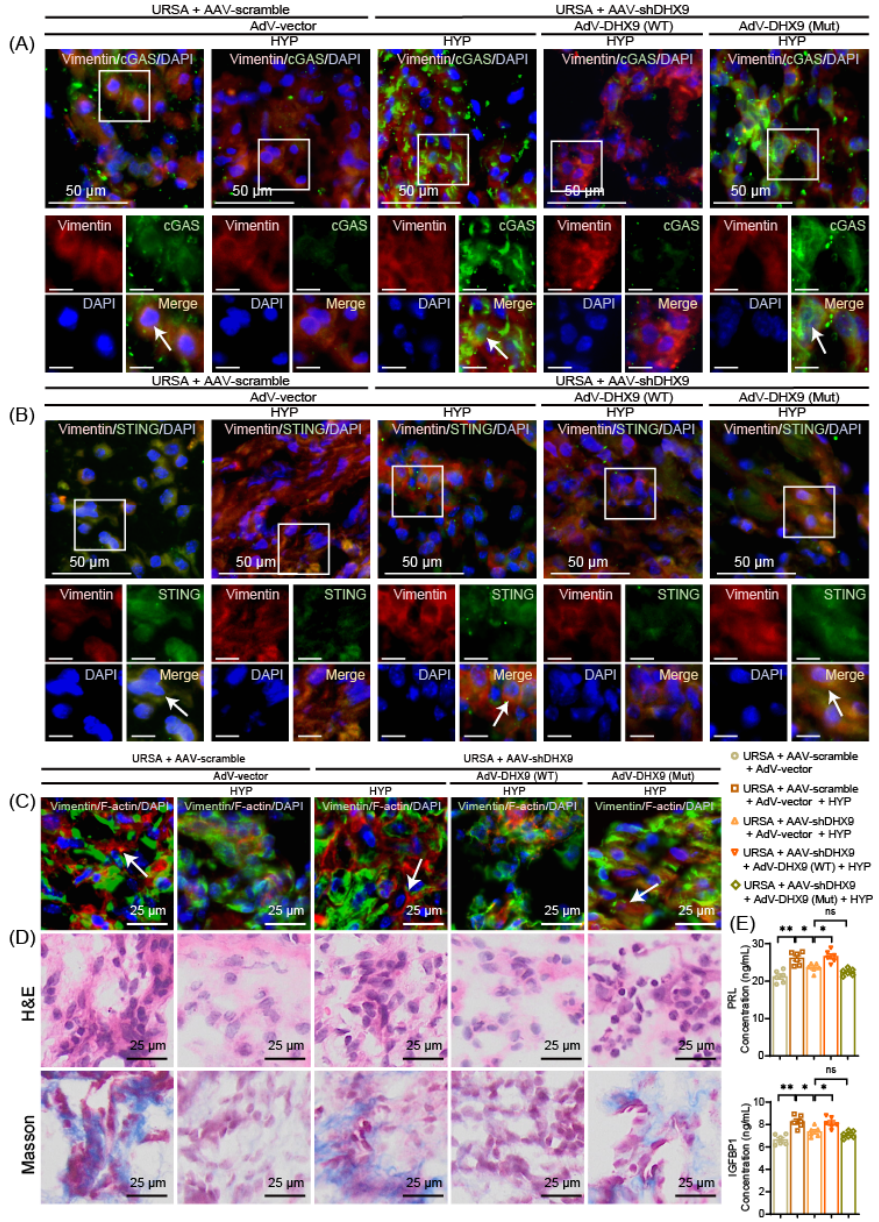


Figure 7. HYP targets a specific DHX9 residue in mice to exert therapeutic effects.

Summary

- In this study, we identified hyperoside as a natural DHX9 modulator.
- Hyperoside targets DHX9 to resolve pathological R-loop accumulation and suppress cGAS-STING-mediated stromal senescence.
- This work reveals R-loop-induced genomic stress as a key mechanism in URSA and proposes a mechanistically distinct therapeutic strategy.

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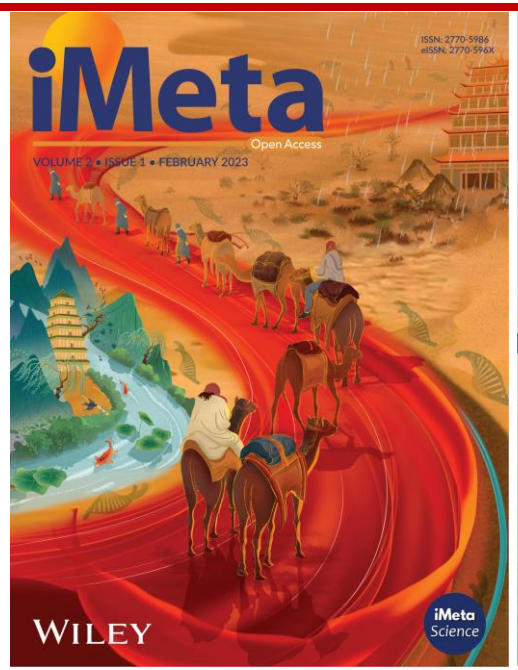

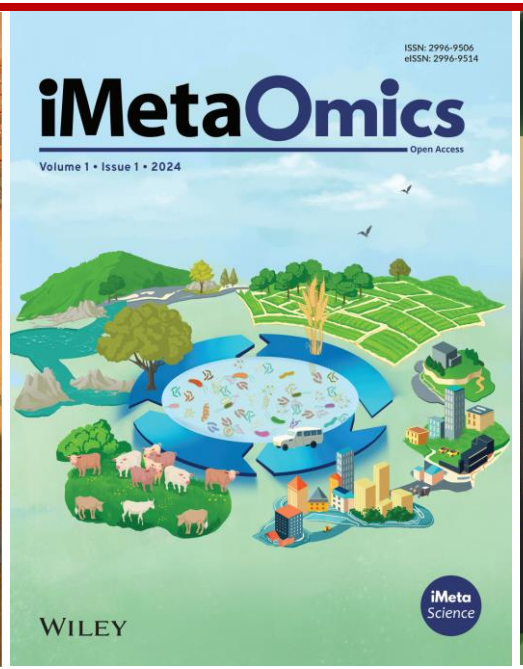

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