

High-throughput screening for host defense peptide-inducing compounds as alternatives to antibiotics

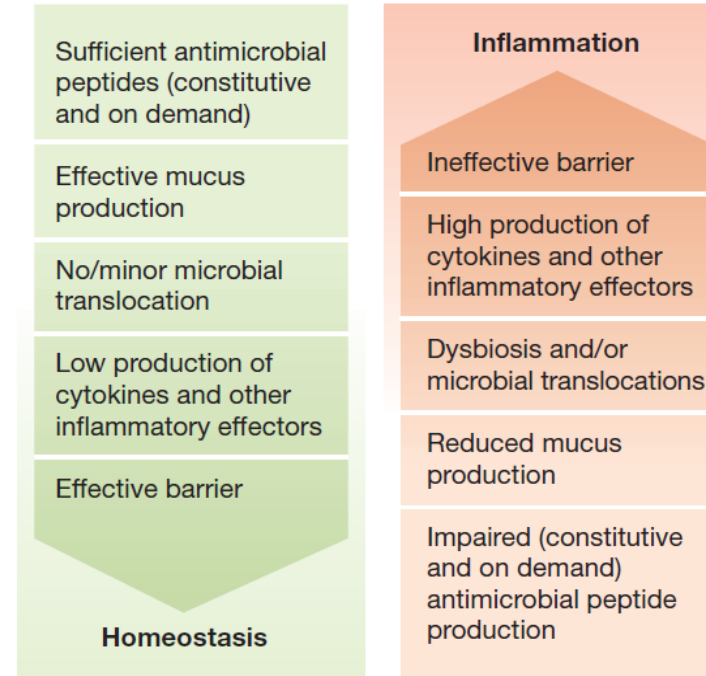
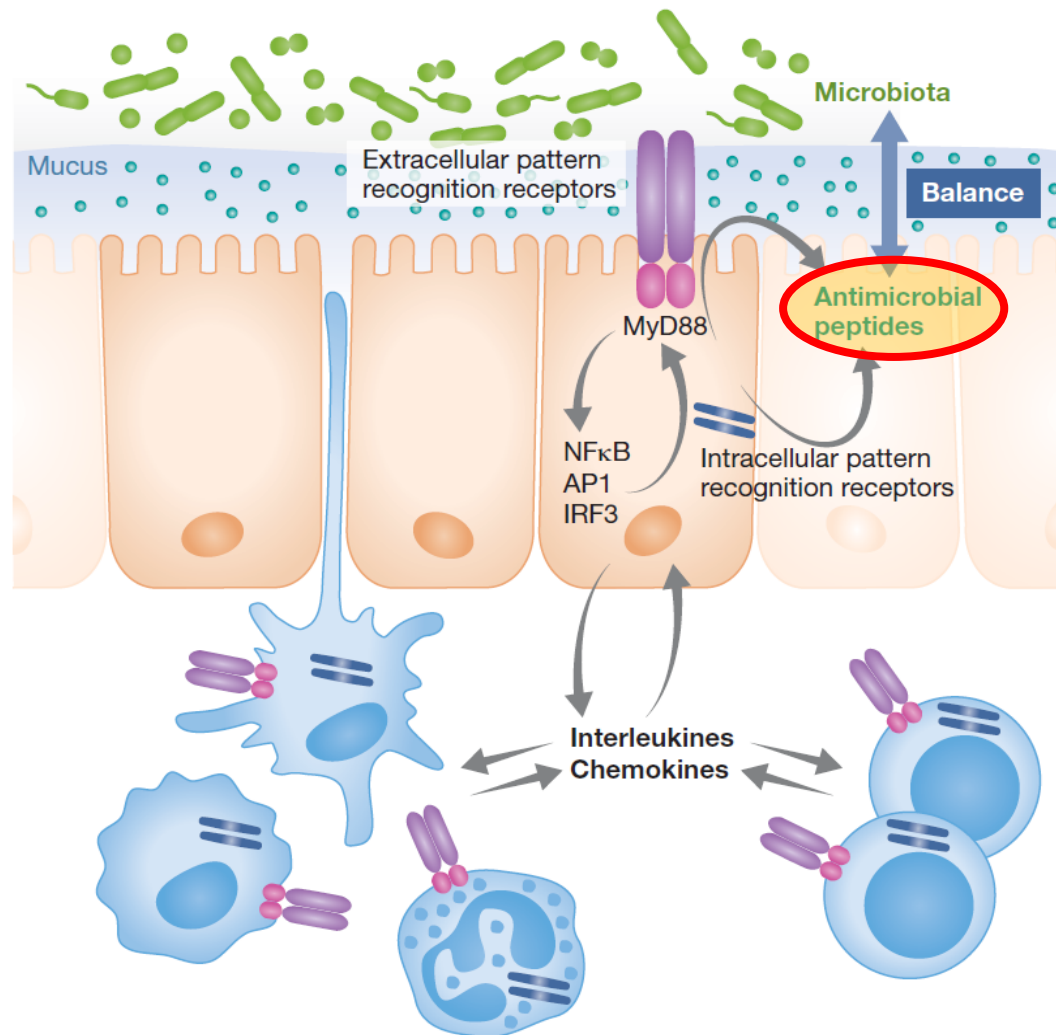
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DEPARTMENT OF
ANIMAL AND FOOD SCIENCES



Role of HDPs in Intestinal Epithelial Defense



EMBO Mol Med 2013, 5: 1465

Our Antibiotic-Alternative Strategy...

- **Approach:** Enhancing the synthesis of endogenous **host defense peptides (HDPs)** to boost animal immunity and disease resistance
- **Goal:** To develop **HDP-inducing compounds** as next-generation antibiotic alternatives



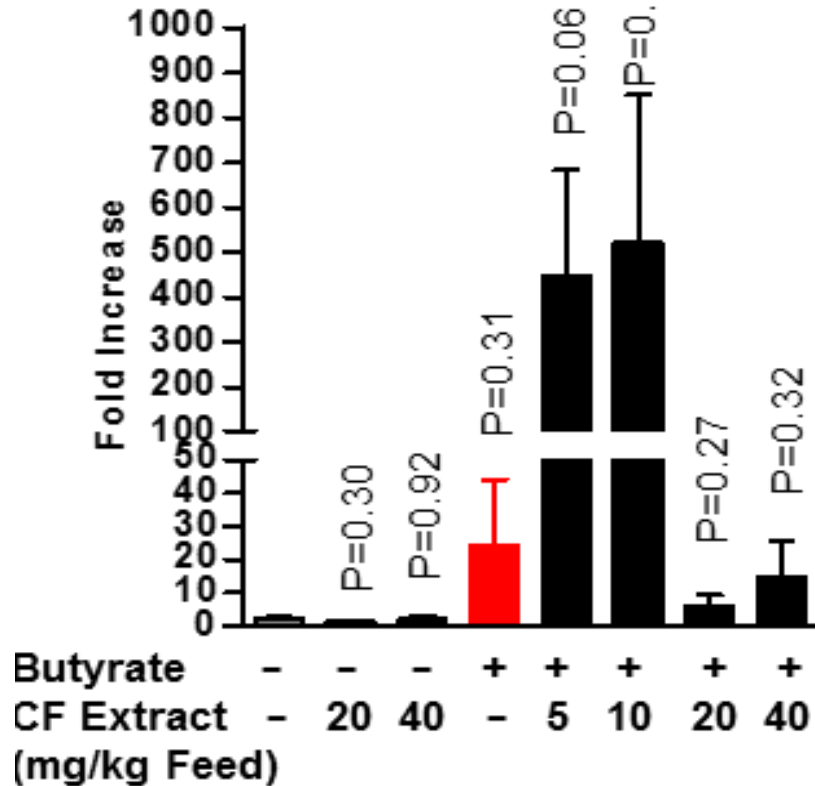
Dietary Modulation of Endogenous HDP Synthesis

- Butyrate enhances disease resistance of chickens by inducing HDP expression ([PLoS One 2011, 6: e27225](#))
- Modulation of HDP expression by SCFAs, MCFAs, and their analogs in chickens, pigs, and humans ([PLoS One 2012, 7: e49558](#); [PLoS One 2013, 8: e72922](#); [Peptides 2013, 50: 129-138](#))
- Synergistic induction of HDP expression and disease resistance by different combinations of dietary compounds ([Mol Immunol 2014, 57: 171-180](#); [Front Cell Infect Microbiol 2018; 8: 191](#))

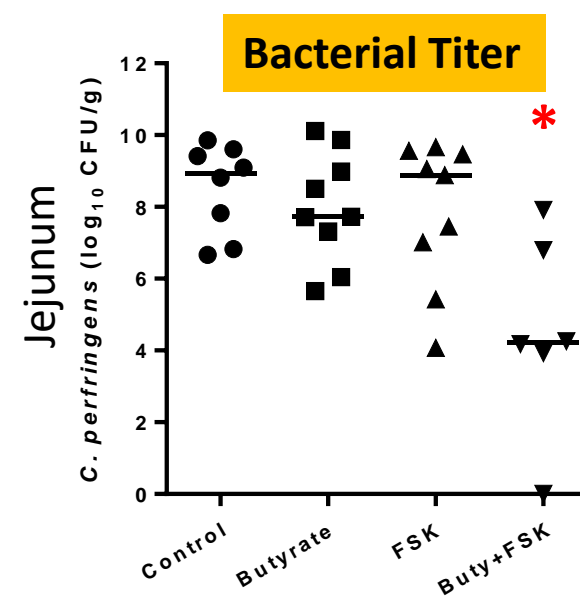
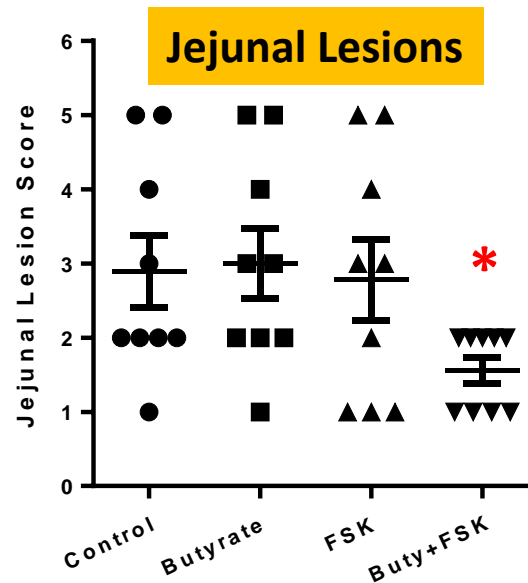
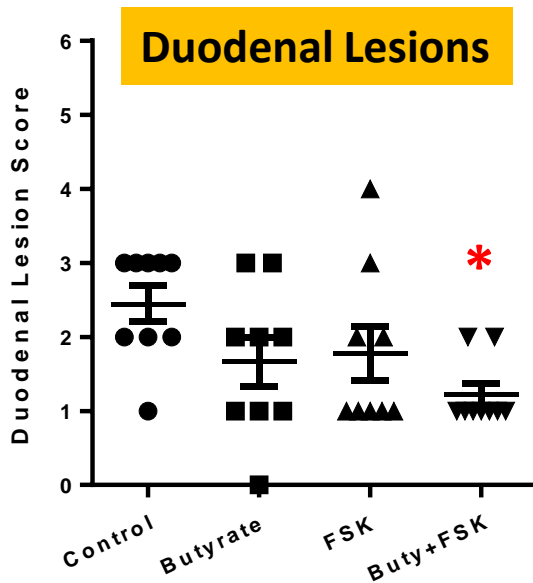
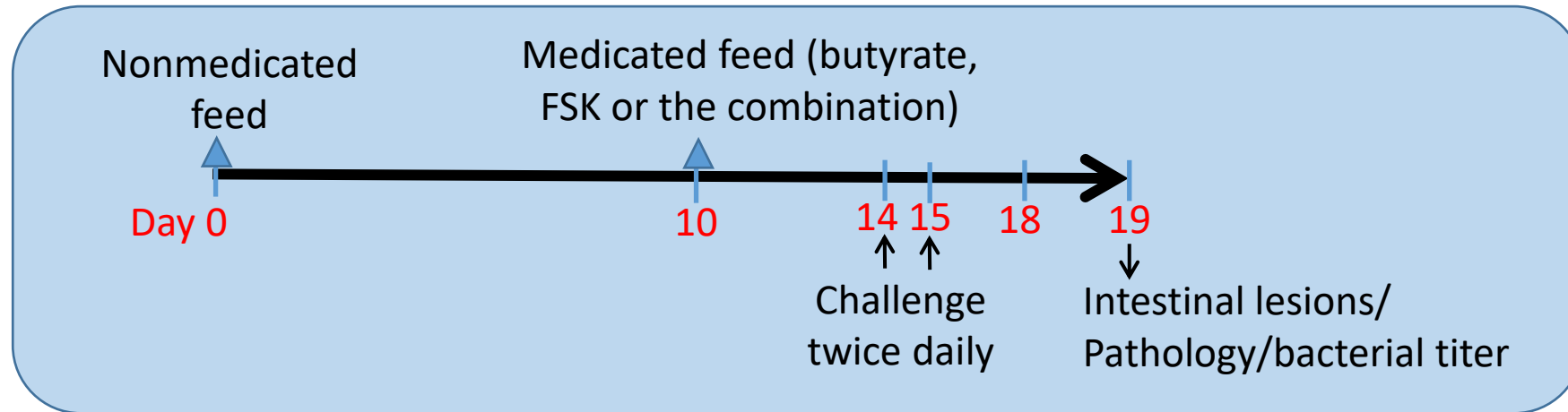


Synergistic HDP Induction without Triggering Inflammation by Butyrate and Forskolin

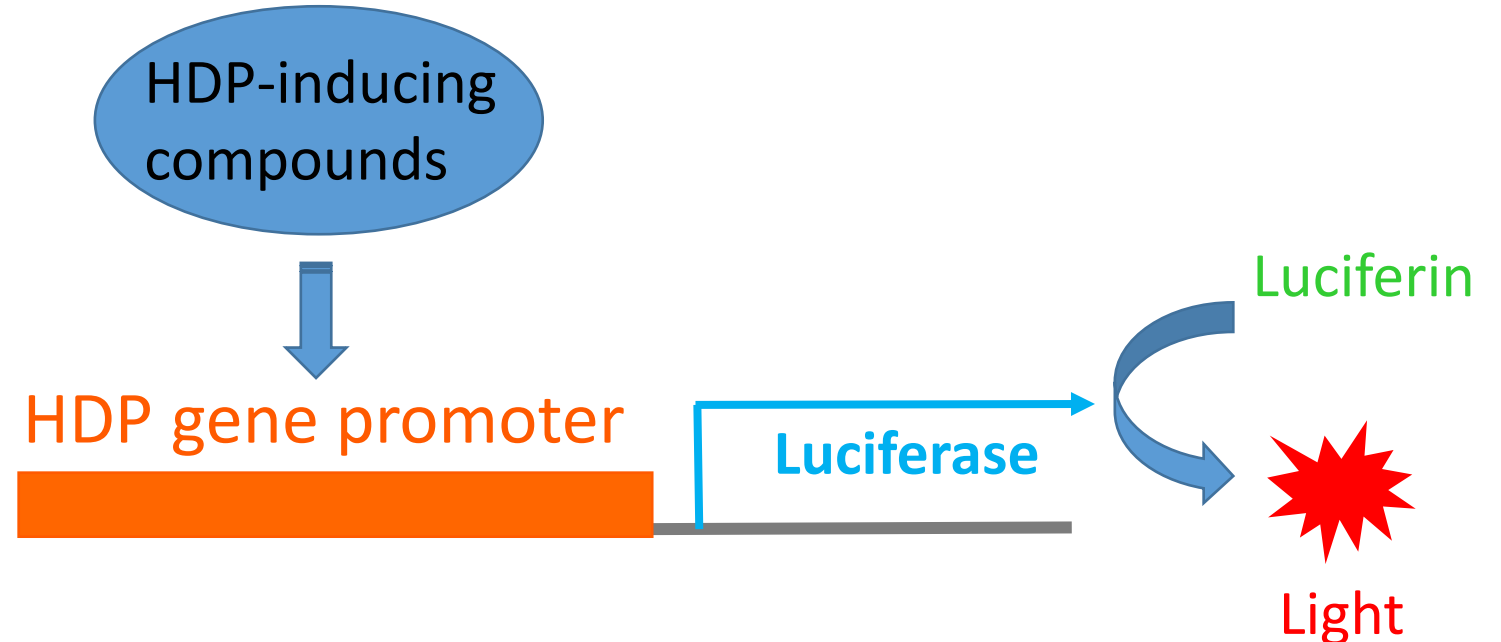
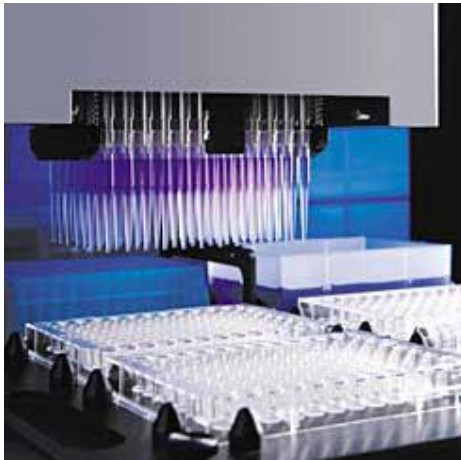
AvBD9/Jejunum



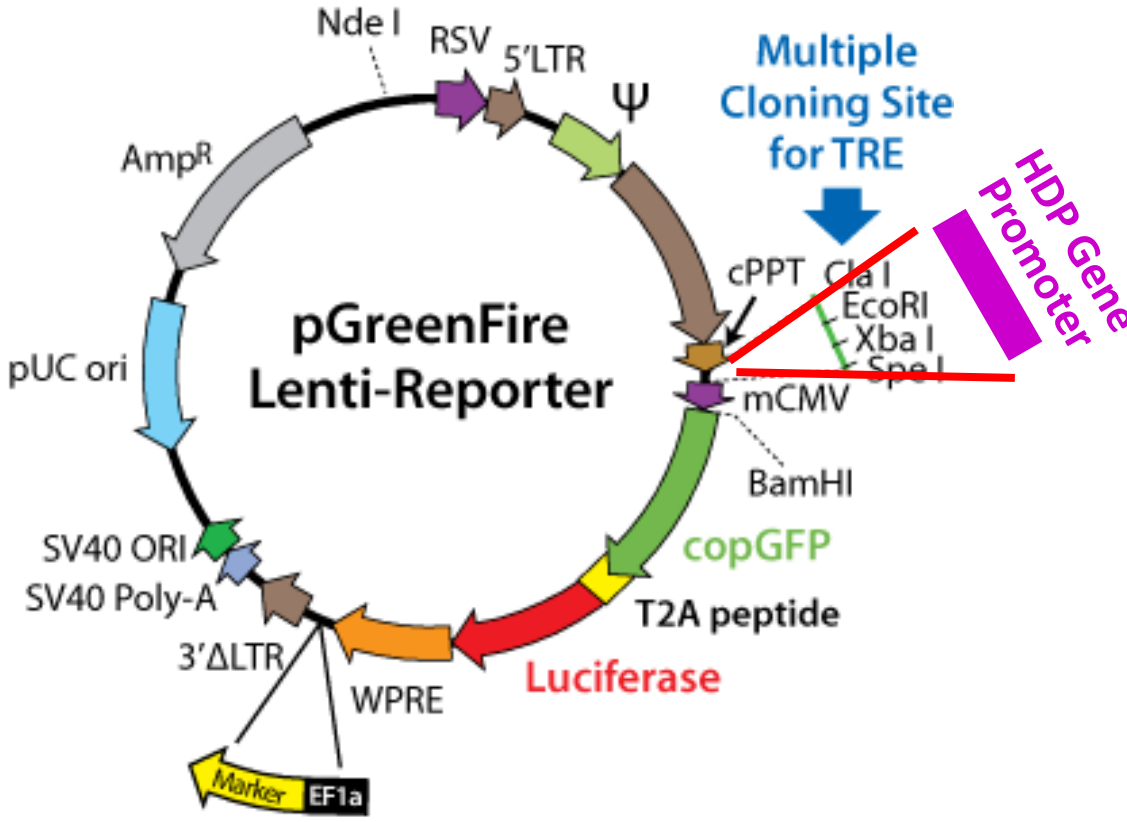
Synergistic Alleviation of Necrotic Enteritis by Butyrate and FSK



Development of stable HDP gene promoter-driven luciferase reporter cell lines for high throughput screening of HDP-Inducing Compounds



Development of an *AvBD9* Promoter-Driven Luciferase Reporter Cell Line

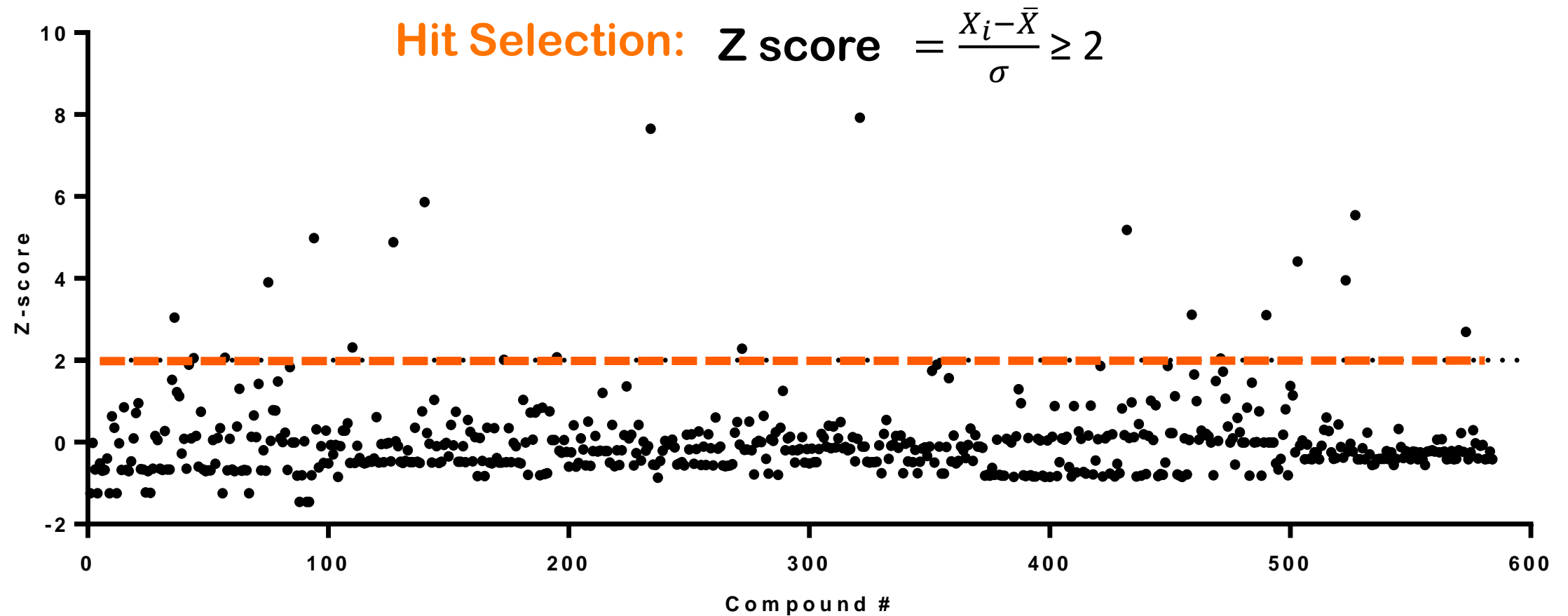


Optional: constitutive Puro or Neo Marker for Easy Cell Line Construction

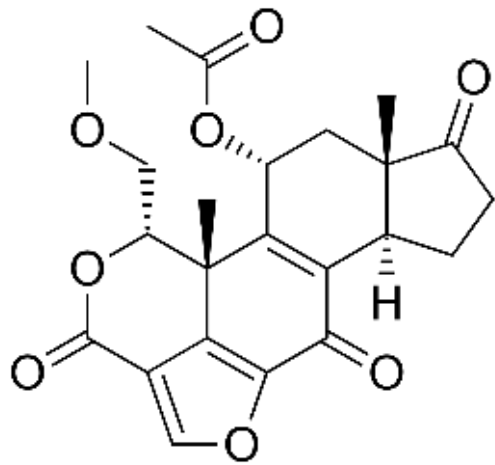
- Pseudo-lentivirus production
- Transduction
- Puromycin selection
- Limiting dilution
- Assay optimization

(Front Cell Infect Microbiol 2018; 8: 191)

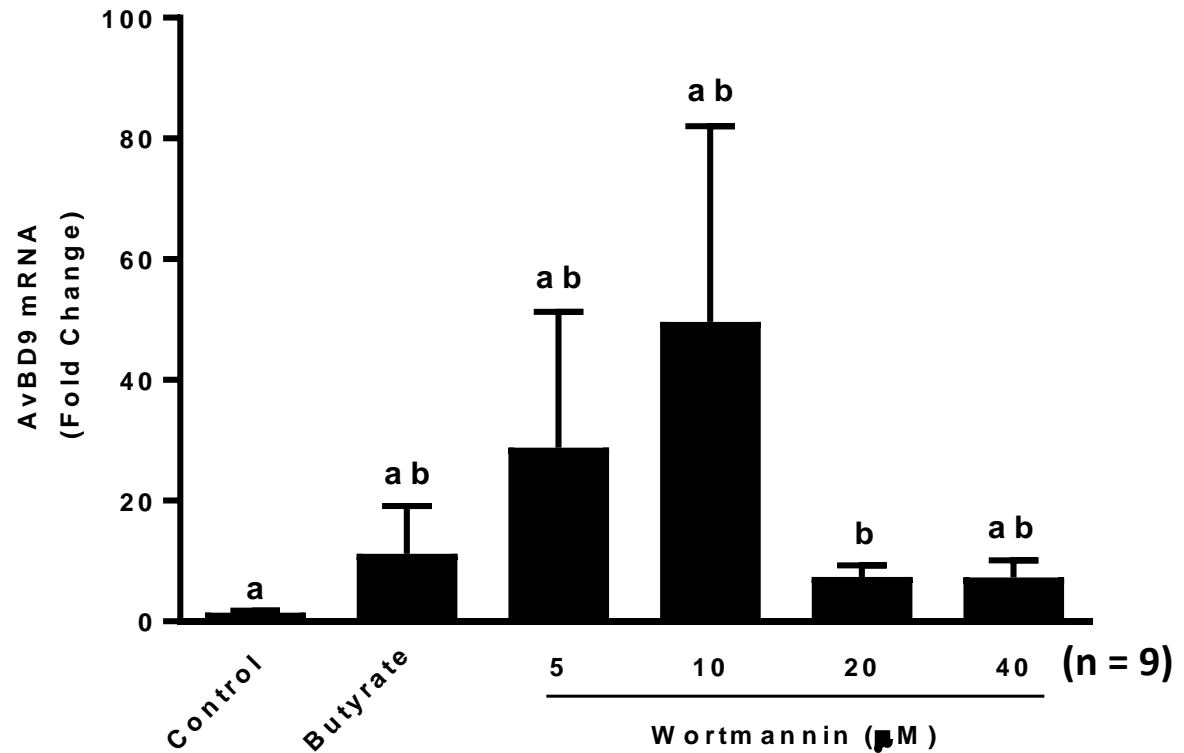
HTS for Natural HDP-Inducing Compounds in HTC/AvBD9-luc Cells



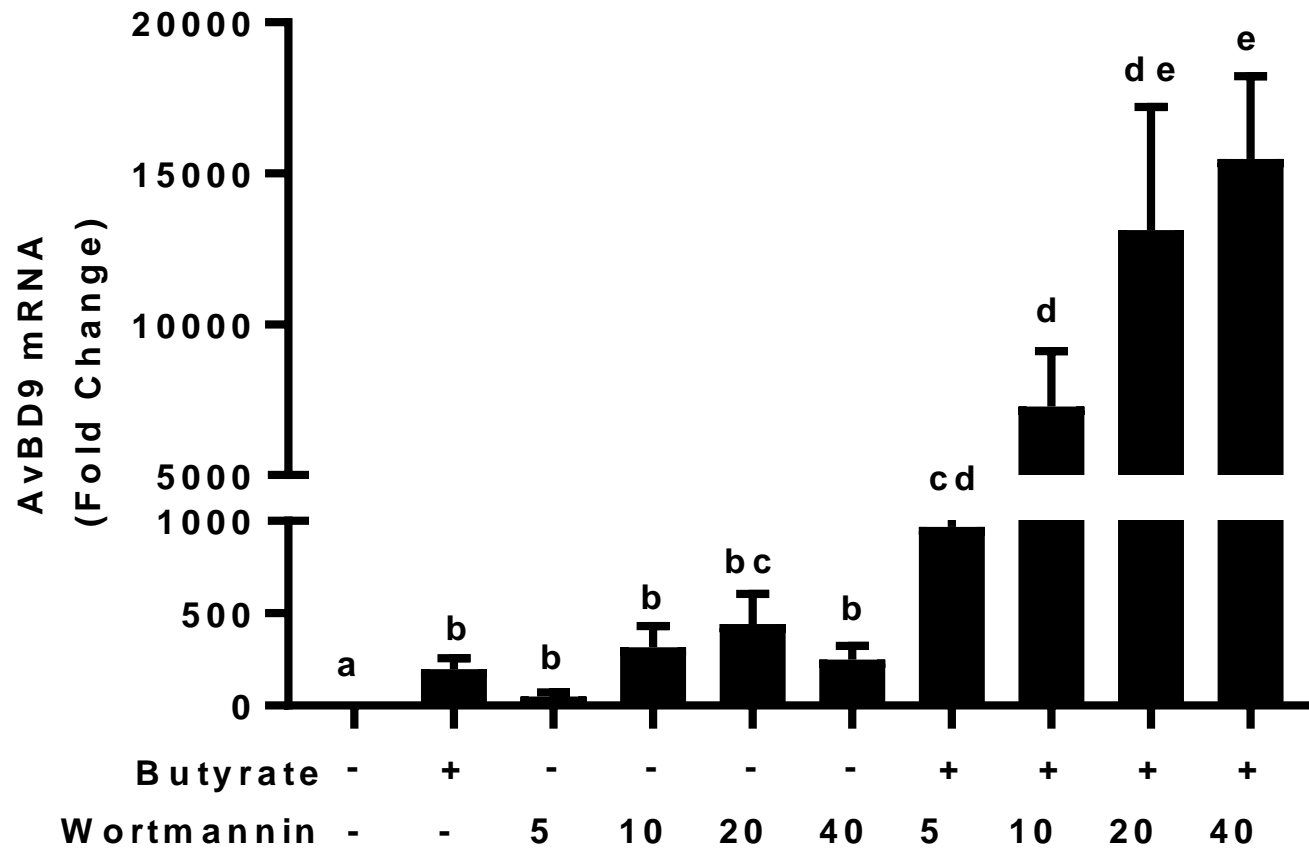
In Vivo Induction of *AvBD9* mRNA Expression in the Duodenum of Chickens by Wortmannin



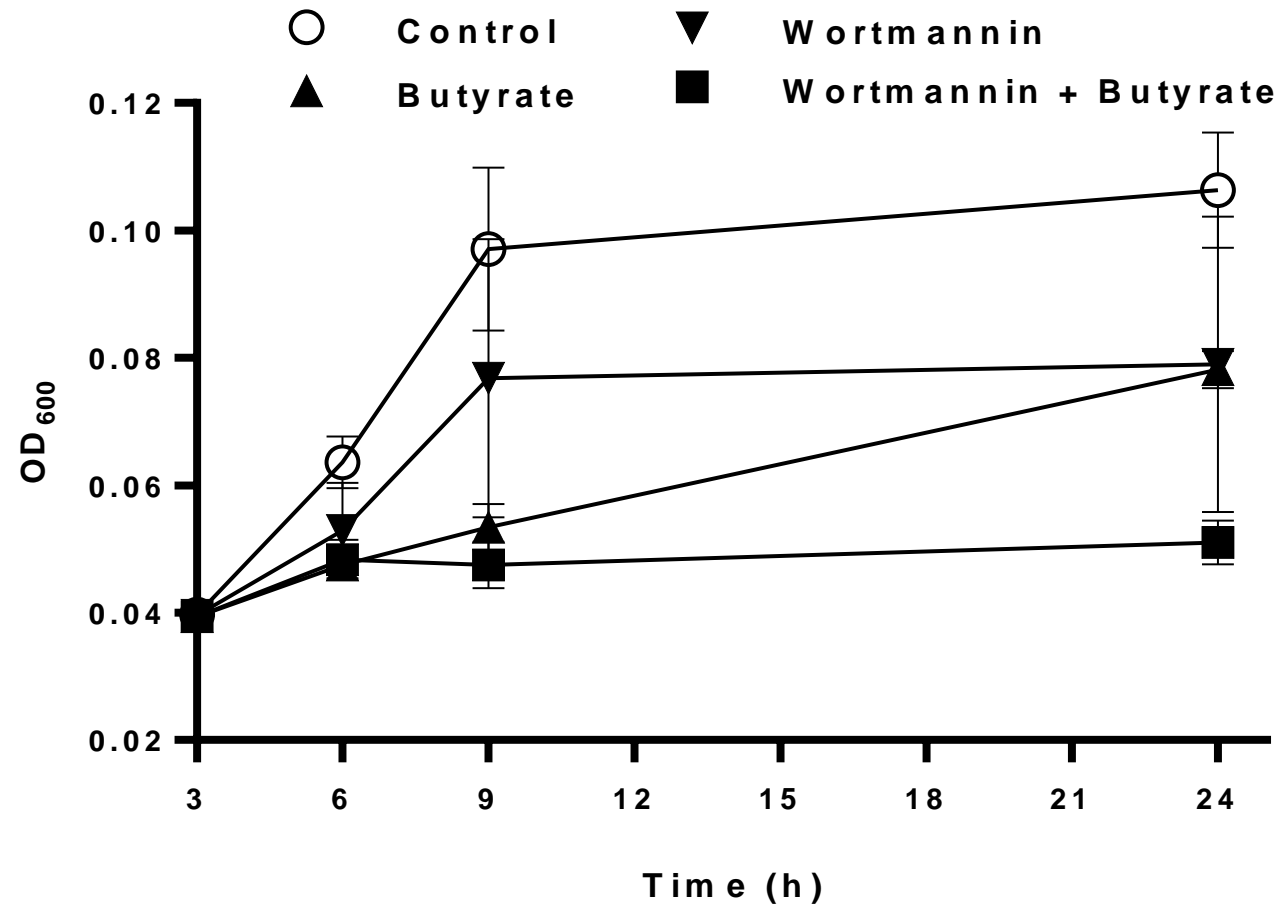
Wortmannin



Synergistic Induction of *AvBD9* mRNA Expression in HTC Cells between Butyrate and Wortmannin



Augmentation of the Antibacterial Activity of Chicken Monocytes by Wortmannin and Butyrate



[< Articles](#)

THIS ARTICLE IS PART OF THE RESEARCH TOPIC

Towards Host-Directed Drug Therapies for Infectious and Non-Communicab

ORIGINAL RESEARCH ARTICLE

Front. Cell. Infect. Microbiol., 11 June 2018 | <https://doi.org/10.3389/fcimb.2018.00191>



High Throughput Screening for Natural Host Defense Peptide-Inducing Compounds as Novel Alternatives to Antibiotics

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Research Article

Development of a Cell-Based High-Throughput Screening Assay to Identify Porcine Host Defense Peptide-Inducing Compounds

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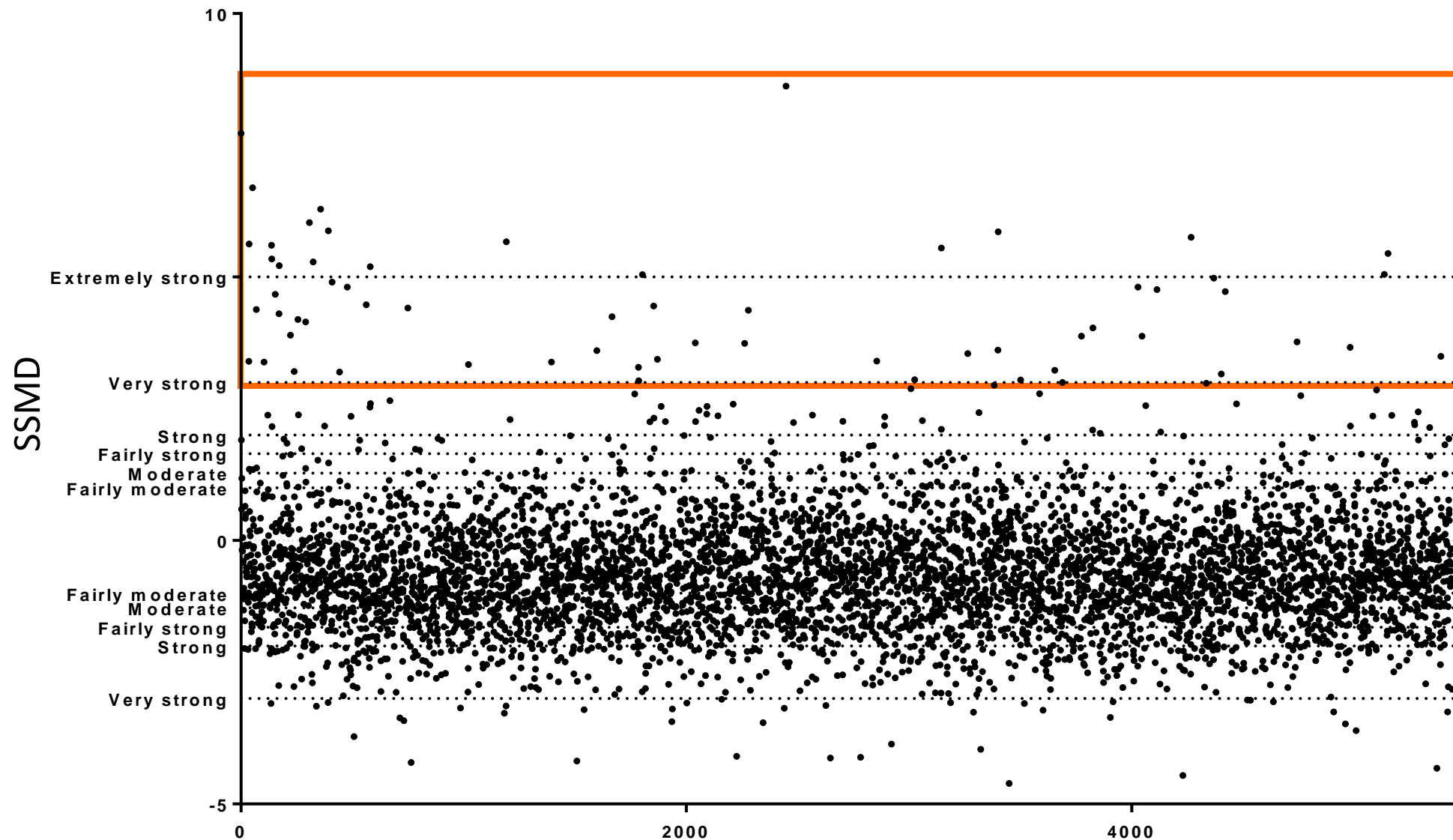
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High Throughput Screening for HDP-Inducing Compounds

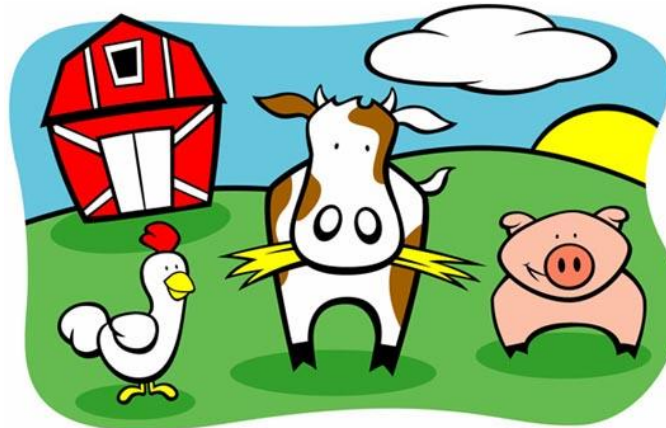


Competitive Advantages of Our technology

- Enhance host immunity without interacting directly with microbes or triggering bacterial resistance
- Anti-inflammatory and barrier protective, without affecting animal growth or meat quality
- Broadly antimicrobial
- Applicable to all animal species and even humans



HDP-inducing compounds = next-generation antibiotic alternatives



Molecular Immunology Lab at Oklahoma State University



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