



## 2017 JITMM

# Anti-protozoan study of a medicinal herb, *Bidens pilosa*

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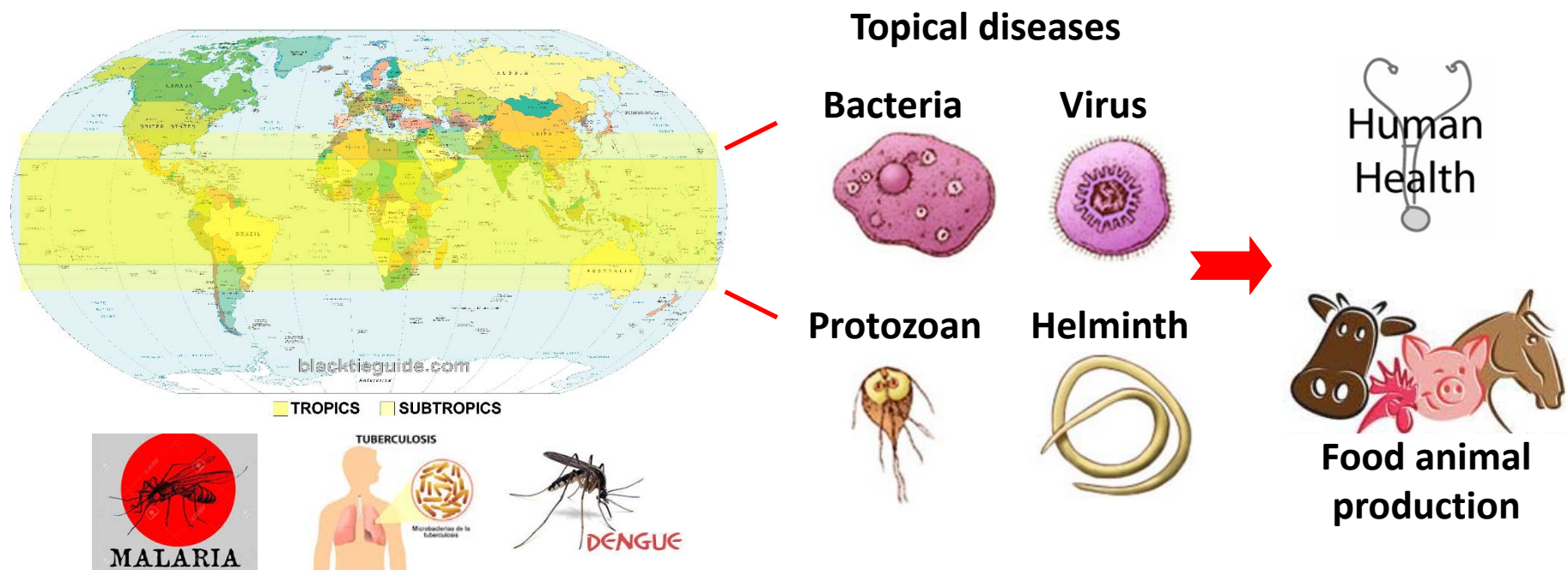
# Outline

- Introduction
  - Tropical diseases and medicine
  - Coccidiosis
  - Current approaches to coccidiosis control
- Results
  - Anti-coccidial properties of BP
  - Anti-coccidial MOA of BP
- Conclusions

# Introduction

# Tropical diseases and medicine

- Tropical diseases are infectious diseases that are prevalent in or unique to tropical and subtropical regions.
- They kill tens of millions of people every year and become one of the greatest challenges of the 21st century.
- Tropical medicine is important to global health and food safety.



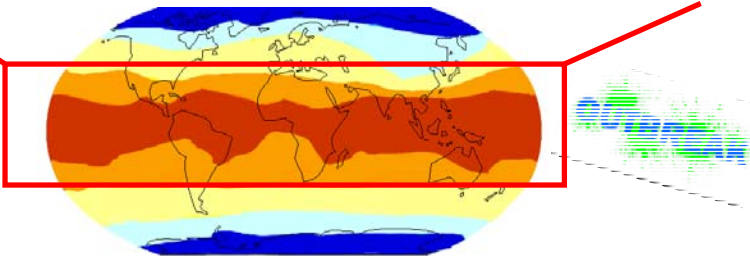
# Coccidiosis in chickens

- Avian coccidiosis, a protozoan disease, is one of the most serious infectious diseases in poultry (*Yang, W.C. (2016) eCAM 2657981*).
- Annual production of chickens is estimated to be 50 billion with a market worth of 60 billion USD.
- Economic loss caused by coccidiosis is estimated to cost over 800 million USD annually (*Intl J Poultry Sci 2004, 3(11): 715-718*).

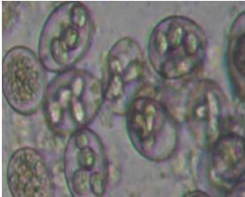


34% protein food for human

Most of poultry industry is in tropical country



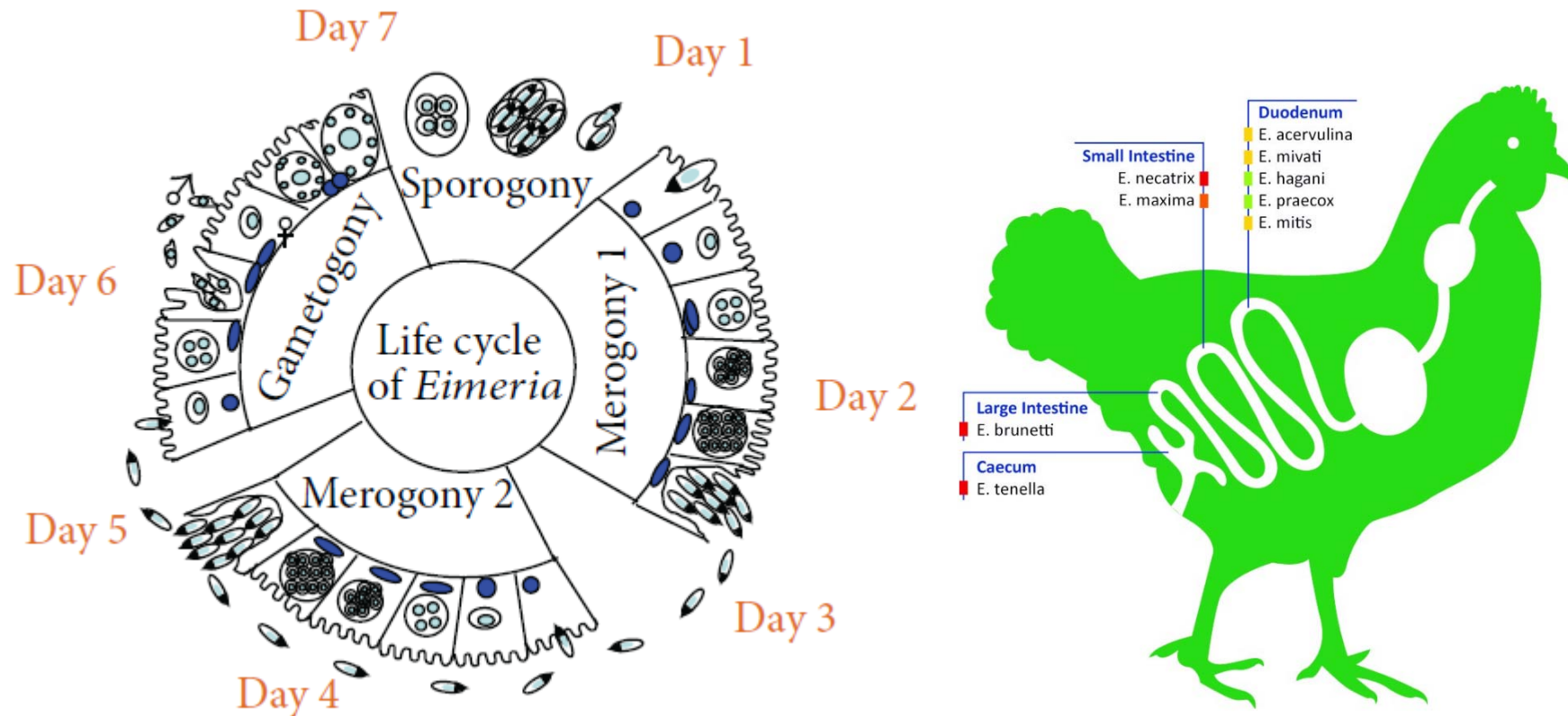
Coccidia  
(*Eimeria* species)



|                       | Looks | Stools | Gut lesions |
|-----------------------|-------|--------|-------------|
| Non-infected chickens |       |        |             |
| Infected chickens     |       |        |             |

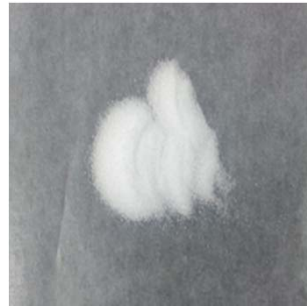
[http://www.betabunny.com/predators/predators\\_bonus.htm](http://www.betabunny.com/predators/predators_bonus.htm); <http://darwinian-medicine.com/protein-fat-and-carbohydrate-how-much-of-each-should-you-eat/>

# The life cycle of *Eimeria* species



Coccidiosis is caused by 9 *Eimeria* species (Yang, W.C. (2016) eCAM 2657981).

# Current approaches to coccidiosis control



|                        | Drugs                           | Vaccines          | Phytoagents                     |
|------------------------|---------------------------------|-------------------|---------------------------------|
| <b>Usage</b>           | <b>Prevention<br/>Treatment</b> | <b>Prevention</b> | <b>Prevention<br/>Treatment</b> |
| <b>Drug resistance</b> | +                               | -                 | ±                               |
| <b>Drug residue</b>    | +                               | -                 | -                               |
| <b>Mode of action</b>  | +                               | +                 | ?                               |

Preventive use of antibiotic chemicals in poultry will be banned by 2021 in Europe and 2017 in USA. Thus, edible plants are emerging as attractive way to control coccidiosis.

## Herbal medicine-*Bidens pilosa*

- Clinical experience for thousands years.
- Plant or plant-derived medicines are used in different categories of diseases.

### *Bidens pilosa* (BP):

- Edible, palatable and easy-to-grow plant.
- Tropical or subtropical areas.
- It is listed as food by FAO of UN and MOHW of Taiwan.
- It has been reported to treat over 40 categories of diseases such as protozoan infection, bacterial infection, gut disorders, immune disorders, etc.
- The anti-coccidial property of BP is still elusive.

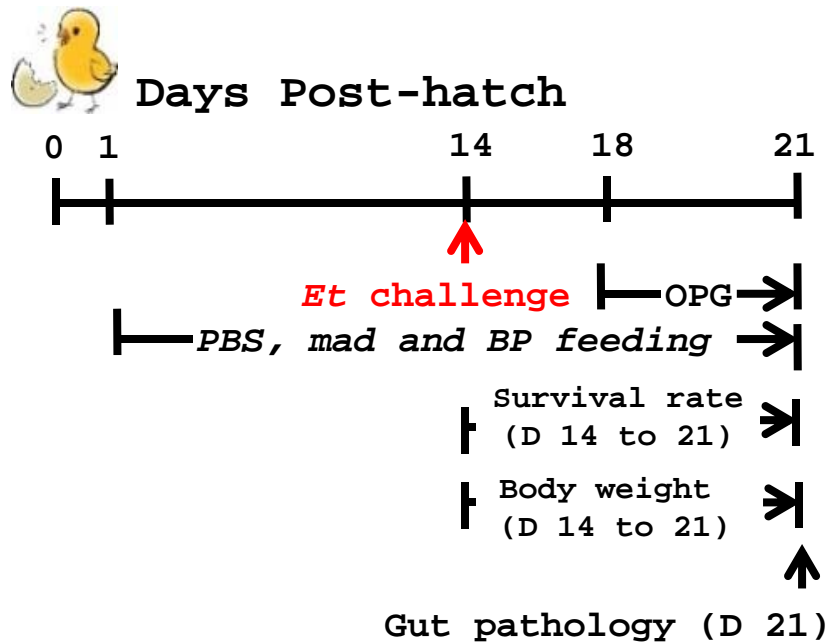
Food and Agriculture Organization of the United Nations (FAO)  
The Ministry of Health and Welfare (MOHW)





# Results

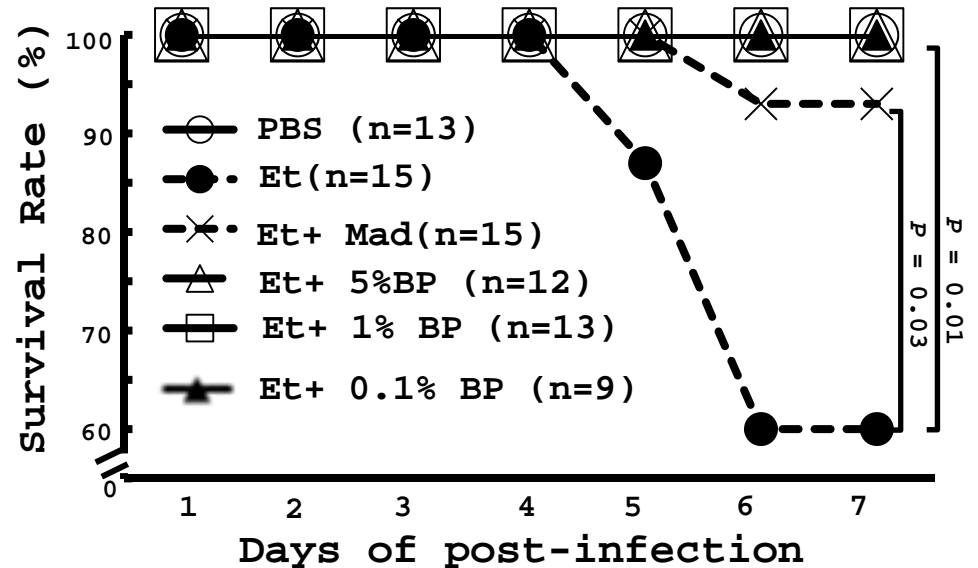
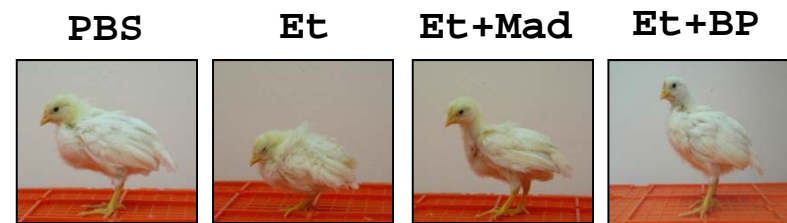
# Anti-coccidial efficacy of BP in chickens.



Mad:maduramycin

BP:*Bidens pilosa*

OPG:oocysts per gram of feces



Research in Veterinary Science 98 (2015) 74–81

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Research in Veterinary Science

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Effect of *Bidens pilosa* on infection and drug resistance of *Eimeria* in chickens

W.C. Yang <sup>a,b</sup>, Y.J. Tien <sup>c</sup>, C.Y. Chung <sup>d</sup>, Y.C. Chen <sup>a</sup>, W.H. Chiou <sup>d</sup>, S.Y. Hsu <sup>d</sup>, H.Y. Liu <sup>d</sup>, C.L. Liang <sup>e</sup>, C.L.T. Chang <sup>d,\*</sup>



# BP increases body weight of chickens.

| Group     | BPP<br>(% of feed) | <i>E. tenella</i><br>(oocysts) | Day 14–21<br>Body weight gain (%) | FCR         |
|-----------|--------------------|--------------------------------|-----------------------------------|-------------|
| 1(CTR)    | 0                  | 0                              | 48.8±3.2                          | 3.3.14±0.27 |
| 2(Et)     | 0                  | 1×10 <sup>4</sup>              | 31.6±11.5                         | 5.16±1.23   |
| 3(BPP)    | 0.5                | 0                              | 52.0±1.6                          | 2.81±0.08   |
| 4(BPP+Et) | 0.5                | 1×10 <sup>4</sup>              | 45.5±5.8                          | 3.71±0.64   |

1. The chickens were given standard diet (Groups 1 and 2) and standard diet supplemented with 0.5% *B. pilosa* product (Groups 3 and 4) from days 1 to 21. On day 14, chickens in Groups 2 and 4 were orally inoculated with *E. tenella* at the dose of  $1 \times 10^4$  sporulated oocysts per chicken.

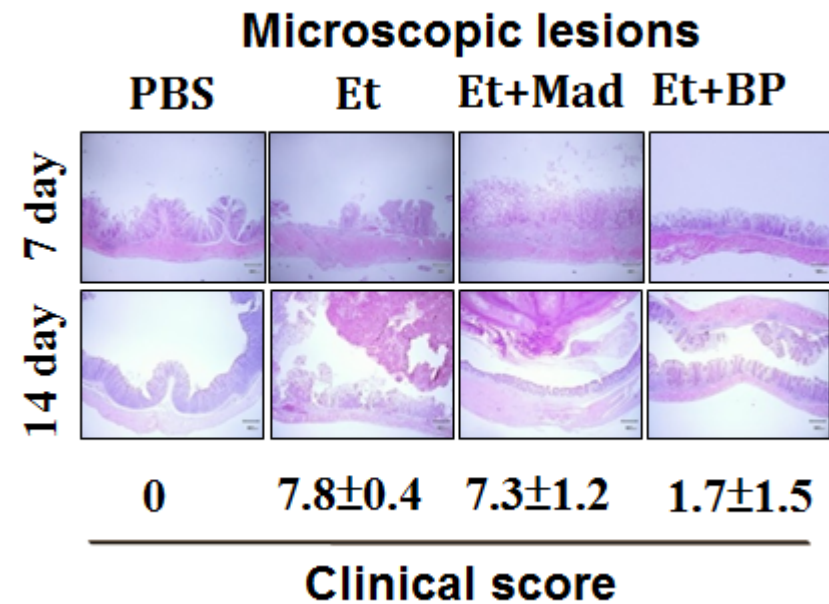
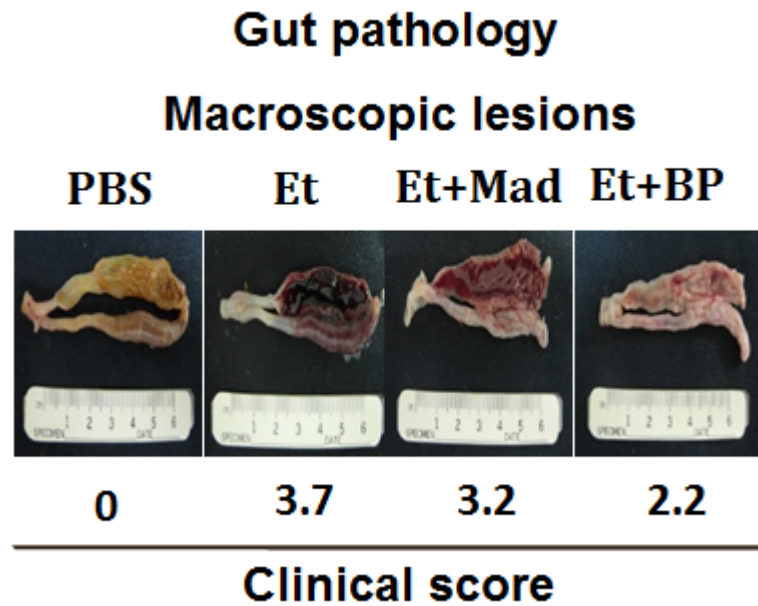
2. Body weight gain (%) was calculated based on the formula:  $100\% \times (\text{body weight on day 21} - \text{body weight on day 14}) / \text{body weight on day 14}$ .

3. FCR stands for feed conversion ratio and it was obtained by normalization of feed intake to body weight gain.

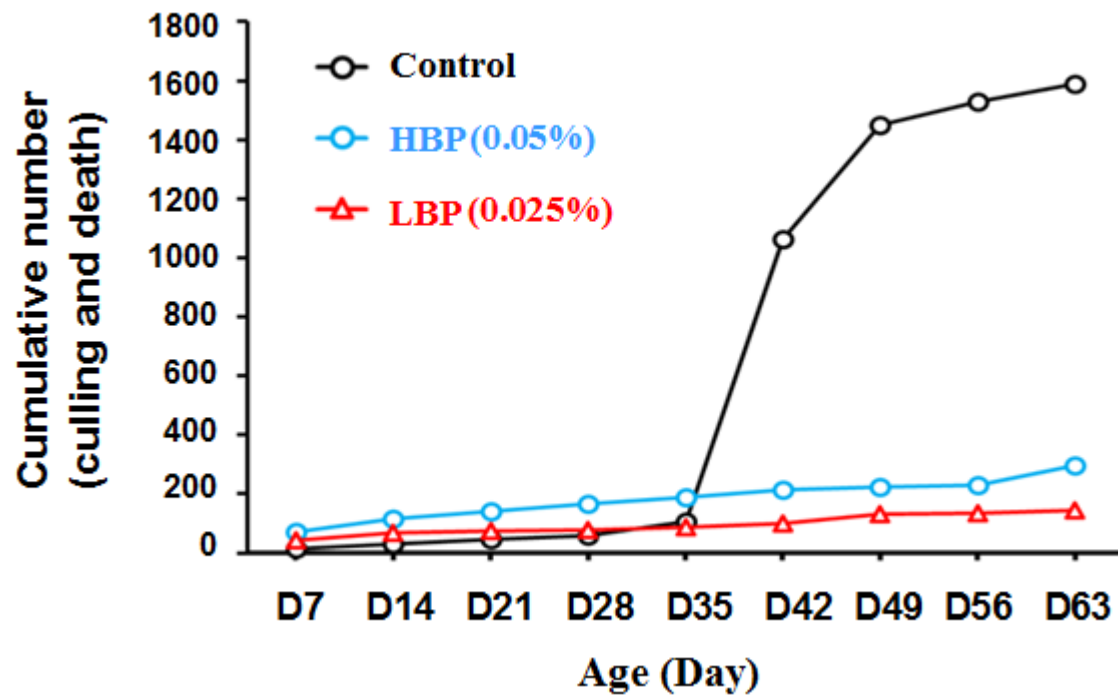
## Beneficial Effect of *Bidens pilosa* on Body Weight Gain, Food Conversion Ratio, Gut Bacteria and Coccidiosis in Chickens

Cicero L. T. Chang<sup>1</sup>, Chih-Yao Chung<sup>1</sup>, Chih-Horng Kuo<sup>2</sup>, Tien-Fen Kuo<sup>3</sup>, Chu-Wen Yang<sup>4\*</sup>, Wen-Chin Yang<sup>3,5,6,7\*</sup>

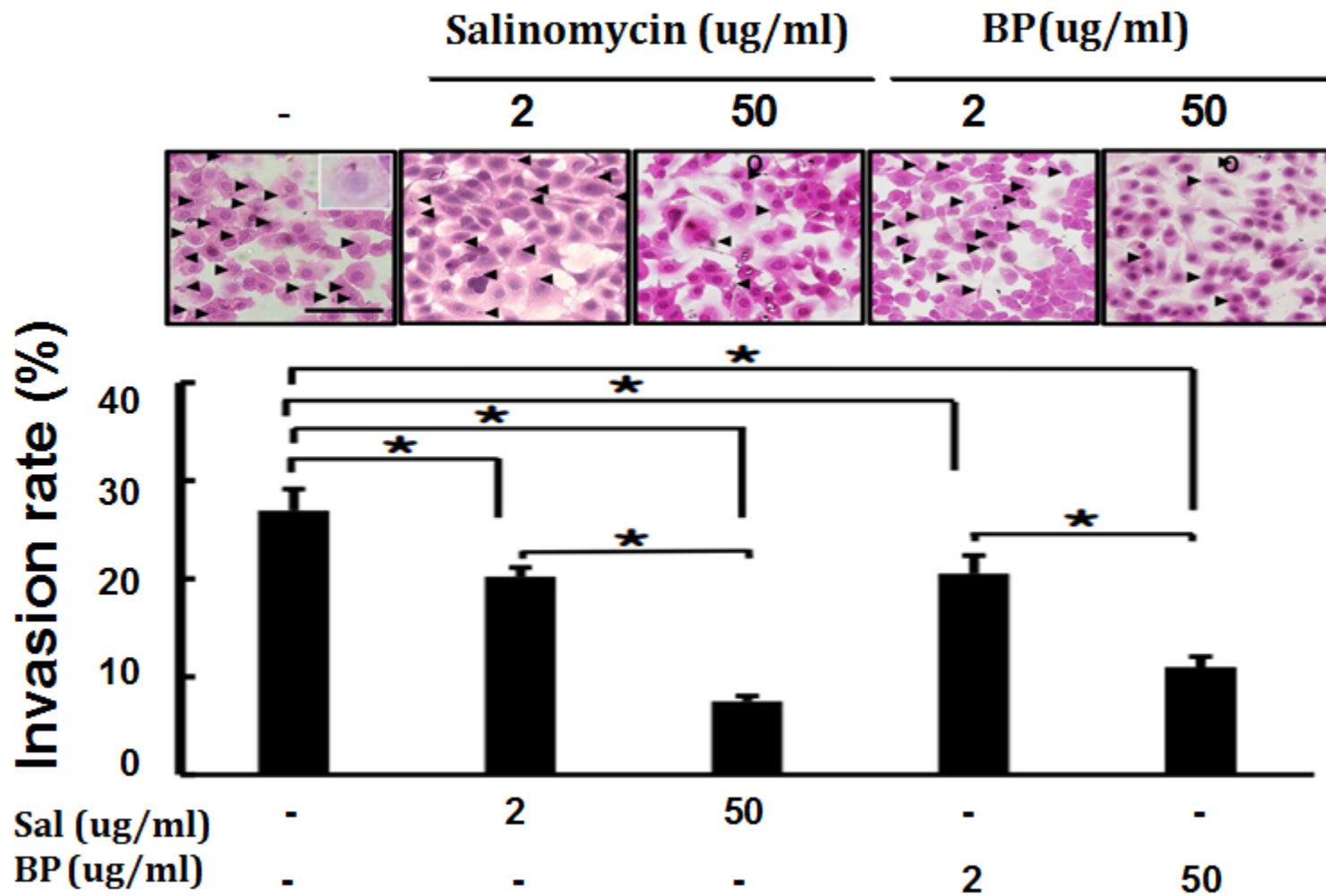
# BP decreases gut pathology of chickens.



## Field trial of BP on coccidiosis in chickens.



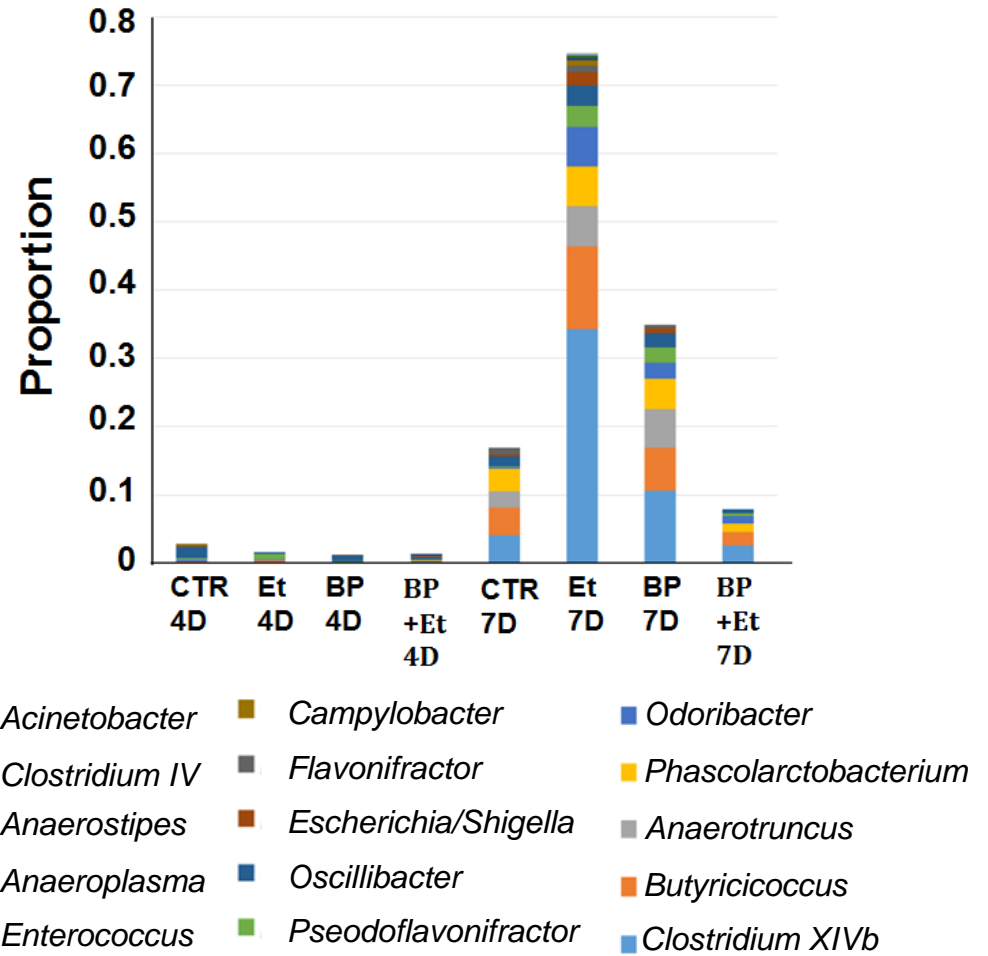
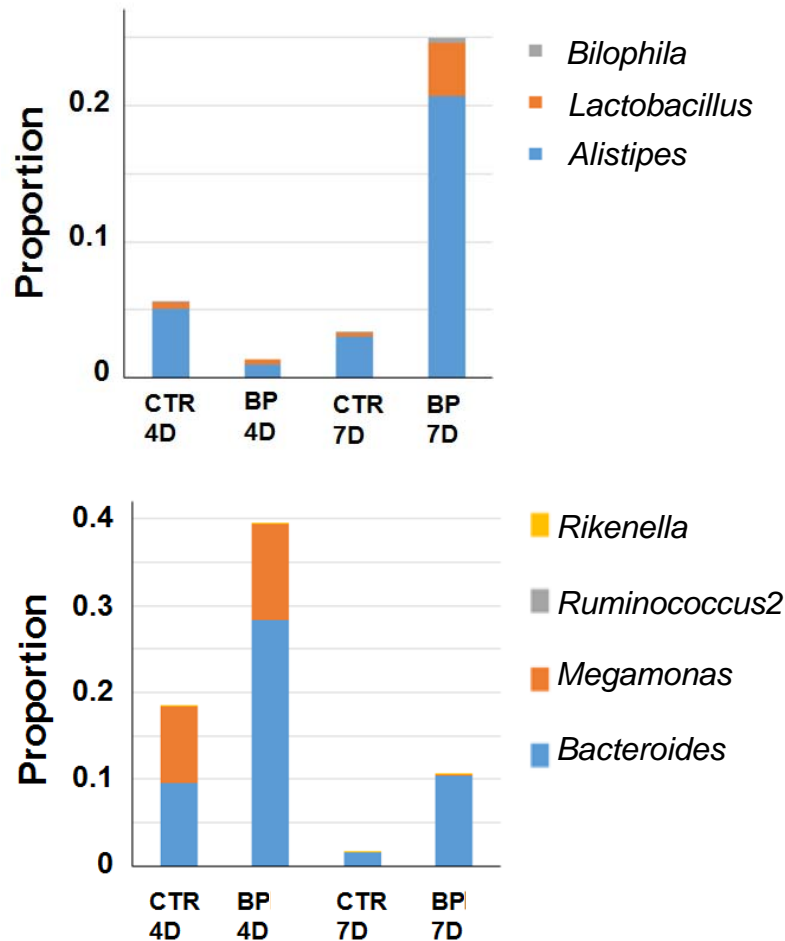
# BP suppresses the invasion of *E. tenella* sporozoites into gut cells.



# Effect of BP on the change of gut microbiota in chickens.

7 beneficial bacteria ↑

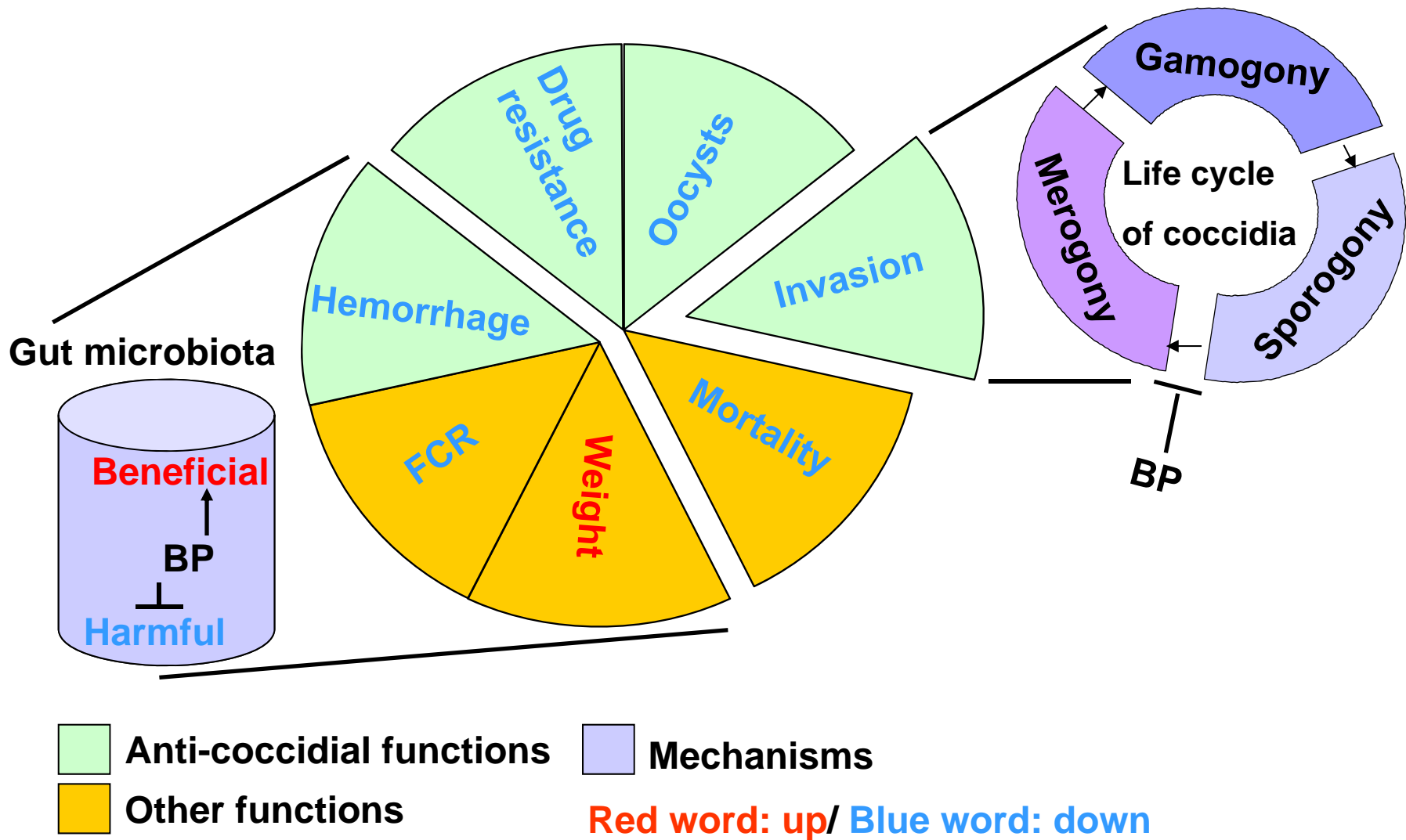
15 harmful bacteria ↓



RESEARCH ARTICLE

Beneficial Effect of *Bidens pilosa* on Body Weight Gain, Food Conversion Ratio, Gut Bacteria and Coccidiosis in Chickens

# A schematic model of BP in coccidiosis of chickens.





## Conclusions

- BP can control coccidiosis via multiple mechanisms, including interference with of *Eimeria* life cycle and modulation of gut bacteria.
- BP can serves as a novel remedy for coccidiosis in chickens.

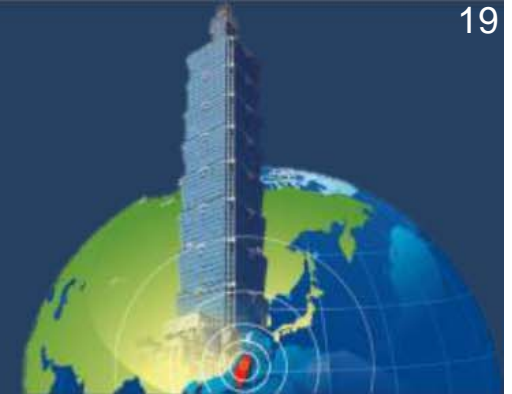
# Acknowledgement

Dr. Wen-Chen Yang and lab crew  
Dr. Cicero L.T. Chang





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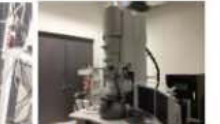
Ultra High-throughput Drug Screening



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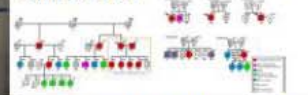


Bioluminescence Facility

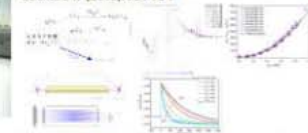


Cryo-EM Facility

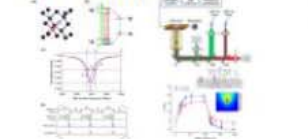
R331W Missense Mutation of Oncogene YAP1 is a Germline Risk Allele for Lung Adenocarcinoma With Medical Actionability, *Journal of Clinical Oncology* 33 (2015): 2303-2310



Direct kinetic measurement of the reaction of the simplest Criegee intermediate with water vapor, *Science* 347 (2015): 751-754



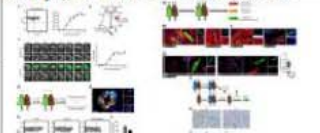
Time-Resolved Luminescence Nanothermometry with Nitrogen-Vacancy Centers in Nanodiamonds, *Nano Letters* 15 (2015): 3945-3952



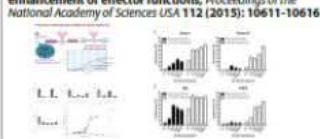
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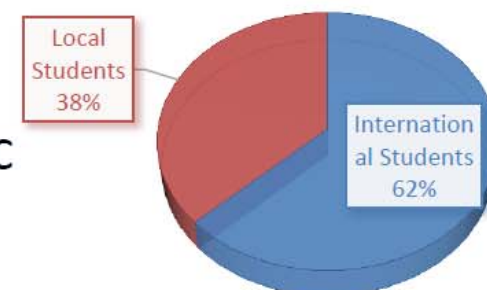
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