Investigating the Immunomodulatory Ability of Peptides Targeting Poultry Pathogens

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Antimicrobial Resistance in Food Systems

Zoonotic transmission of antibiotic-resistant bacteria

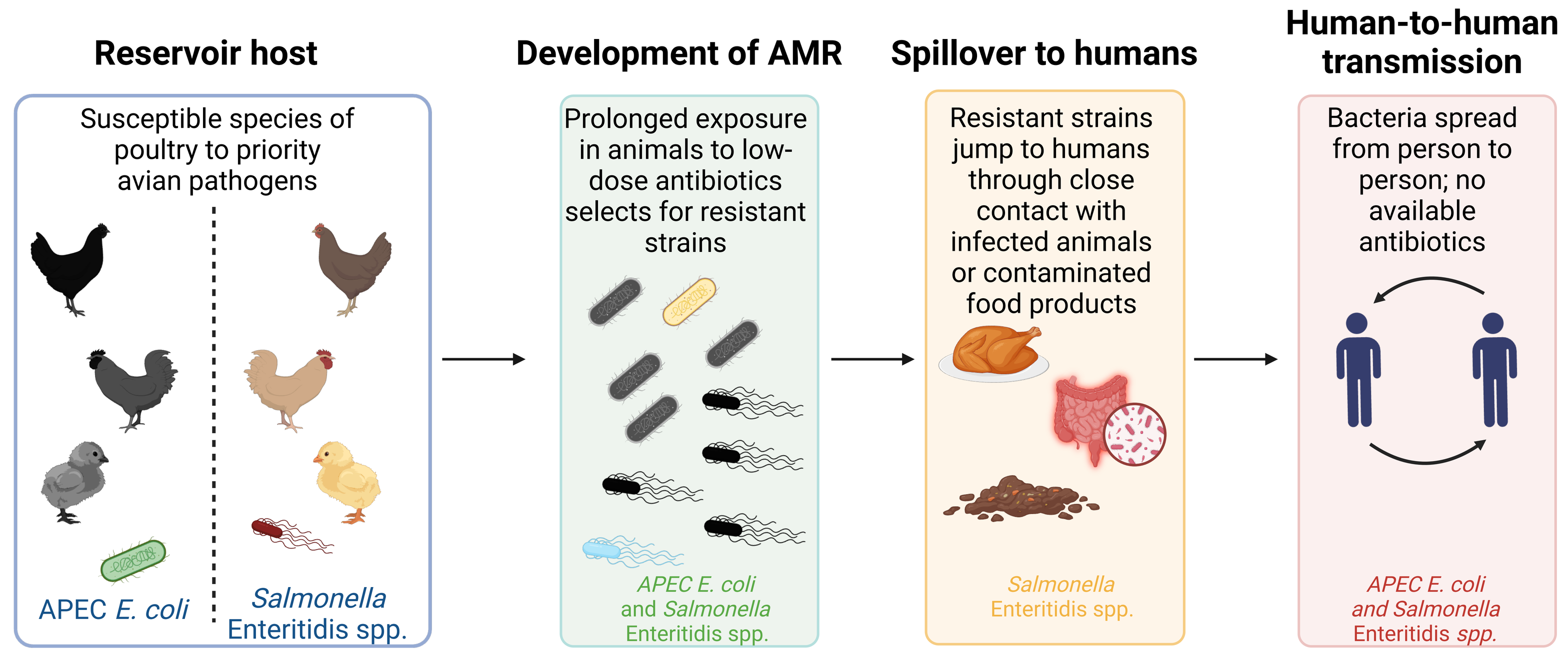

Figure 1. Zoonotic transmission of AMR bacteria from susceptible poultry species to humans. Illustrates potential harm to human resulting from increased antibiotic use in farm settings.[1]

Antimicrobial Resistance (AMR) is an evolving global health crisis driven by the inappropriate use of antibiotics in agricultural and medical settings.[2] Traditional antibiotics act via a singular mechanism in targeted pathogens. Selective pressure ensues on resistant strains to the incoming assault, allowing for the continued success and transmission of surviving microbes.[3] An ever-increasing number of multi-drug-resistant microbes poses a significant worldwide health concern requiring coordinated action and novel solutions.[4]

AMPs as a Novel Antibiotic Replacement

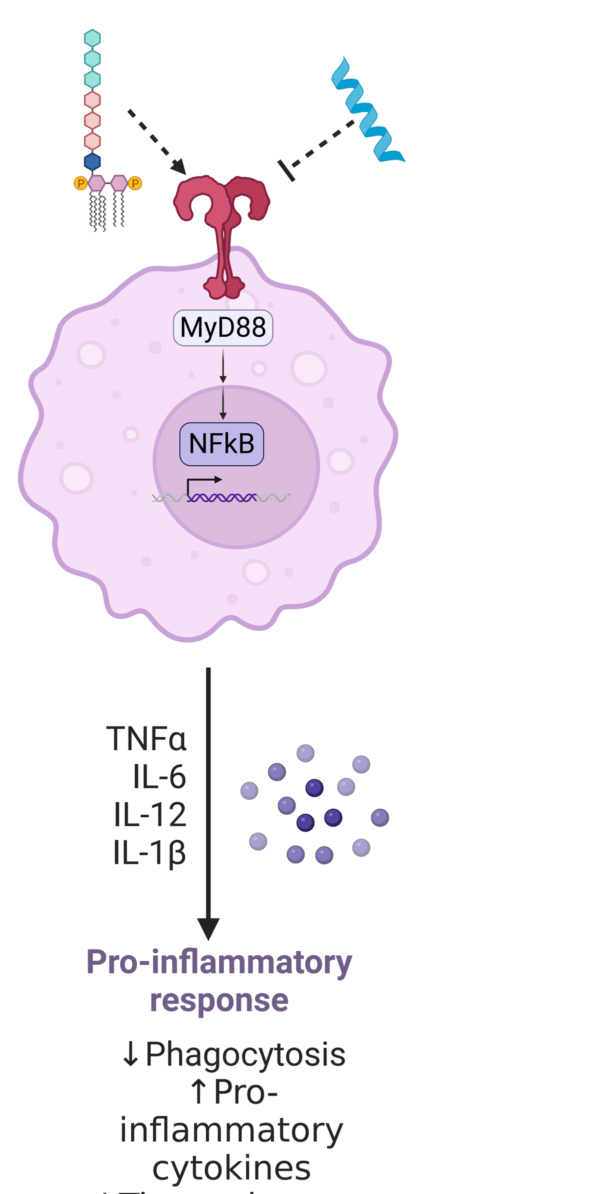

Figure 2. Schematic depiction proposed mechanism of action for dampened pro-inflammatory response by AMP-attenuation of LPS induced inflammation through TLR4 signalling.[7]

Antimicrobial peptides (AMPs) are a promising alternative to conventional antibiotics since they act on multiple targets, alleviating selective pressure on microbes and thereby mitigating AMR.[5] PeptAID is a collaborative project utilising machine-learning technologies to rapidly discover and identify AMP candidates in a streamlined process. Selected candidates undergo further testing to measure their efficacy against common avian pathogens with the ultimate aim to limit the widespread use of antibiotics in the poultry industry.[6]

PeptAID

Materials and Methods

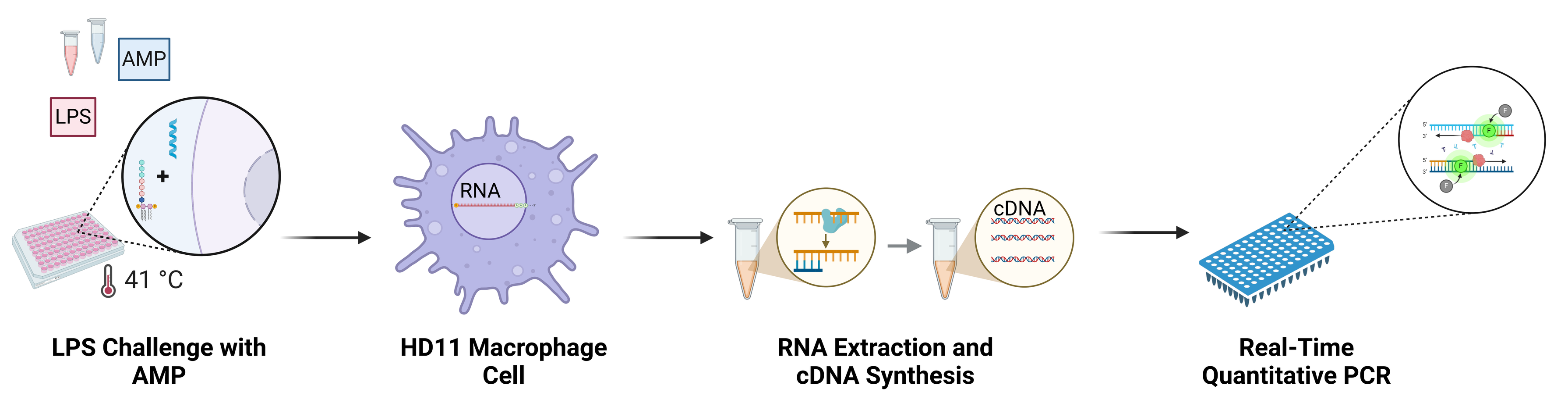

Figure 3. Methods. HD11 chicken-macrophage-like cells challenged with LPS in the presence of PeptAID AMPs for 3 hours. Macrophage RNA extracted and converted to cDNA for RT qPCR analysis of cytokine and chemokine transcripts.

TeBi1

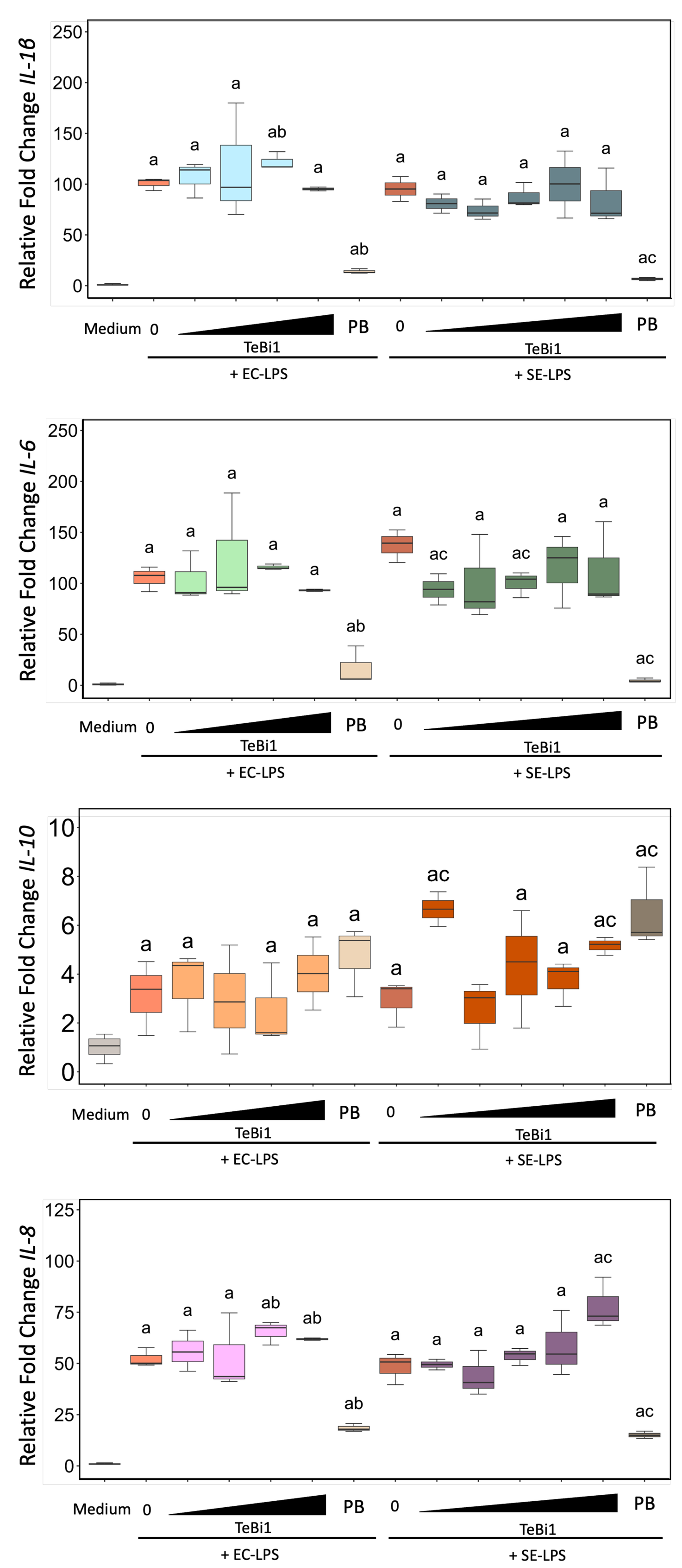

Figure 4. Relative fold change (RFC) for cytokine (IL1b, IL6, IL10) and chemokine (IL8) transcript abundance as determined via RT-qPCR following treatment of HD11 cells with 25 ng/mL EC-LPS or SE-LPS and 8 ug/mL Polymixin B or 1-16 ug/mL TeBi1. LPS-Results exclude 4 ug/mL TeBi1 with EC-LPS Data generated by CMV and SEM.

TeRu4

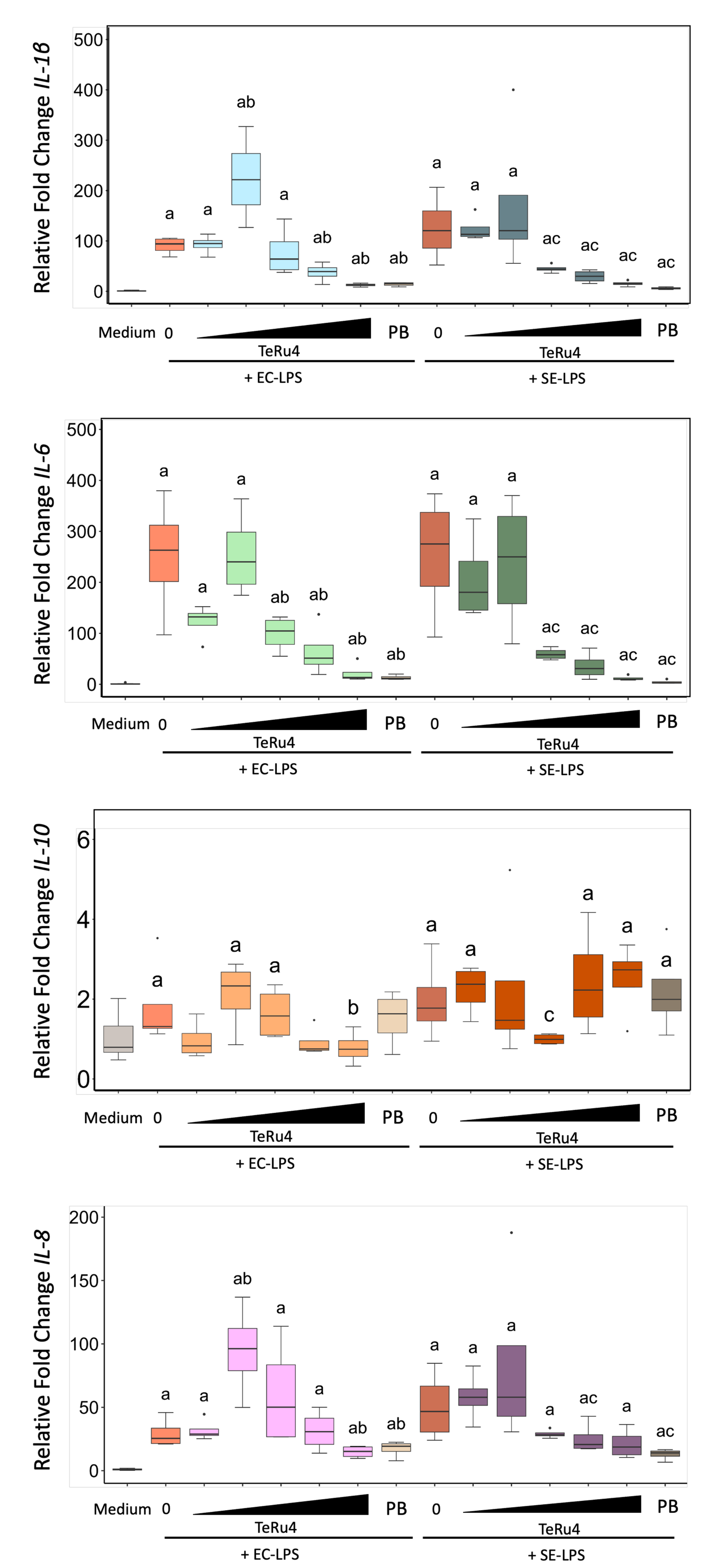

Figure 5. Relative fold change (RFC) for cytokine (IL1b, IL6, IL10) and chemokine (IL8) transcript abundance as determined via RT-qPCR following treatment of HD11 cells with 25 ng/mL EC-LPS or SE-LPS and 8 ug/mL Polymixin B or 1-16 ug/mL TeRu4. Data generated by SEM.

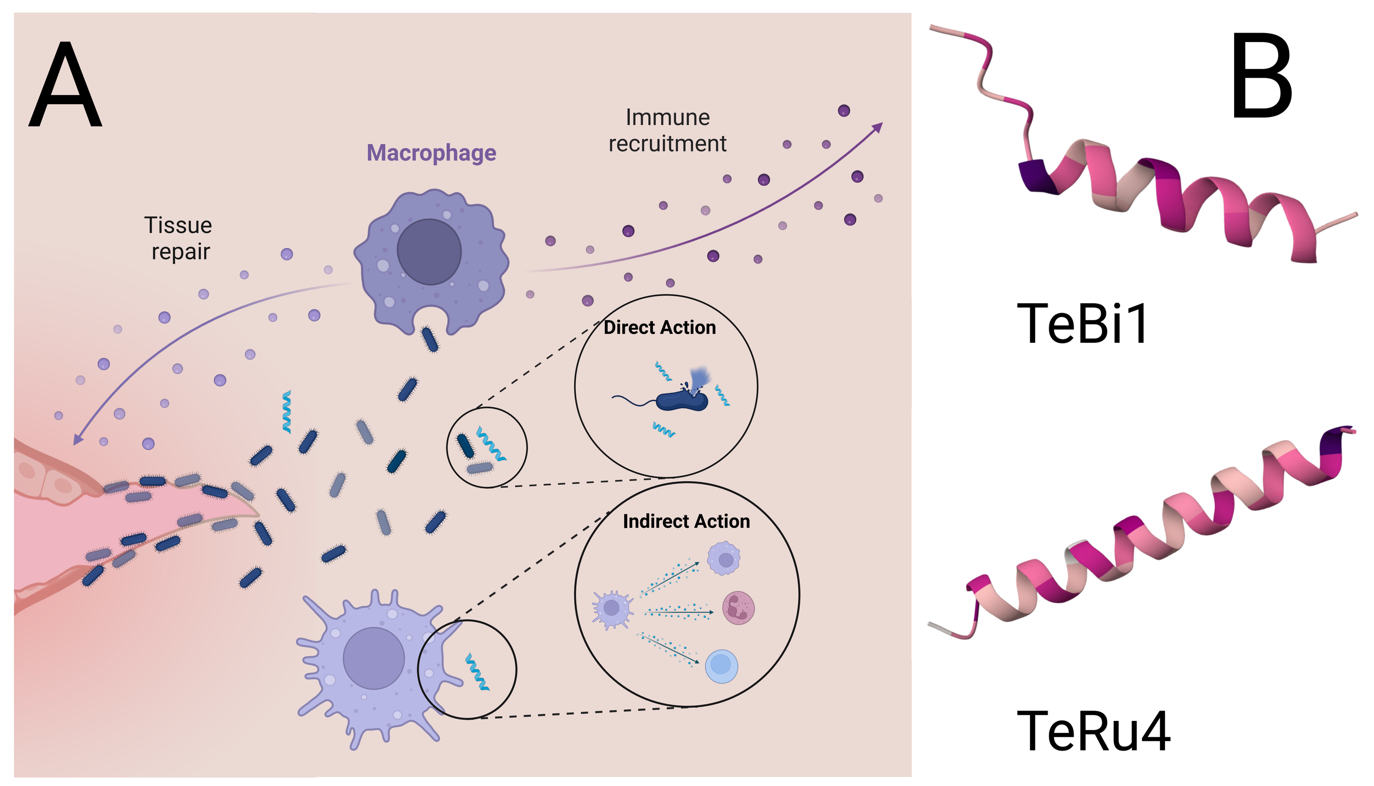

Figure 6. A. AMPs exert direct effects through pore-formation at bacterial cell walls, resulting in pathogen lysis. Indirect activity of AMPs involves host immune modulation to recruit immune cells to the site of infection.[5] **B.** Colabfold structural predictions of TeBi1 and TeRu4, colours in alignment with hydrophobicity properties.[8]

Conclusions and Future Directions

- PeptAID AMPs TeBi1 and TeRu4 can reduce the transcript abundance of pro-inflammatory cytokine signatures in LPS-stimulated HD11 cells
- TeRu4 attenuates LPS-induced inflammatory responses, whereas TeBi1 does not confer a strong anti-inflammatory effect on LPS-challenged cells
- Future experiments will seek to elucidate the mechanism of attenuation of LPS-induced inflammation by AMPs as direct AMP-LPS binding or AMP-mediated modulation of HD11 immune response
- Expansion of AMPs will test for similar, or more effective candidates to be used in agriculture, or medical applications
- Research findings will extend into *in vivo* trials in poultry, with later implications in other animals and settings

Acknowledgments and References

[9]acknowledge and respect the Lək ̓ əŋən (Songhees and Xʷsepsəm/ Esquimalt) Peoples on whose territory this UVic-based researched was undergone, and the Lək ̓ əŋən and WSÁNEĆ Peoples whose historical relationships with the land continue to this day.

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