UNIVERSITY OF MINNESOTA
Swine Disease Eradication Center

October 8, 2012
Volume 1, Issue 8

www.cvm.umn.edu/sdec

SDEC Partners Research Update

Project Update: Genes expressed by pathogenic and non-pathogenic *Lawsonia intracellularis* isolates

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Funded by the SDEC and University of Minnesota Emerging, Zoonotic Diseases Mentored Research and CNPq of Brazil.

Background

- *Lawsonia intracellularis* is the obligate, intracellular bacterium responsible for proliferative enteropathy.
- Non-pathogenic variants of *Lawsonia* are obtained through multiple passages in cell culture and do not cause disease.
- However, low passage *Lawsonia* isolates cause clinical and pathological changes typical of proliferative enteropathy.

Objective

The objective of this study was to determine whether genes differentially expressed between pathogenic (low passage) and non-pathogenic *Lawsonia* variants encode potential bacterial virulence factors.

Results

- A larger number (401) of genes were exclusively expressed by the pathogenic *Lawsonia* variant as compared to the non-pathogenic variant.
- This wider transcriptional landscape of the pathogenic variant was distributed in the chromosome and three plasmids (Fig.1).
- Only genes from the pathogenic *Lawsonia* variant were expressed by plasmid A, suggesting a potential role of this plasmid in the pathogenesis of proliferative enteropathy.
- There was no significant difference (Log (RPKM) > 2; p-value < 0.05) in the comparison of all 319 genes commonly expressed in both variants.
- Those commonly expressed genes demonstrated positive correlation (Fig.2), indicating the involvement of gene silencing (switching off) mechanisms to attenuate virulence of the pathogenic variant through cell passages.

Results

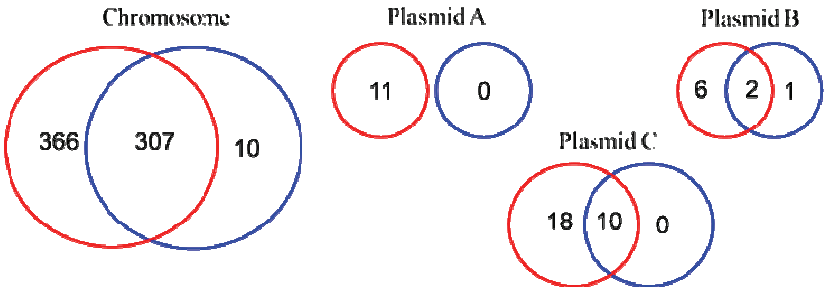

Figure 1.(left) Schematic representation of the *Lawsonia* genome. Distribution of genes expressed by pathogenic (red circles) and non-pathogenic (blue circles) variants. Overlapping zones represent genes expressed in both variants.

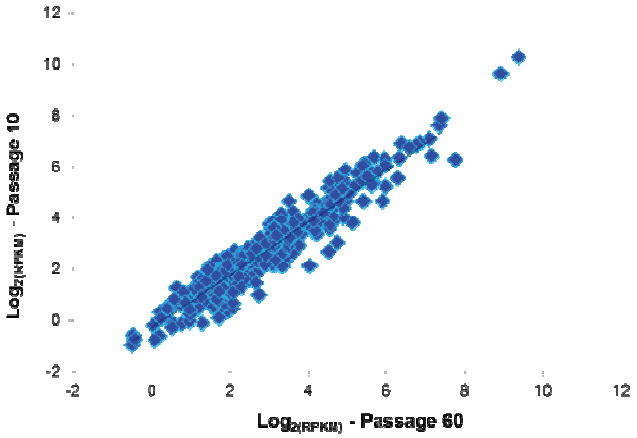

Figure 2. (right) Expression levels of 319 genes commonly expressed by the pathogenic and non-pathogenic *Lawsonia* variants.

Conclusions

- The pathogenic *Lawsonia* variant has a wider transcriptional landscape, which may represent an important contribution from plasmids.
- The entire gene repertoire of plasmid A was repressed in the non-pathogenic variant, suggesting its significant role in the virulence of the pathogenic variant.
- Gene silencing (switching off) mechanisms during loss of virulence (spontaneous attenuation) may occur in vitro.
- Genetic pathways found in the pathogenic *Lawsonia* variant include membrane transporters, stress-related responses and many highly expressed, but uncharacterized, proteins.

Implications

- This study is the first report characterizing the transcriptional profile of *Lawsonia*.
- Specific properties of genes expressed by *Lawsonia* at high levels in both variants or exclusively in the pathogenic variant may now be studied in order to: 1) understand the pathogenesis of proliferative enteropathy– e.g. identify virulence factor-encoding genes and 2) develop new diagnostic tools – e.g. differentiate naturally infected from vaccinated animals (DIVA).
- These results open a new research field for studying target genes involved in the pathogenesis, diagnosis and control of proliferative enteropathy.

The full article, entitled "Comparative transcriptional analysis of homologous pathogenic and non-pathogenic *L.intracellularis* isolates in infected porcine cells" by F.Vannucci, D.Foster, and C.Gebhart, has been published in PLOS ONE and is available online at http://dx.plos.org/10.1371/journal.pone.0046708 .