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Homogeneity among *Lawsonia intracellularis* isolates

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Intra-species heterogeneity in some pathogenic bacteria presents challenges for disease diagnosis and control. A range of sophisticated phenotypic and genotypic approaches can be employed to subdivide some bacterial species into "strains". A strain can be defined as a subgroup of a bacterial species that differ only in minor characteristics but measurably from others within the same species. The term "strain" is often used interchangeably with "isolate", although the former requires evidence of measurable differences from other members of the same species while the latter is simply an organism obtained in pure culture from a specimen. Detection of potential heterogeneity becomes more challenging with obligately intracellular organisms such as *L. intracellularis*. Obligate intracellular bacteria are highly adapted to their hosts and literally depend upon them for their survival. Genomic alterations characteristic of obligately intracellular bacteria include reduction in genome size, an evolutionary adaptation that likely reflects loss of genes unnecessary for survival in the relative stability of the intracellular niche provided by host cells.

There is little to suggest host-species specificity or distinct pathotypes of *L. intracellularis* since experimental infections with porcine isolates can reproduce disease in other animals [**1,2**] and PHE isolates can reproduce both PIA and PHE. Currently it is known that 16S rRNA sequences of multiple *L. intracellularis* are very highly conserved even among isolates of different mammalian origin [**3**]. The gene encoding LsaA, the immunological target of a monoclonal antibody used widely in immunohistochemical detection of *L. intracellularis* was detected by PCR in all of 5 isolates [**4**]. Up to twenty two additional outer membrane proteins (OMPs) common to six *L. intracellularis* isolates have been reported [**5**]. Also supporting antigenic conservation in *L. intracellularis* is the capacity to detect infected animals from disparate origins by serological assays employing a limited range of *L. intracellularis* isolates as antigen. The demonstration of immunological cross-protection [**6**] is suggestive of immunologic conservation among isolates from disparate geographical origins (i.e. North America and Europe). Gebhart et al [AASV, Toronto, Canada, 2005] reported detection of VNTRs (variable number tandem repeats) within the *L. intracellularis* genome which provides targets for detecting genomic heterogeneity. VNTRs were able to distinguish geographically- and temporally-distinct *L. intracellularis* isolates as well as isolates from two pathologically-distinct forms of disease – intestinal adenomatosis (PIA) and proliferative hemorrhagic enteropathy (PHE). Differences were shown between multiple (n=3) PHE cases and between four recent field outbreaks. These genomic differences appear to be intergenic - occurring between rather than within functional genes - and do not encode for any detectable phenotypic trait or correlate to pathogenicity. However the VNTRs could be potentially valuable as epidemiologic markers.

Conclusion

From available evidence, *L. intracellularis* appears to be phenotypically homogeneous. Immunochemical and serological tests indicate a marked degree of antigenic conservation among *L. intracellularis* isolates. Experimental challenges indicate a single pathotype and immunologic cross-protection. Therefore, at present it appears that the intergenic variation observed in *L. intracellularis* does not correspond to any observed phenotypic or immunologic differences and this species appears to be monotypic.

References

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