InSignia has the capacity to shift the standard of infection diagnosis and guided therapy

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Background (=107 words)

Diagnostic tests can affect the timely and appropriate management of infectious diseases. Currently, NAATs cannot accurately determine infection status, or confirm cure after treatment, due to residual nucleic acids persisting after cell death. Guidance on appropriate therapy is limited to slow culture methods or NAATs targeting only strictly defined resistance mechanisms. InSignia overcomes these gaps by ascertaining a ratio of RNA to DNA, quantifying active transcription associated with viable pathogens. Further, perturbation of the ratio by antibiotics allows assessment of pathogens' susceptibility profiles. Overall, InSignia can be used to determine organism viability before or after treatment and/or resistance or sensitivity to antibiotics, facilitating guidance towards appropriate therapy.

Methods (=54 words)

Total Nucleic Acid was extracted, and specific *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) targets amplified through Reverse Transcriptase-qPCR. To analyse susceptibility profiles, a rapid 10-minute incubation with antibiotics was performed prior to extraction. Results from PCR are measured as an Index, elucidating viability and/or whether antibiotics could induce changes compared to untreated controls.

Results (=94 words)

The sensitivity and specificity of pathogen detection using InSignia was high, comparable to conventional NAATs. However, more information was ascertained since viability was also assessed, and in some instances indicating potential overtreatment of asymptomatic individuals. The analysis of viability was independent of target concentration of non-viable organisms.

The susceptibility or resistance of NG isolates to ciprofloxacin was accurately determined, with concordance between antibiotic breakpoints and InSignia Index values. This revealed a correlation between the defined susceptibility and the transcriptional response to antibiotic exposure. Other commonly used antibiotics also produced promising data in preliminary studies.

Conclusion (=65 words)

InSignia™ is an informative new test, with capacity to shift the paradigm away from presumptive and imperative treatment to appropriate guided therapy. It is an informative molecular-phenotypic test required to support antimicrobial stewardship efforts and slow the fast-evolution of antimicrobial resistance. Employable in centralised labs and POC settings, it is a versatile test with ability to transform infectious disease management, providing insights not currently met.