Klebsiella pneumoniae sugar import suppresses hypermucoviscosity

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Background: *Klebsiella pneumoniae* is significant cause of community- and hospital-acquired infections, impacting both immunocompromised and immunocompetent individuals. The co-emergence of drug-resistance and hypervirulence in *K. pneumoniae* has severely limited therapeutic options. Hypermucoviscosity (HMV) is an important *K. pneumoniae* virulence factor that manifests as a 'tacky' bacterial colony due to changes in capsule chain length. Two genetically encoded mechanisms regulating HMV are the regulator of mucoidy phenotype (*rmpD*) and *wzc* activity. We have previously shown that difference in growth medium also alters HMV, but specific nutrient signals and mechanisms involved are still unclear. To address this knowledge gap, we hypothesized that extracellular nutrients such as sugars distinctly induce changes in *K. pneumoniae* HMV without impacting capsule abundance.

Methods: To investigate, we cultured K. pneumoniae strain KPPR1 in M9 minimal medium supplemented with varying sugar concentrations, and measured HMV and capsule production using sedimentation resistance assay and uronic acid quantification, respectively.

Results: Our results demonstrated that all tested sugars, including metabolizable and non-metabolizable sugars, significantly suppressed the mucoidy, while capsule abundance was not impacted similarly. This finding indicates that sugar import in *K. pneumoniae* distinctly regulates HMV. Moreover, sugar supplementation led to significant downregulation of *rmpADC*. To further elucidate the mechanism tying sugar transport to *rmpD* transcription and mucoidy, we screened a transposon library covering ~70% of the KPPR1 genome to identify genes required for suppressing mucoidy in sugar-supplemented M9 medium. The transposon screen identified genes involved in carbohydrate and amino acid transport and metabolism, suggesting their role in sugar-mediated HMV suppression.

Conclusion: These findings collectively suggest that host-derived sugars could act as nutrient signals, selectively regulating *K. pneumoniae* hypermucoviscosity during infection. Further defining the mechanism by which sugars modulate hypermucoviscosity and how this observed phenotype manifests *in vivo* would contribute to better understanding of *K. pneumoniae* pathogenesis.

