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Genome-scale investigation of the metabolic determinants generating bacterial fastidious growth

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High proliferation rate and robustness are vital characteristics of bacterial pathogens to successfully colonize their hosts. The observation of drastically slow growth in some pathogens is thus paradoxical and remains unexplained. In this study, we sought to understand the strikingly slow, designated as fastidious, growth of the plant pathogen *Xylella fastidiosa*. Using genome-scale metabolic network reconstruction, modeling and experimental validation, we explored its metabolic capabilities. Despite genome reduction and slow growth, the pathogen's metabolic network is complete but strikingly minimalist and lacking robustness. Most alternative reactions were missing, especially those favoring a fast growth, replaced by less efficient paths. We also unraveled that the production of virulence factors is inefficient and imposes a heavy burden on growth. Interestingly, some specific determinants of fastidious growth were also found in other slow-growing pathogens, enriching the view that these metabolic peculiarities are a pathogenicity strategy to remain at low population level.

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