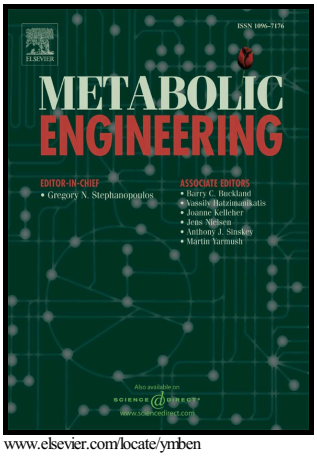

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Engineering of *Halomonas bluephagenesis* for Low Cost Production of Poly(3-hydroxybutyrate-*co*-4-hydroxybutyrate) from Glucose

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Abstract

Poly(3-hydroxybutyrate-*co*-4-hydroxybutyrate) [P(3HB-*co*-4HB)] is one of the most promising biomaterials expected to be used in a wide range of scenarios. However, its large-scale production is still hindered by the high cost. Here we report the engineering of *Halomonas bluephagenesis* as a low-cost platform for non-sterile and continuous fermentative production of P(3HB-*co*-4HB) from glucose. Two interrelated 4-hydroxybutyrate (4HB) biosynthesis pathways were constructed to guarantee 4HB monomer supply for P(3HB-*co*-4HB) synthesis by working in concert with 3-hydroxybutyrate (3HB) pathway. Interestingly, only 0.17mol% 4HB in the copolymer was obtained during shake flask studies. Pathway debugging using structurally related carbon source located the failure as insufficient 4HB accumulation. Further whole genome sequencing and comparative genomic analysis identified multiple orthologs of succinate semialdehyde dehydrogenase (*gabD*) that may compete with 4HB synthesis flux in *H.*

[1] These authors contributed equally to this work.