

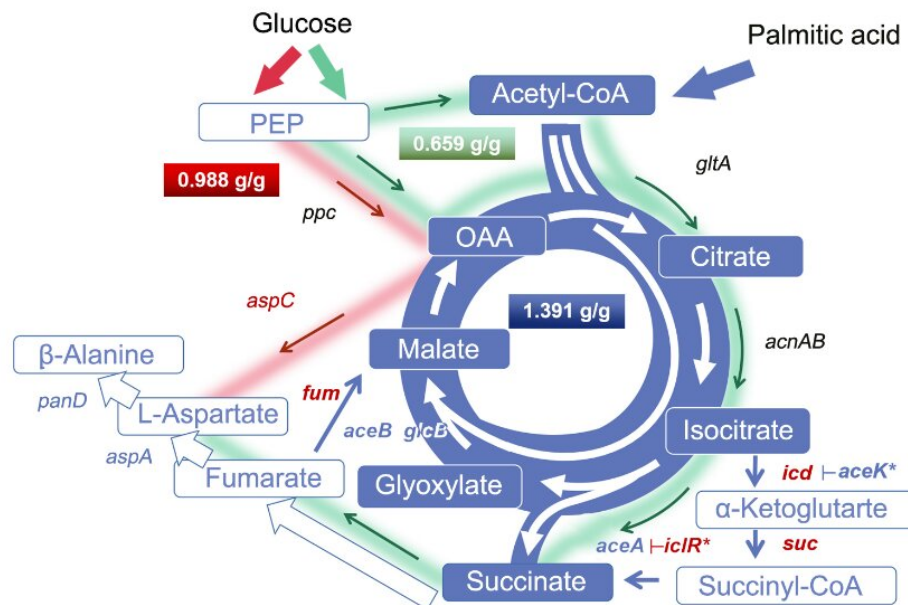
Fatty acid feedstocks enable a highly efficient glyoxylate-TCA cycle for high-yield production of β -alanine

September 1 2022

(A)

Glucose/glyoxylate shunt	$\text{Glucose} \rightarrow \text{Oxaloacetate} + 2\text{CO}_2 + 2\text{ATP} + 6\text{NADH} + \text{FADH}_2$	0.734 g/g materials
Glucose/PEPC pathway	$\text{Glucose} + 2\text{CO}_2 \rightarrow 2\text{Oxaloacetate} + 2\text{NADH}$	1.467 g/g materials
FAs/glyoxylate-TCA cycle	$\text{C16} + \text{ATP} \rightarrow 4\text{Oxaloacetate} + 15\text{NADH} + 11\text{FADH}_2$	2.064 g/g materials

(B)



(A) Comparison of metabolic pathway routes of bioproduction of C4 tricarboxylic acid (TCA) cycle intermediates (OAA) from FA or glucose

feedstocks. (B) Design of glyoxylate-TCA cycle for efficient production of TCA cycle-derived chemicals. Credit: *mLife* (2022). DOI: 10.1002/mlf2.12006

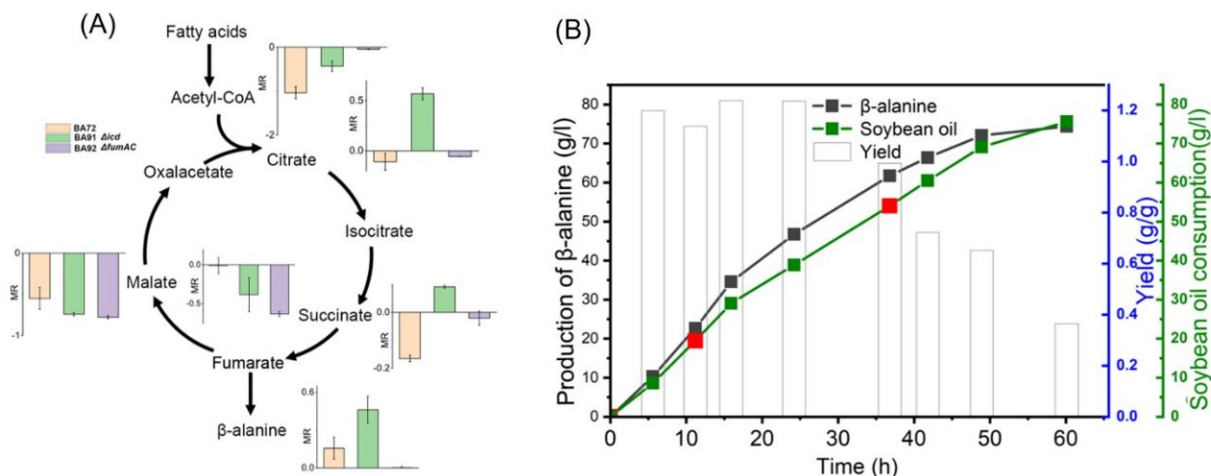
This study is led by Dr. Yong Tao (Institute of Microbiology, Chinese Academy of Sciences), Dr. Weifeng Liu (Institute of Microbiology, Chinese Academy of Sciences) and Dr. Bo Liu (Microcyto Co. Ltd.,). Fatty acids are promising alternative feedstocks to glucose and can be easily obtained from various sources, including waste oil, crude oil, and oil by-products. In recent years, Prof. Yong Tao 's group has been committed to develop economically and ecologically competitive bioproduction processes using alternative biomass. They mainly focused on fatty acid-based biomass resources.

Both Dr. Weifeng Liu and Bo Liu are the key members of this research team. "Fatty acids have a higher degree of reduction and carbon content per mass compared to glucose. Fatty acid catabolism can generate abundant acetyl-CoA serving as the precursor of many important chemicals. Meanwhile, their catabolism allows generation of more reducing equivalents required for biosynthesis and can produce chemicals with higher yield," Weifeng says.

β -Alanine is an important nonprotein amino acid derived from TCA cycle intermediates. It can be used as precursors for producing pantothenic acid, acrylamide, and acrylonitrile, which are widely applied in the production of food additives, pharmaceuticals, and bulk chemicals. β -Alanine could be produced from [fatty acids](#) with a theoretical yield of 1.391 g/g [raw materials](#) ([palmitic acid](#)), which is much higher than any route from glucose.

In this work, they found that fatty acid feedstocks could enable high-yield production of β -alanine, while maintaining an efficient and

balanced metabolic flux of the glyoxylate-TCA cycle, which is favorable for both product synthesis and [cell growth](#).



(A) Identification of the bottleneck of β -alanine yield. (B) Bioconversion of strains producing β -alanine. Credit: *mLife* (2022). DOI: 10.1002/mlf2.12006

Eventually, an efficient microbial cell factory for the sustainable production of β -alanine from fatty acid feedstocks was developed. "The production metrics are the highest reported so far. We anticipate that the principles elucidated here would provide insights into developing novel bioproduction routes in the future," Weifeng says.

The research was published in *mLife*.

More information: Yingchun Miao et al, Fatty acid feedstocks enable a highly efficient glyoxylate-TCA cycle for high-yield production of β -alanine, *mLife* (2022). [DOI: 10.1002/mlf2.12006](https://doi.org/10.1002/mlf2.12006)

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