Docket #: S21-271

Enzymatic Detoxification of Aberrant NAD(P)H Tautomers for Improved Biosynthesis of Proteins and Biochemical Commodities

Stanford researchers in the Swartz lab have developed a method for improving the productivity of biosynthetic processes via enzymatic detoxification of aberrant forms of NAD(P)H.

The 1,6- and 1,2-NAD(P)H tautomers of the reducing equivalent carrier NAD(P)H are strong inhibitors of enzyme-catalyzed redox reactions that are critical for protein synthesis and other biosynthetic processes. Since the detoxification of these aberrant forms of NAD(P)H requires molecular oxygen as a substrate, they can accumulate in anaerobic industrial bioprocesses. Even in aerobic cell-free bioprocesses, the native oxidases present are often not sufficient to detoxify these byproducts, hampering overall productivity.

In this invention, scientists in the Swartz lab have developed methods to detoxify 1,6- and 1,2-NAD(P)H with enzymes (e.g., renalase or 1,6-NAD(P)H/1,2-NAD(P)H oxidases) that use molecular oxygen to convert these aberrant forms back into the original NAD(P)H. For the case of anaerobic bioprocesses, this invention also provides methods for establishing a secondary bioreactor for this aerobic reaction and for managing the input and removal of molecular oxygen as the biosynthetic mixture leaves and reenters between the main anaerobic reactor and a secondary aerobic bioreactor. When added to an existing industrial biosynthesis process, this technology can greatly improve the efficiency of the production of proteins and other biochemicals at scale by removing these inhibitory byproducts.

Related Technologies
Swartz lab inventions S21-276 and S21-281 can be combined with this technology in

a carbon-negative process for synthesizing biochemical commodities.

Applications

- Cell-free protein synthesis
- Biofuel production
- Biopharmaceutical production
- Bioproduction of agricultural commodities

Advantages

- **Improved productivity**: Enzymatic conversion of aberrant NAD(P)H tautomers back to NAD(P)H improves efficiency of redox reactions in both aerobic and anaerobic biosynthetic reactors
- **Novel**: No method or device yet exists for removal of these inhibitory forms of NAD(P)H

Patents

- Published Application: WO2024215747
- Published Application: 20260275396

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