The uracil metabolism in the Tetanus vaccine fermentation process.

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Clostridium tetani is an anaerobe pathogen that causes tetanus by producing one of the most potent toxin known, the tetanus neurotoxin (TeNT). Extensive immunisation programs have kept the disease controlled in humans. However, despite more than half a century of industrial fermentation for vaccine production, the physiological behaviour controlling toxin production in bioreactors is not well understood. This makes production inefficient and costly, with batch-to-batch variability and irregular toxin yields.
In order to have an insight of the intricate toxin regulation mechanisms, *C. tetani* was grown in bioreactors using two conditions, yielding different toxin yields. Using intracellular and extracellular metabolomics, we compared the bacteria metabolic responses to these two conditions and we complemented the approach using time course transcriptomics. We focused our analysis on amino acid, vitamin and nucleotides and we observed that the uracil consumption was different in the two conditions. Our data showed that the uracil consumption behavior in this bacterium regulates the *de novo* pyrimidine biosynthesis as well as other metabolic pathways, such as toxin synthesis. Ultimately, the extensive metabolomics dataset will contribute to a better understanding of the Tetanus vaccine fermentation process and will be used for the future design of a chemical defined medium to avoid the inherent variability.
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