

CLAIMS

What is claimed is:

1. An engineered microbial cell comprising:
 - a plurality of microbial cells;
 - the microbial cells expressing at least two exogenous polypeptides, including a first exogenous polypeptide and a second exogenous polypeptide;
 - the first exogenous polypeptide is a uric acid degrading polypeptide; and
 - the second exogenous polypeptide is a uric acid transporter that brings in uric acid from outside of the microbial cells.
2. The engineered microbial cell of claim 1, further comprising:
 - the uric acid transporter is at least 60% homologous to a uric acid transporter selected from a group, or a combination selected from the group, consisting of: *Aspergillus nidulans* UapA [SEQ ID NO: 9], *Aspergillus nidulans* UapC [SEQ ID NO: 10], *Aspergillus fumigatus* UapC [SEQ ID NO: 11], *Candida albicans* Xut1 [SEQ ID NO: 12], *Schizosaccharomyces pombe* Q9HE12 [SEQ ID NO: 13], *Bacillus subtilis* PucK [SEQ ID NO: 14], *Bacillus subtilis* PucJ [SEQ ID NO: 15], *Escherichia coli* YgfU [SEQ ID NO: 16], *Zygosaccharomyces parabailii* AQZ18664 [SEQ ID NO: 17], or *Spirosoma sp.* KCTC 42546 WP_142773020 [SEQ ID NO: 18].
3. The engineered microbial cell of claim 2, further comprising:
 - the microbial cells are fungal cells.

4. The engineered microbial cell of claim 3, further comprising:
the uric acid degrading polypeptide is a uricase.
5. The engineered microbial cell of claim 4, further comprising:
the uricase is a fungal uricase.
6. The engineered microbial cell of claim 5, further comprising:
the fungal uricase is selected from a group, or a combination selected from the group,
consisting of: *Candida utilis* [SEQ ID NO: 1], *Aspergillus flavus* [SEQ ID NO: 2],
Schizosaccharomyces pombe [SEQ ID NO: 5], or *Zygosaccharomyces parabailii*
[SEQ ID NO: 7].
7. The engineered microbial cell of claim 4, further comprising:
the uricase is a bacterial uricase.
8. The engineered microbial cell of claim 7, further comprising:
The bacterial uricase is selected from a group, or a combination selected from the
group, consisting of: *Arthrobacter globiformis* [SEQ ID NO: 2], *Bacillus subtilis*
[SEQ ID NO: 6], or *Spirosoma sp.* [SEQ ID NO: 8].
9. The engineered microbial cell of claim 4, further comprising:
the uricase is a mutant uricase, including chimera and/or overexpression variants of
the uricase.

10. The engineered microbial cell of claim 9, further comprising:
the mutant uricase is a porcine-baboon chimera uricase [SEQ ID NO: 4].
11. The engineered microbial cell of claim 2, further comprising:
the microbial cells are bacterial cells.
12. The engineered microbial cell of claim 11, further comprising:
the uric acid degrading polypeptide is a uricase.
13. The engineered microbial cell of claim 12, further comprising:
the uricase is a fungal uricase.
14. The engineered microbial cell of claim 13, further comprising:
the fungal uricase is selected from a group, or a combination selected from the group,
consisting of: *Candida utilis* [SEQ ID NO:1], *Aspergillus flavus* [SEQ ID NO: 2],
Arthrobacter globiformis [SEQ ID NO: 3], Chimeric porcine baboon [SEQ ID
NO: 4], *Schizosaccharomyces pombe* [SEQ ID NO: 5], or *Zygosaccharomyces
parabailii* [SEQ ID NO: 7].
15. The engineered microbial cell of claim 12, further comprising:
the uricase is a bacterial uricase.

16. The engineered microbial cell of claim 15, further comprising:

The bacterial uricase is selected from a group, or a combination selected from the group, consisting of: *Arthrobacter globiformis* [SEQ ID NO: 2], *Bacillus subtilis* [SEQ ID NO: 6], or *Spirosoma sp.* [SEQ ID NO: 8].

17. The engineered microbial cell of claim 12, further comprising:

the uricase is a mutant uricase, including chimera and/or overexpression variants of the uricase.

18. The engineered microbial cell of claim 17, further comprising:

the mutant uricase is porcine-baboon chimera uricase [SEQ ID NO: 4].

19. A method of lowering uric acid in the gastrointestinal tract of a recipient, comprising the steps of:

preparing a therapeutically effective dose of the engineered microbial cell selected from a group, or a combination selected from the group, consisting of: claims 1-18;

orally administering the therapeutically effective dose; and

allowing time for the selected engineered microbial cell to transport and degrade uric acid.

20. A method for treating a patient suffering from a condition selected from a group, or a combination selected from the group, consisting of: gout, rheumatoid arthritis, cerebral stroke, heart disease, arrhythmia, chronic renal disease, and chronic refractory gout; the method comprising the steps of:
- determining whether the patient has a serum uric acid level of ≥ 6.8 mg/dl prior to initiating urate lowering therapy; and
 - if the patient has a serum uric acid level of ≥ 6.8 mg/dl prior to initiating urate lowering therapy, then orally administering the engineered microbial cell selected from a group, or a combination selected from the group, consisting of: claims 1-18, in an amount of 10^6 to 10^{12} microbial cells.
21. The method for treating a patient of claim 20, further comprising:
- the amount of microbial cells orally administered is approximately 10^9 cells.
22. The method for treating a patient of claim 20, further comprising:
- the condition selected from a group, or a combination selected from the group, is chronic refractory gout.
23. The method for treating a patient of claim 20, further comprising:
- the engineered microbial cell selected from a group, or a combination selected from the group, is administered with a pharmaceutically acceptable carrier.
24. A method for determining uric acid degradation, comprising the steps of:
- creating an assay solution including an assay buffer and a uric acid solution;
 - selecting a cell;
 - washing and suspending the cell in the assay solution;

incubating the cell in the assay solution at conditions acceptable for uric acid degradation;
sampling aliquots of the assay solution at intervals; and
measuring absorbance of the aliquots in a spectrophotometer at substantially a wavelength of 293nm.

25. A method of identifying uric acid degrading polypeptides, comprising the steps of:

selecting a cell that expresses a uric acid transporter polypeptide;
operatively linking a promoter that is functional in the cell to a nucleotide sequence encoding a putative uric acid degrading polypeptide;
introducing the promoter linked to the nucleotide sequence encoding the putative uric acid degrading polypeptide into the cell;
performing the method of claim 24; and
identifying and quantifying whether uric acid degrading increased.

26. The method of identifying uric acid degrading polypeptides of claim 25, further comprising the steps of:

the uric acid transporter polypeptide of the cell is selected from a group, or a combination selected from the group, consisting of: SEQ ID NO: 9-18.

27. A method of identifying uric acid transporters, comprising the steps of:
- selecting a cell that expresses a uric acid degrading polypeptide;
 - operatively linking a promoter that is functional in the cell to a nucleotide sequence encoding a putative uric acid transporter polypeptide;
 - introducing the promoter linked to the nucleotide sequence encoding the putative uric acid transporter polypeptide into the cell;
 - performing the method of claim 24; and
 - identifying and quantifying whether uric acid degrading increased.
28. The method of identifying uric acid transporter of claim 27, further comprising the steps of:
- the uric acid degrading polypeptide of the cell is selected from a group, or a combination selected from the group, consisting of: SEQ ID NO: 1-8.
29. An engineered microbial cell, comprising:
- a cell expressing the uric acid degrading polypeptide identified by the methods of either claim 25 or claim 26; and
 - the cell expressing the uric acid transporter polypeptide identified by the methods of either claim 27 or claim 28.