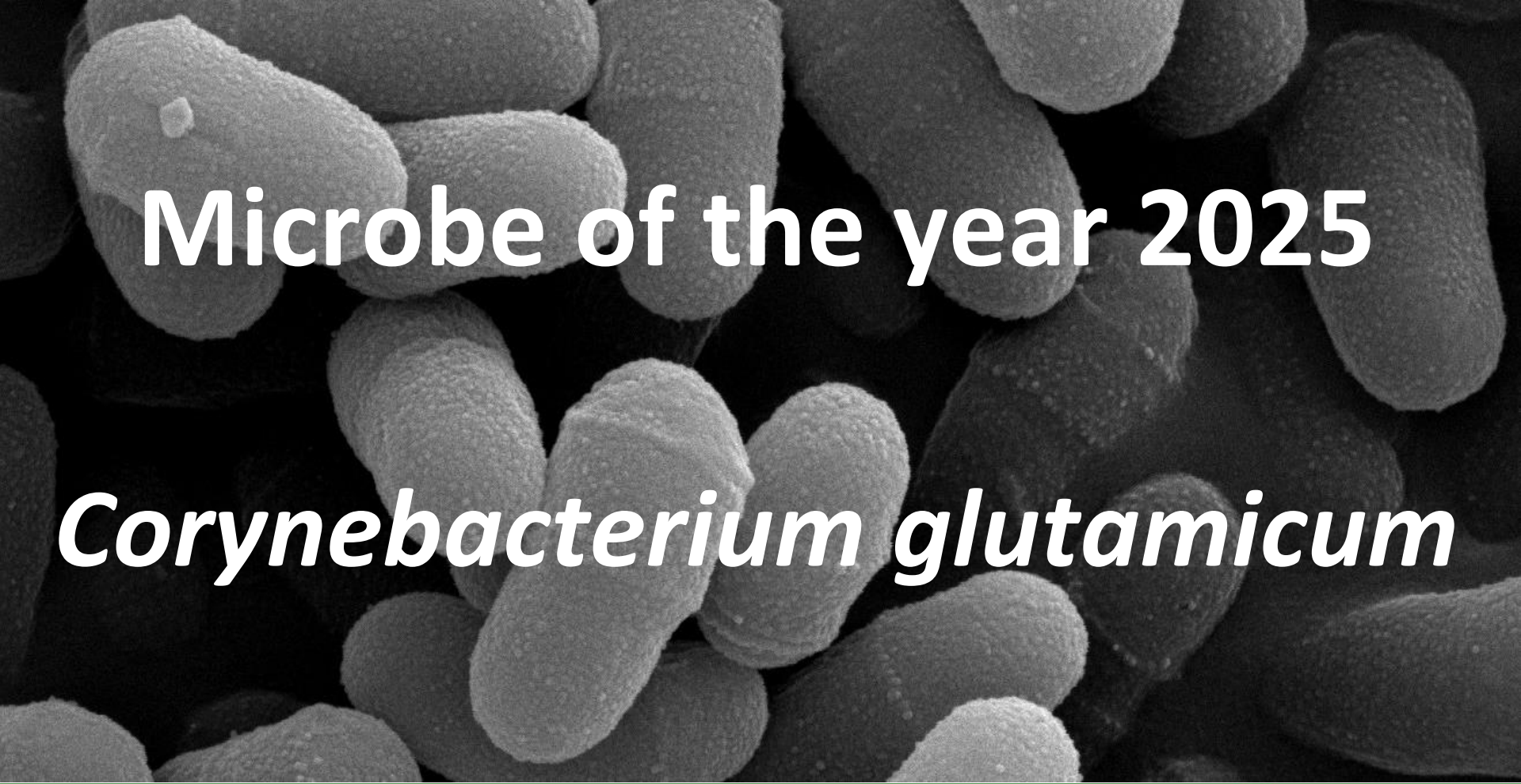
Mikrobe des Jahres

Vereinigung für Allgemeine und Angewandte Mikrobiologie



Microbe of the year 2025

Corynebacterium glutamicum

Scanning electron micrograph by Meike Baumgart (FZ Jülich),
Mareike Hoß and Hiltrud Königs (RWTH Aachen)

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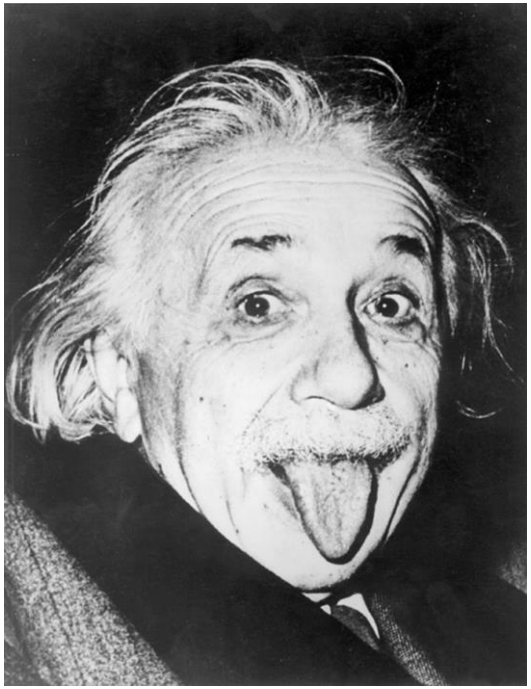
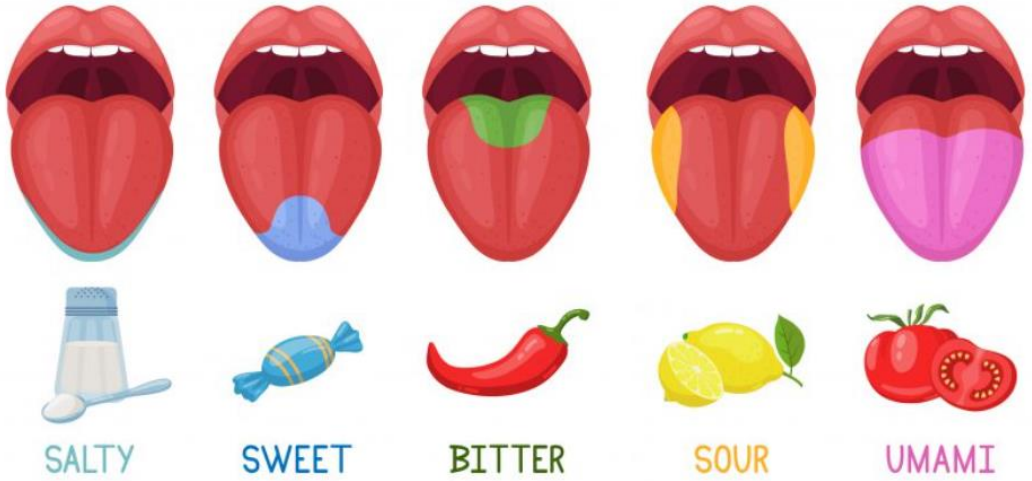
Microbe of the Year 2025



© picture-alliance/akg-images
Photo by Arthur Sasse 1951



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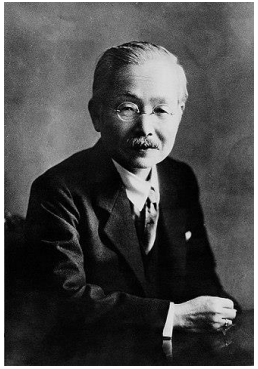
The basis of the umami taste

Monosodium glutamate (MSG)



1908: Prof. Kikunae Ikeda identifies monosodium glutamate (MSG), which he isolated from the seaweed Kombu, as being responsible for a taste he called „Umami“. The word is derived from „umai“ (jap.: うまい) for delicious and „mi“ (jap.: 味) for taste. Together with a partner Prof. Ikeda founded the company Ajinomoto, which marketed MSG isolated from hydrolyzed plant proteins.

Photo: Hashimoto (2016)
Adv Biochem Eng Biotechnol

Photos: Umami information center

Corynebacterium glutamicum

A natural glutamate-secreting microbe

1957: Dr. Shigezo Udaka and Dr. Shukuo Kinoshita of the company Kyowa Hakko Kogyo isolate *Corynebacterium glutamicum* (originally *Micrococcus glutamicus* strain no. 534) in a screen for glutamate-secreting bacteria.

1958: industrial glutamate production with *Corynebacterium glutamicum* started and marked the birth of fermentative amino acid production, which today is a multibillion dollar business.

The soil sample from which *Corynebacterium glutamicum* was isolated came from the Ueno Zoo in Tokyo.

Fig. 2 Bioassay screening of glutamate-producing microorganisms. Glutamate productivity of the test strain can be estimated by the scale of the halo formed around the strain. The photo is reprinted under the kind permission of Kyowa Hakko Bio Co. Ltd.

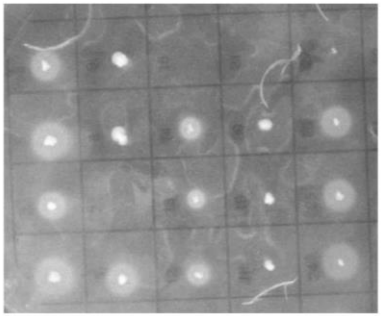


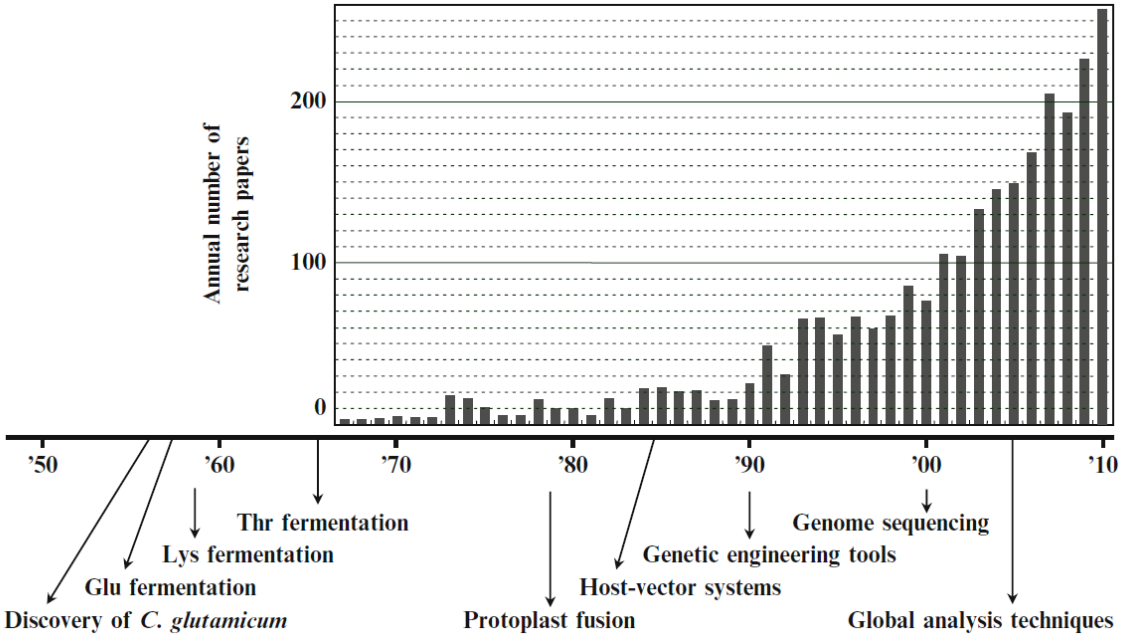
Photo: Hashimoto (2016) Adv Biochem Eng Biotechnol

Photo: picture cells / Shutterstock.com

Hashimoto 2017 Discovery and History of Amino Acid Fermentation. Advances in Biochemical Engineering and Biotechnology 159: 15–34

Corynebacterium glutamicum

History of amino acid fermentation and strain development



German microbiologists at Forschungszentrum Jülich and Bielefeld University started research on the metabolism and the development of genetic tools for *Corynebacterium glutamicum* around 1985.

Ikeda and Takeno (2013) Corynebacterium glutamicum – Biology and Biotechnology, 1st. ed., Springer Verlag

Mikrobe des Jahres

Corynebacterium glutamicum

Major academic research spots in Germany

JÜLICH Forschungszentrum

UNIVERSITÄT BIELEFELD

UNIVERSITÄT ZU KÖLN

universität ulm

FAU Friedrich-Alexander-Universität Erlangen-Nürnberg

UNIVERSITÄT DES SAARLANDES

RUHR UNIVERSITÄT BOCHUM RUB

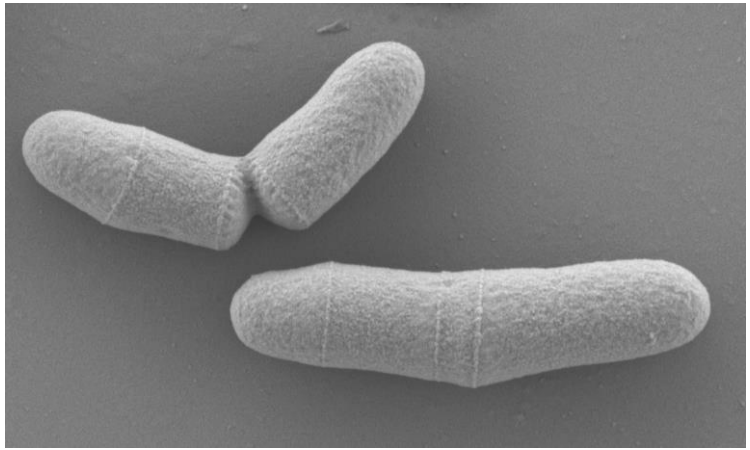
CAU Kiel University Christian-Albrechts-Universität zu Kiel

Technische Universität München

Corynebacterium glutamicum

The club-shaped bacterium

- member of the *Actinobacteria*, order *Mycobacteriales*
- non-pathogenic, immobile, no spore formation, circular genome of 3.3 million basepairs
- typically rod-shaped or “club-shaped” (coryneform)
- “V-snapping” - this unique arrangement is due to the one-sided cracking after cell division
- prefers aerobic growth, limited potential for anaerobic growth by nitrate respiration and mixed-acid fermentation
- moderate growth rate of about 0.3-0.6 h^{-1}, maximum reported 0.94 h^{-1} (doubling time 70-140 minutes)



Scanning electron micrograph by Urska Repnik & Marc Bramkamp (Kiel)

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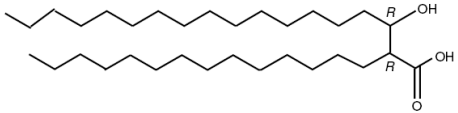
Corynebacterium glutamicum

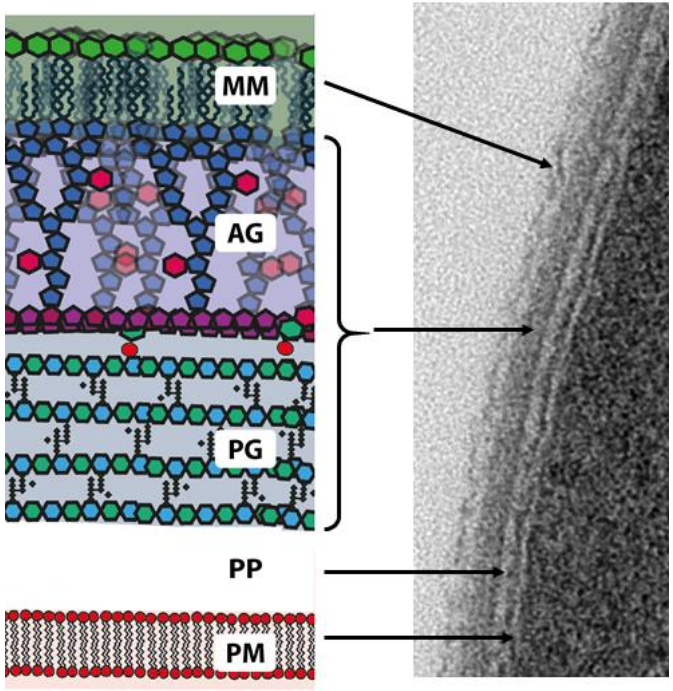
The complex cell envelope

- after the cytoplasmic membrane (PM) and the periplasm (PP) the cell envelope is composed of a thick peptidoglycan layer (PG), an arabinogalactan layer (AG), and an outer membrane of mycolic acids, also called mycomembrane



2-Alkyl 3-hydroxy fatty acids

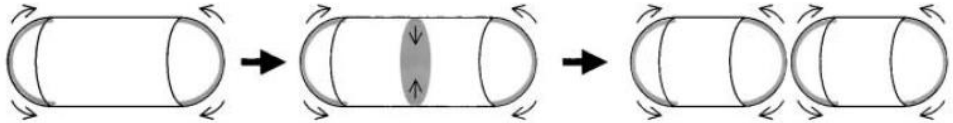
- mycolic acids are 2-alkyl 3-hydroxy fatty acids that form esters with the disaccharide trehalose; the length of the mycolic acids can strongly vary
- *Corynebacterium* species have short mycolic acids, whereas *Mycobacterium* species have very long mycolic acids, rendering them acid-fast and very resistant against antibiotics



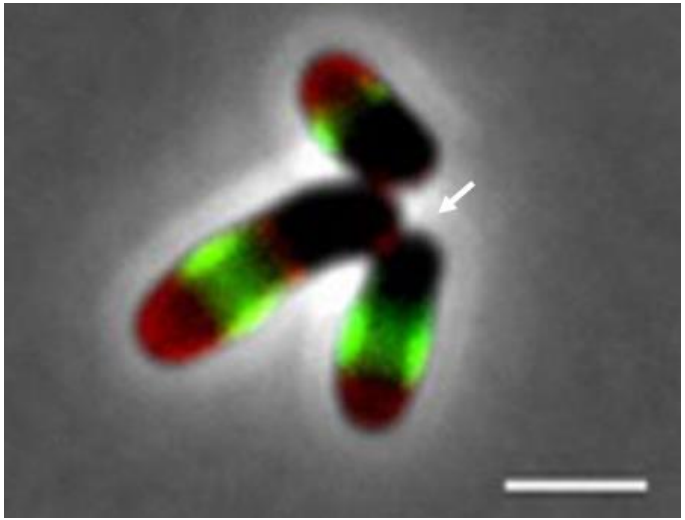
adapted from Meyer et al. (2023) The Cell Surface

Corynebacterium glutamicum

Polar growth



- cells grow at their cell poles (like all actinobacteria)
- apical cell growth is coordinated by a conserved scaffold protein, DivIVA
- the old cell pole initially grows faster, while the young cell pole catches up in the course of the cell cycle (asymptotic linear growth)
- this atypical growth mode enables the maintenance of a relatively homogeneous cell length distribution



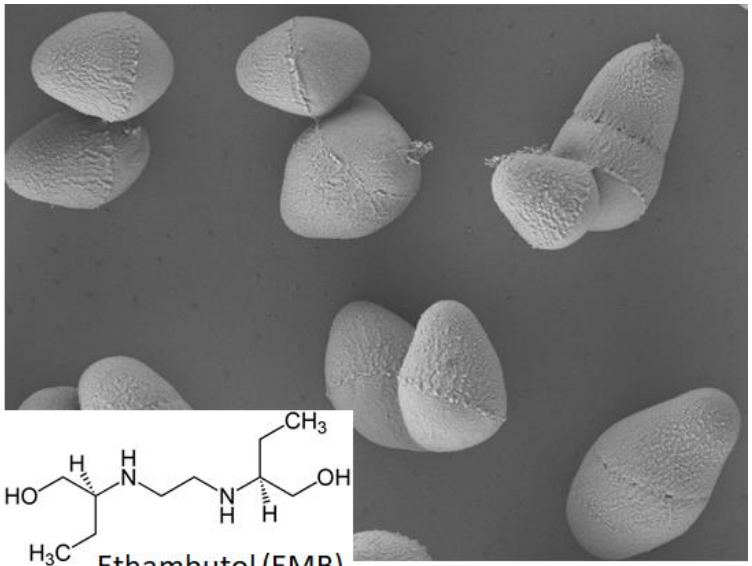
Bioorthogonal labeling of active cell wall synthesis after “pulse-chase” with two dyes (first green and then red). Old poles are more strongly colored than the young cell poles (white arrow).
Schubert et al. (2017) mBio

Daniel and Errington (2003) Cell
Schubert et al. (2017) mBio, Meyer and Bramkamp (2024) Curr Opin Microbiol

Corynebacterium glutamicum

The pathogenic relatives

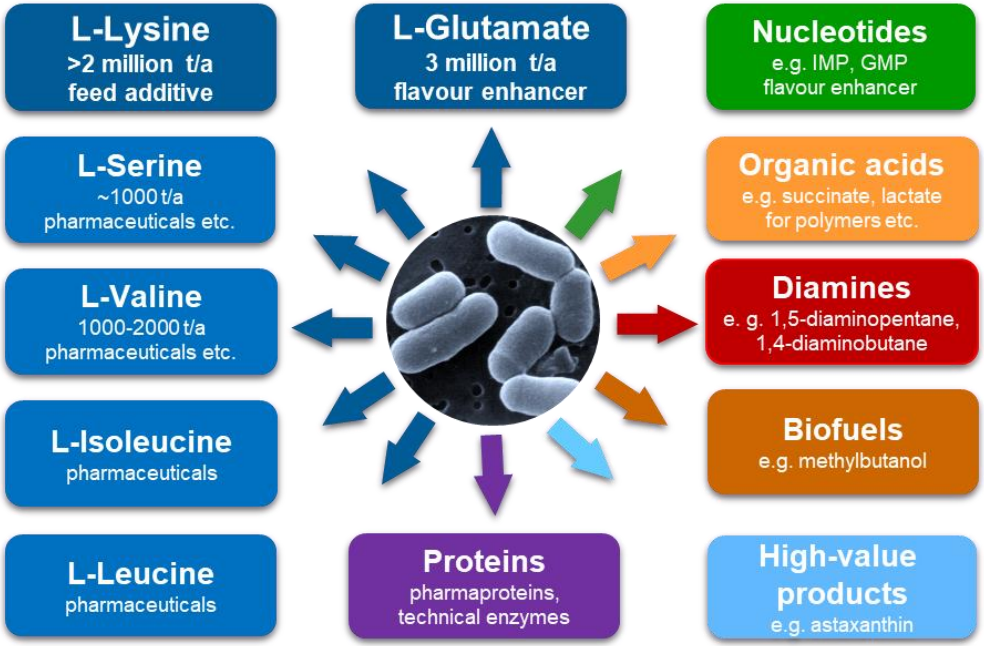
- ***Corynebacterium diphtheriae*** causes diphtheria by the diphtheria toxin (DT); major cause of child death until the beginning of the 20th century
- Emil von Behring received first Nobel Prize for Physiology or Medicine in 1901 for the development of serum therapy, in particular for DT antitoxin
- ***Mycobacterium tuberculosis***, the causative agent of tuberculosis, is still the deadliest infection caused by a single microorganism
- many antibiotics used for treating tuberculosis inhibit cell envelope synthesis, such as ethambutol; also corynebacteria are sensitive to these cell-wall targeting antibiotics



Scanning electron micrograph of EMB-treated cells by Urska Repnik & Marc Bramkamp (Kiel)

Corynebacterium glutamicum

An important industrial cell factory for amino acids and more



The main products produced by *Corynebacterium glutamicum* are the amino acids L-glutamate and L-lysine. In addition, production strains have also been developed for many other amino acids and a broad spectrum of other products.

Companies using *Corynebacterium glutamicum*:

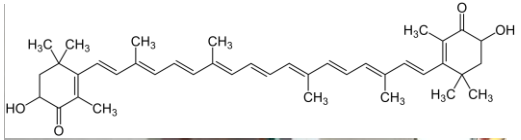
- Ajinomoto (Japan)
- ADM (USA)
- CJ (South-Korea)
- Evonik (Germany)
- Meihua (China)

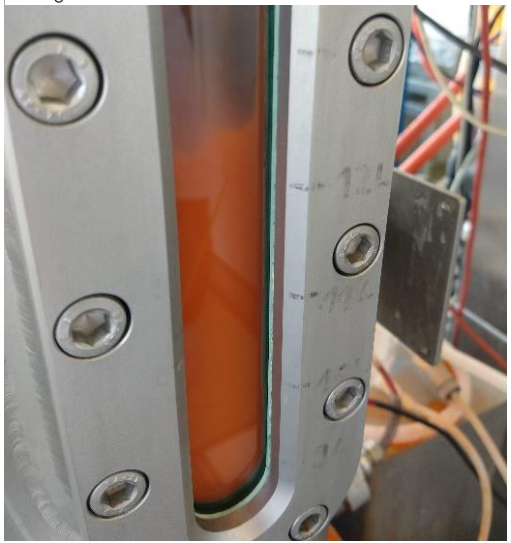
Eggeling and Bott (2015) Appl Microbiol Biotechnol,
Wendisch et al. (2016) World J Microbiol Biotechnol, Wolf et al. (2021) Essays Biochem

Corynebacterium glutamicum

High value products: Astaxanthin

- the metabolism of *C. glutamicum* was specifically optimized for the production of the antioxidant carotenoid astaxanthin, which has an intense red color (see photo on the right)
- strains were developed for the co-production of astaxanthin and the amino acid L-lysine, both of which are used as feed additives; astaxanthin remains bound to the cells, L-lysine is excreted into the medium
- in addition to glucose and sucrose, pentoses (C5 sugars) or waste materials from salmon aquacultures can also be used as carbon sources and enable a circular bioeconomy





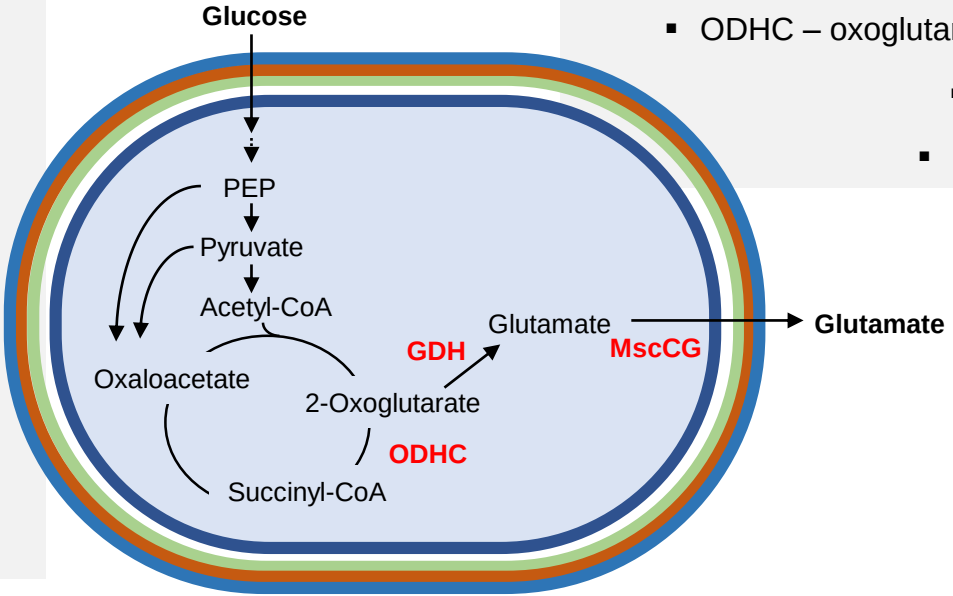
Henke et al. (2018) Bioresource Technology
Photo by Florian Meyer (Bielefeld University)

Corynebacterium glutamicum

Towards the secrets of glutamate excretion

Conditions inducing glutamate secretion by the wild type affect cell envelope composition and integrity:

- biotin limitation □ reduced fatty & mycolic acid synthesis
- ethambutol □ inhibits arabinogalactan synthesis
- penicillin □ disturbed peptidoglycan synthesis
- Tween 40 □ altered cell envelope



Key players for glutamate synthesis and secretion:

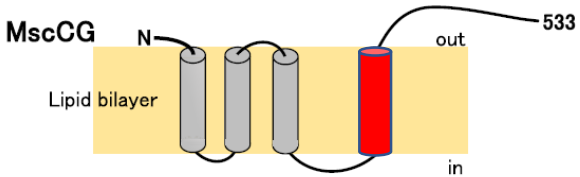
- ODHC – oxoglutarate dehydrogenase complex
- Glutamate dehydrogenase
- MscCG – glutamate exporter

Schultz et al. (2007) Appl Microbiol Biotechnol
Nakamura et al. (2007) Appl Environm Microbiol

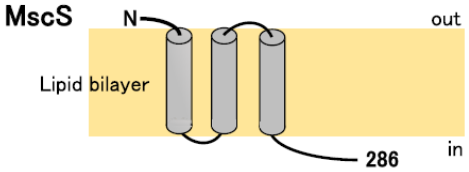
Corynebacterium glutamicum

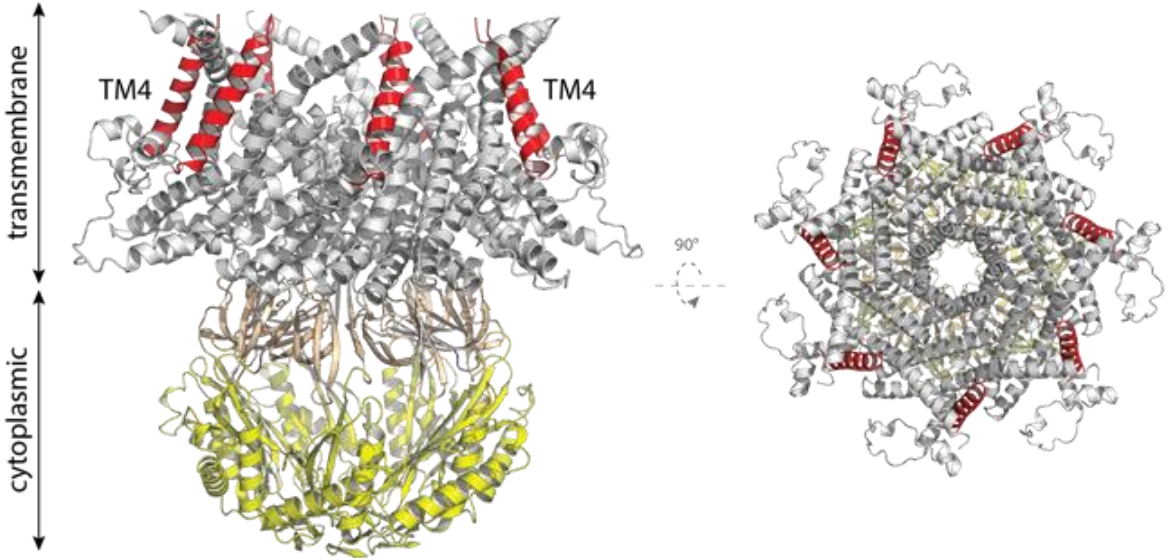
An unusual mechanosensitive channel for glutamate secretion

C. glutamicum MscCG



Escherichia coli MscS



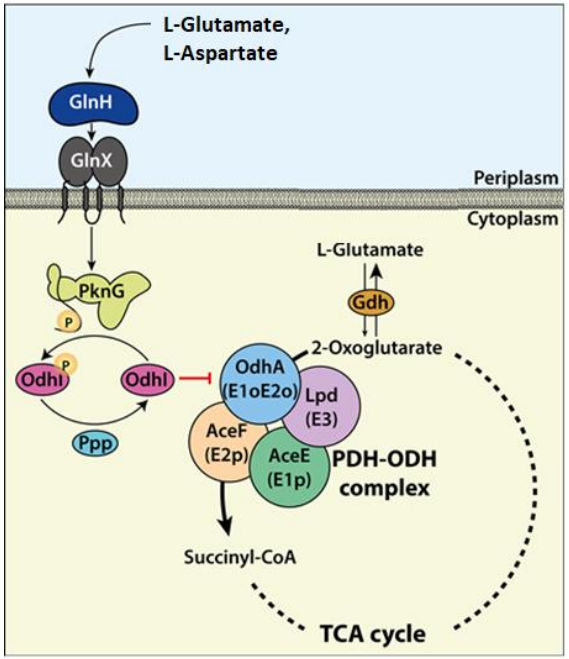


AlphaFold model of the MscCG heptamer without unstructured regions (residues 292-348 and 422-533)

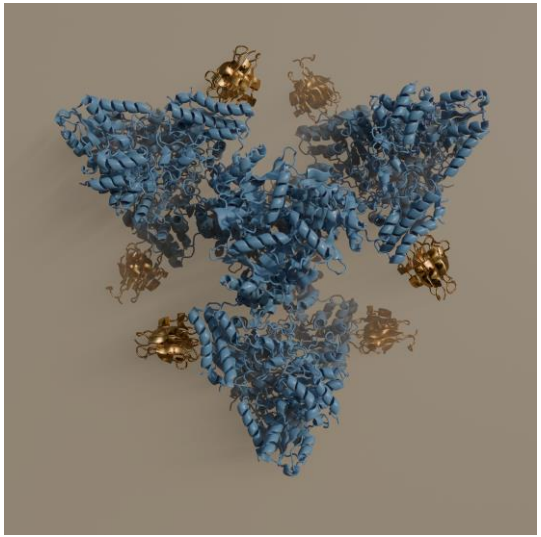
Kawasaki & Martinac (2020) Curr Opin Chem Biol
Becker & Krämer (2015) Eur Biophys J

Corynebacterium glutamicum

An atypical 2-oxoglutarate dehydrogenase



- forms a hybrid complex with pyruvate dehydrogenase composed of four subunits AceE, OdhA, AceF, Lpd
- hybrid complex localized at the cell poles
- ODH activity is controlled by OdhI, which binds to OdhA subunit and inhibits ODH
- ODH inhibition relieved by phosphorylation of OdhI via Ser/Thr protein kinase PknG
- PknG activity is controlled by a signal transduction cascade composed of the proteins GlnH and GlnX



Cryo-EM structure of the hexameric OdhA-OdhI complex
Yang et al. (2023) Nat Commun

Niebisch et al. (2006) J Biol Chem; Bott (2007) Trends Microbiol
Sundermeyer et al. (2022) Microbiol Spectr; Sundermeyer et al. (2023) Microbiol Spectr

Mikrobe des Jahres

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