Self-assembling amino acid therapeutics

Yukio Nagasaki University of Tsukuba, Japan

Amino acids are important molecules for health and life

Many types of amino acid supplements are available on the market.

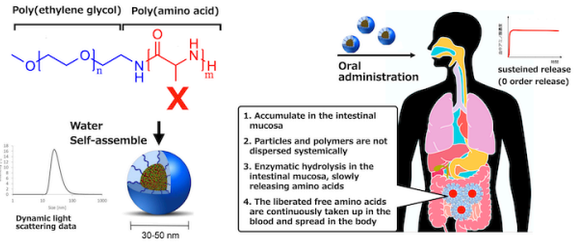
The effect is insufficient for the following reasons.
1. Rapid metabolism
2. Rapid excretion

New strategy must be required!

筑波大学長崎研究室

Design of novel amino acid delivery system

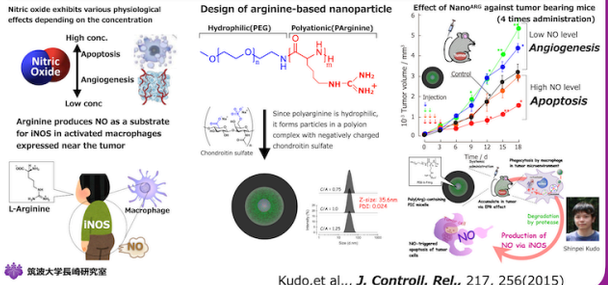
We designed a diblock copolymer micelle with poly (amino acid) as one of the segments. Peptide groups are enzymatically hydrolyzed, slowly releasing the corresponding amino acids and preventing their rapid metabolism.



筑波大学長崎研究室

Design of arginine based nanoparticle (Nano^{ARG}) against cancer therapy

Arginine is known to have various physiological activities, and in particular, it is known to generate NO as a substrate for nitric oxide synthase (NOS). The physiological activity of NO differs depending on its concentration, and low concentration induces angiogenesis and blood flow increase, and high concentration induces apoptosis. Therefore, if NO can be generated in the vicinity of the tumor at a high level, it can be expected to suppress the growth of cancer cells. However, NO has a short life span and spreads quickly, making it difficult to act in the vicinity of the tumor. Therefore, self-assembled nanoparticles were prepared and evaluated as shown below.

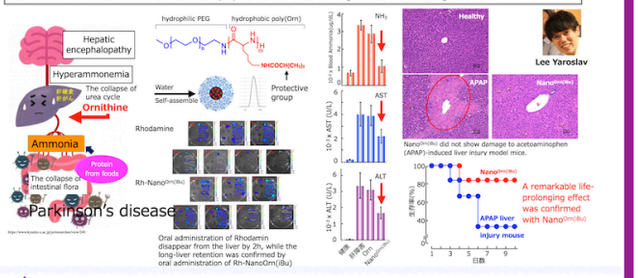


Kudo,et al.,, ***J. Controll. Rel.,*** 217, 256(2015)

筑波大学長崎研究室

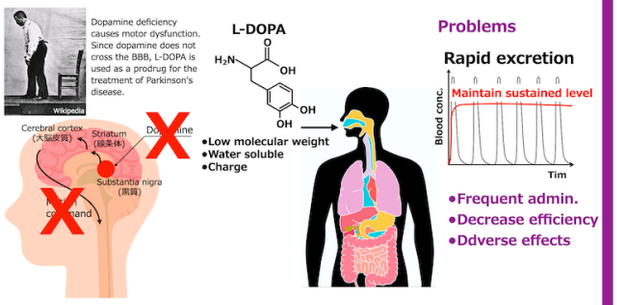
Ornithine nanoparticle and liver injury

The urea cycle is a pathway that produces urea from ammonia, mainly in the liver, and is composed of four amino acids: ornithine, citrulline, argininosuccinic acid, and arginine. Urea cycle abnormality refers to a group of diseases that develop due to symptoms such as hyperammonemia due to a congenital abnormality in the metabolic system of the urea synthesis pathway. Although improvement is attempted by administering ornithine, the water-soluble small molecule ornithine is metabolized rapidly and has little effect. We designed nano-ornithine and got the effect.



Vong, et al., ***J. Controll. Rel.***,310, 74 (2019)

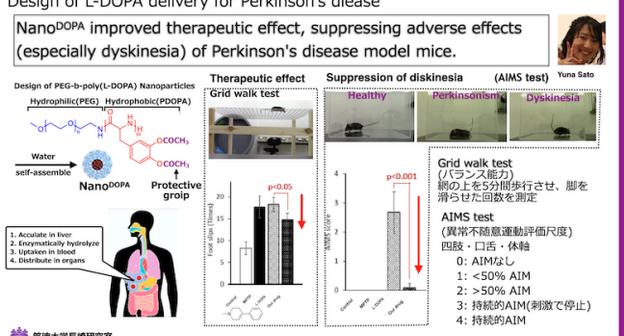
筑波大学長崎研究室



筑波大学長崎研究室

Design of L-DOPA delivery for Perkinson's diease

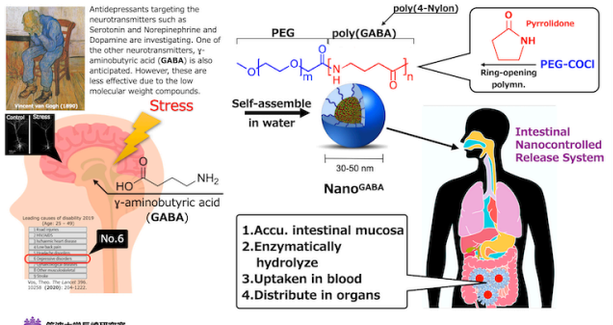
Nano^{DOPA} improved therapeutic effect, suppressing adverse effects (especially dyskinesia) of Perkinson's disease model mice.



Vong, et al., ***Acta Biomaterialia, 109, 220(2020)***

筑波大学長崎研究室

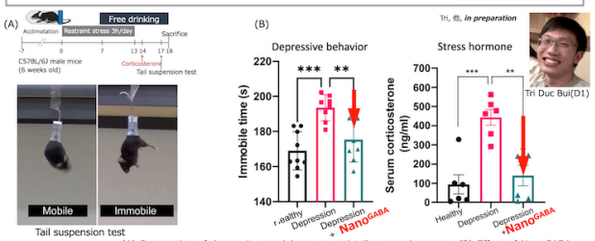
Major depressive disorder (鬱病) and Nano^{GABA}



筑波大学長崎研究室

Effect of Nano^{GABA} to Major depressive disorder (鬱病)

Although it is not an amino acid, γ-aminobutyric acid (GABA) has various physiological and pharmacological activities. Because its metabolism is very fast, it is only provided as a supplement. Therefore, we have designed it as a self-assembling drug and confirmed that a high effect was observed for the depression model mouse. γ-Aminobutyric acid: NH_2-$CH_2CH_2CH_2$-COOH



(A) Preparation of depression model mouse and tail suspension tests; (B) Effect of NanoGABA on depression model mice [(Left) tail suspension test, (Right) Blood corticosterone level.

筑波大学長崎研究室

Conclusion

Contact address: nagasaki@ims.tsukuba.ac.jp

The newly designed PEG-b-poly(amino acid) block copolymers were self-assembled in water (Nano^{AA}). Nano^{AA} accumulated in the intestinal mucosa by oral administration, hydrolyzed by intestinal enzymes, released corresponding amino acids, and were taken up in the blood. As a result, there was no unpleasant odor, amino acids were continuously supplied, and side effects were reduced almost completely. As a result, it functions effectively for various diseases such as cancer, liver injury, Perkinson's disease, and depression. Therefore, Nano^{AA}s are expected as promising novel drugs.