

Tick Tock: a new test for rapid Lyme disease diagnosis

With a wealth of experience in Lyme disease (LD) research, **Dr Maria Gomes-Solecki** from the University of Tennessee has turned her attention and expertise to LD diagnosis. A new device, developed by Dr Gomes-Solecki (Immuno Technologies, Inc) in collaboration with Dr Sam Sia (Columbia University), provides rapid diagnosis of LD at the point of care, allowing prompt prognosis decisions and treatment delivery.

Lyme disease (LD) is the most common tick-borne illness in the US and is also highly prevalent throughout Northern Hemisphere temperate regions, including Europe, Mongolia and China. As reported by the Centres for Disease Control and Prevention, the spread of LD is a rapidly growing problem, affecting more people year on year. Cases of the disease are estimated to have doubled in the US over the last decade, and an estimated 300,000 people contract the disease there each year.

Sufferers of LD can experience a wide range of non-specific symptoms that develop gradually as the disease progresses from early to late stage. The disease can affect the skin, joints, heart and nervous system and symptoms often overlap with other illnesses, presenting significant difficulties in diagnosis. If progressed to late stage, LD can result in permanent damage to the musculoskeletal and nervous systems, antibiotic-refractory arthritis and post-treatment Lyme disease syndrome (ongoing fatigue, pain, and joint and muscle aches that persist after treatment is completed).

A HISTORY OF SUCCESS

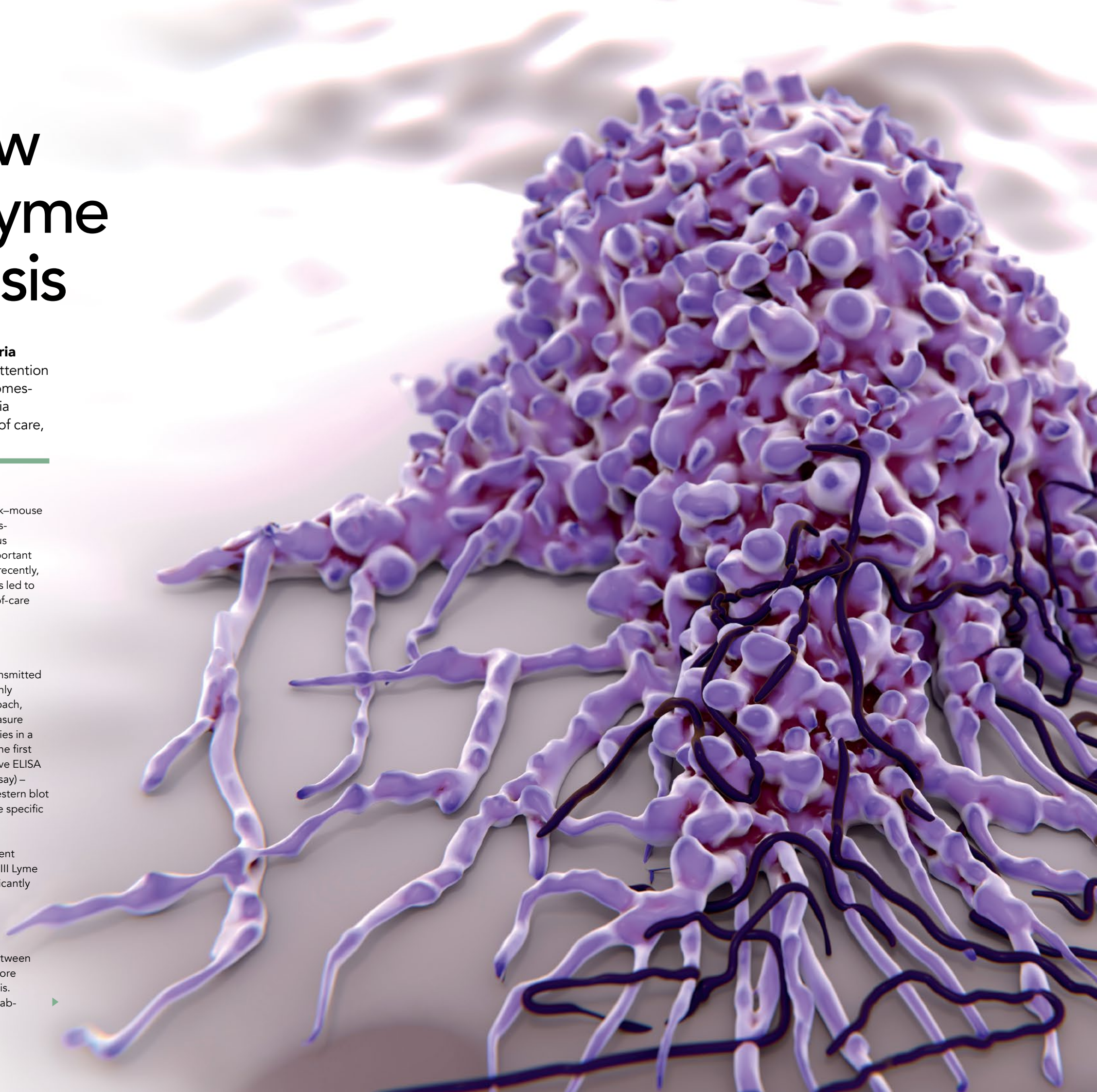
Dr Gomes-Solecki has an impressive track record when it comes to LD research. In a previous project, an oral bait vaccine developed in Dr Gomes-Solecki's laboratory

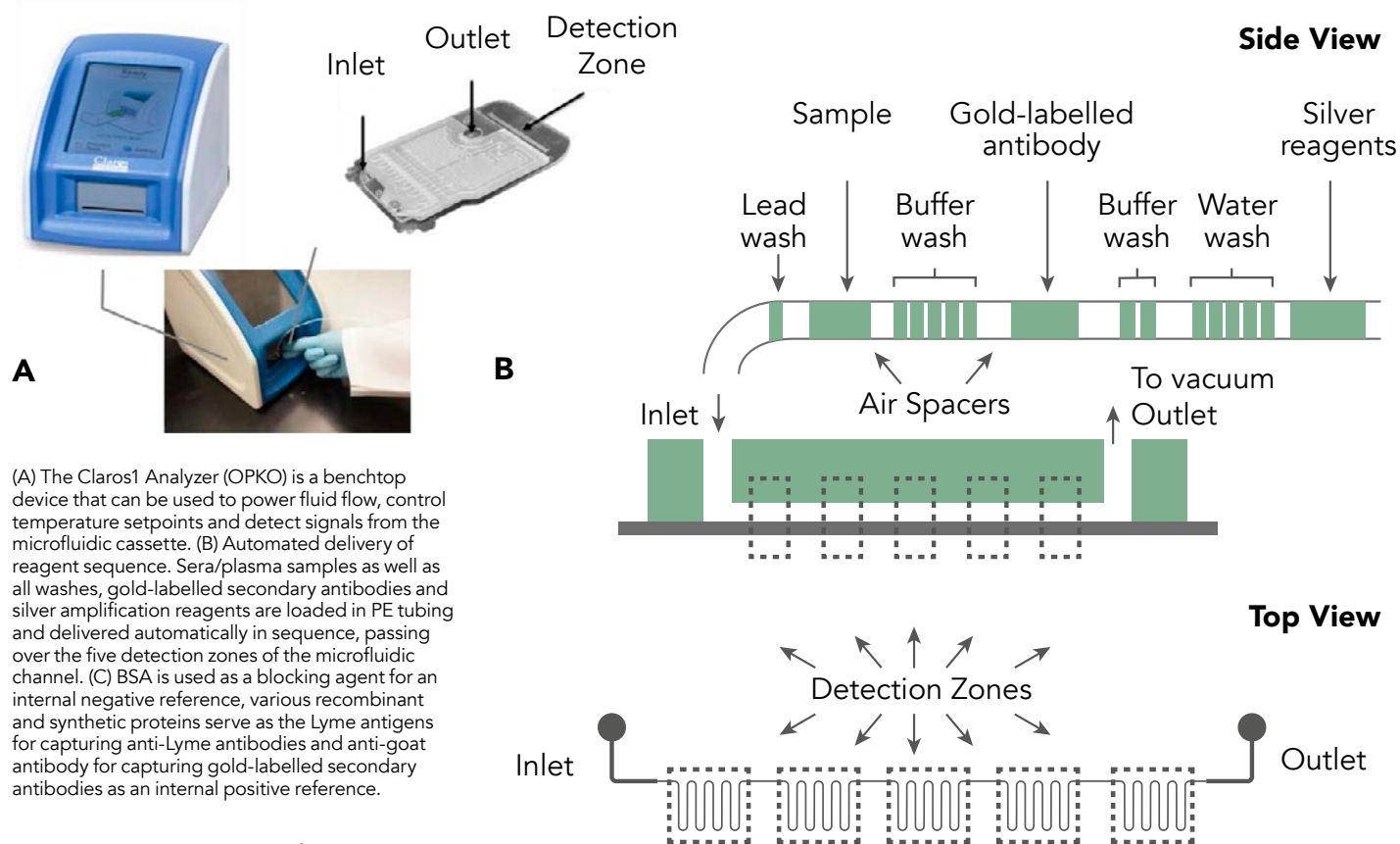
was shown to break the cycle of tick-mouse LD transmission. In 2014, Dr Gomes-Solecki was awarded the prestigious MBQ Innovation Award for this important contribution to LD research. More recently, her continued focus in LD diagnosis led to the development of a rapid point-of-care diagnostic test.

A MATTER OF TIME

Lyme disease is caused by *Borrelia burgdorferi*, a bacterial species transmitted by ticks. Current diagnosis commonly uses a two-tiered serological approach, a series of lab-based tests that measure the *B. burgdorferi*-specific antibodies in a patient's blood sample. Typically, the first assay is comprised of a very sensitive ELISA (Enzyme-linked immunosorbent assay) – which, if positive, is followed by Western blot analysis, an assay that is much more specific than ELISA.

Although these tests display excellent sensitivity (96–100%) for late stage III Lyme disease, the test sensitivity is significantly reduced in earlier stages of the disease (35–56% for early stage I). The current approach to testing also has significant limitations. Tests are unable to differentiate between early- and late-stage LD and therefore cannot be used to predict prognosis. Furthermore, the current tests are lab-



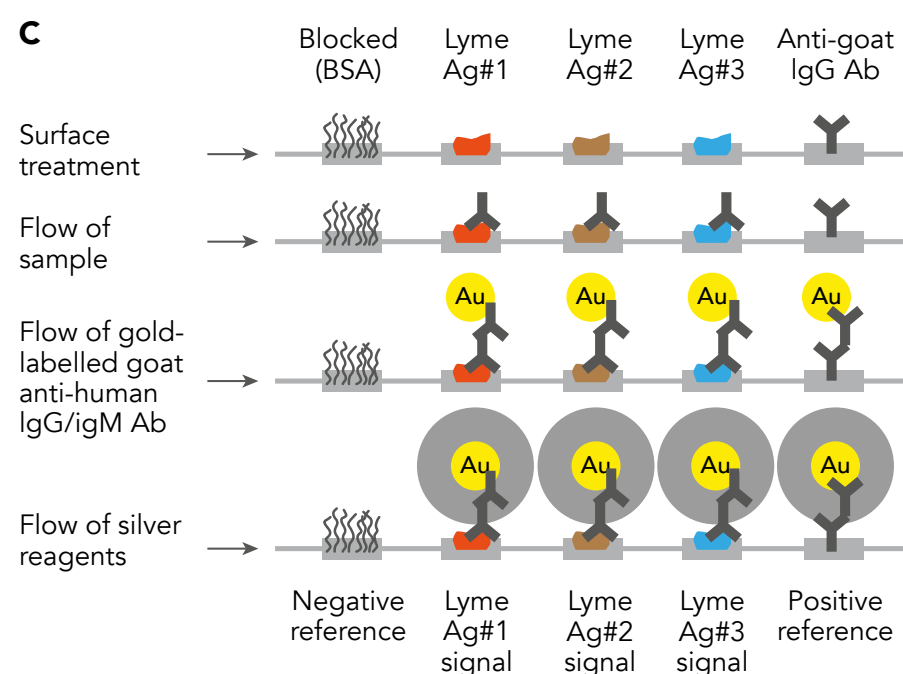


dependent, resulting in significant delays between obtaining a blood sample and receiving results. Given the risks associated with later stages of LD, rapid diagnosis and treatment is vital to limit serious injury and optimise treatment outcomes.

Dr Gomes-Solecki has recently developed in collaboration with Dr Sam Sia (Columbia University) a pioneering new device that uses ultrasensitive microfluidics technology to diagnose LD. Called the mChip-Ld, this device facilitates rapid diagnosis at the point of care, eliminating the need for laboratory-dependent tests.

THE FUTURE OF LYME DISEASE DIAGNOSIS

The mChip-Ld device consists of two main components: a microfluidic plastic cassette which is the base for all the biochemical steps and a light-detection device. Bound to the surface of the cassette are five Lyme antigens, substances that induce the production of an immune response in the body. When a patient blood sample is added, any Lyme-specific antibodies present in the sample will bind to the respective antigen on the cassette. Pre-loaded washes, gold-labelled secondary antibodies and silver amplification reagents are then delivered. The binding of these antibodies and reagents affects silver ion production on the surface of the cassette.



The mChip-Ld facilitates rapid diagnosis at the point of care. It helps the doctor make a decision regarding best course of treatment in the clinic

Q&A

The number of cases of Lyme disease in the US has rapidly increased over the last decade. What are the main factors contributing to this rise?

In the past, there was about 10x the amount of under-reporting of the disease by doctors who patients. Recently, awareness of the disease has become much greater. In addition to growing awareness of LD, there has also been recent expansions of tick habitats into new areas.

Why is it difficult to diagnose LD in the very early stages of the disease?

Most diagnostic assays for LD detect the presence of the bacteria indirectly by assessing immunoglobulins made by the immune cells in the blood. It usually takes 7–21 days for the body to produce enough immunoglobulins (G and M) for detection. Therefore, if the patient presents to the doctor the same day as he/she was bitten by a tick, there is a high likelihood that the patient's serological assay will be negative.

At what stages of disease progression can the mChip-Ld device detect LD?

The mChip-Ld device can detect early disseminated (convalescent) and late Lyme disease.

The mChip-Ld device can identify the presence of multiple different antibodies. What can these results tell us about LD in a patient?

Knowing which antigens induced a positive immune response can give indications of the stage of the disease at that time. OspC, for example, is a good indicator for early Lyme Disease. Other proteins can also detect early Lyme as well as late Lyme.

What are the next steps to getting the mChip-Ld device used regularly in clinical practice?

The assay needs to go through optimisation (early product development) and FDA approval.

The detection component consists of an LED paired with a photodiode for each antigen. Light emitted from the LEDs passes through the cassette and is detected by the photodiodes. As it is transmitted through the cassette, light is absorbed by silver ions present on the cassette. Thus, greater silver production is inversely proportional to light detected by the photodiodes. Quantification of the light sensed by the photodiodes allows simultaneous detection of multiple Lyme-specific antibodies, and subsequent diagnosis for LD.

Importantly, to carry out the analysis, the cassette is inserted into a benchtop analyser (OPKO Diagnostics LLC). This analyser controls fluid flow, temperature and signal detection. In addition, the delivery of samples, washes, antibodies and reagents is programmed to occur automatically and sequentially, allowing the mChip-Ld to be used by non-specialist practitioners.

LONG-TERM BENEFITS

In a series of tests, the mChip-Ld device was found to have comparable performance to traditional diagnostic methods. In addition, it

also provides a broad spectrum of associated benefits. Primarily, the mChip-Ld is portable and facilitates point-of-care diagnosis in 10-15 minutes. A rapid diagnosis allows for prompt treatment and a subsequent reduction in the risk of developing serious and chronic illnesses associated with late stage LD. Furthermore, the separation of antigens and their corresponding detection zones allows for future differentiation between early and late stage LD and informs antigen-based diagnostic decisions. Lastly, at about \$1.50 the cassettes are low-cost and the automated nature of the device means it can be used by medical practitioners with minimal training.

The ability to rapidly diagnose Lyme disease, at the point of care, will have extended benefits. While the wider research community strives to reduce LD transmission, a rapid diagnosis, together with rapid treatment, is key to ensuring the best possible outcomes for the many people who contract LD each year. Dr Gomes-Solecki, in collaboration with Dr Sia, has developed a device that is all about saving time, but the benefits to LD patients will reach far into the future.

Detail

RESEARCH OBJECTIVES

Dr Gomes-Solecki has a long track record in research and development of vaccines and diagnostic assays for Lyme disease.

FUNDING

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COLLABORATORS

Sam Sia, PhD, Columbia University

BIO

Originally from Portugal, Maria earned her DVM from the University of Lisbon in 1992. After completing her Fellowship at the National Institute of Technology in Lisbon, she moved to New York, where she completed her post-doctorate work at Stony Brook University.

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