Press Release

Keio University

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Development of a Glowing Paper Chip That Detects Antibodies—

Towards the Early Detection of Infectious Diseases

A testing chip that can rapidly test for infectious diseases has been jointly developed by Professor Daniel Citterio's laboratory at Keio University's Department of Applied Chemistry, Faculty of Science and Technology, and Professor Maarten Merkx's laboratory at Eindhoven University of Technology in the Netherlands. The testing chip is made of paper and is about 1 cm in size. The test only requires a drop of blood to be applied to the paper chip and a picture to be taken with a digital camera. Results can be confirmed by the blue-green light that is emitted from the chip after about 20 minutes. In addition to reducing the cost and time required to perform tests at hospitals, there are expectations that this paper chip could be used as a quick and easy test to detect tropical diseases in developing nations.

The outcomes of this research have been published in the German scientific journal "Angewandte Chemie International Edition."

1. Background of Research

The human body creates specific antibodies to protect itself against viruses and germs that invade it. Through tests which detect such antibodies in the blood using the paper chip that was developed by the researchers of this study, the presence of an infectious disease can be confirmed. Similar to the home pregnancy test kit, this easy to use and cheap testing chip that detects antibodies has been gathering attention as an alternative to tests at hospitals that can be both expensive and time-consuming. Moreover, in recent times, antibody drugs are increasingly being used to treat chronic diseases such as cancer or rheumatism. However, for an effective course or treatment using antibody drugs, an optimal dose must be determined for each patient, meaning that there is a need to regularly monitor the concentration of antibodies within the blood after the medicine has been administered. This paper chip is also ideal as a method to test the state of these patients.

2. Content of Research and Results

This paper chip, which has been jointly developed by Professor Daniel Citterio's laboratory at Keio University's Department of Applied Chemistry, Faculty of Science and Technology, and Professor Maarten Merkx's laboratory at Eindhoven University of Technology in the Netherlands, is as easy to use as pH test papers. A biochemical reaction takes place about 20 minutes after a drop of blood is applied to the test paper, emitting a blue-green light from the bottom of the paper chip. The bluer this light is, the greater the concentration of the target antibody. A digital camera on a mobile phone is sufficient to detect the light that is emitted and it is possible to clearly determine the results.

All of the functions and reagents necessary for the test is consolidated into a single paper chip. It has a multilayer structure patterned in several areas or pretreated with various reagents. Even a process to remove red blood cells from the blood sample, which obstruct the emission of the blue-green light, is embedded in this paper chip. The only procedure required by the user is to apply a blood sample, after which the sample and the detection reagents will be properly mixed, a biochemical reaction will take place, and light will be emitted. The light emission of the paper chip is due to a development at Eindhoven University of Technology that is commonly known as a "bioluminescent sensor protein." This sensor protein uses the same type of enzyme found in light-emitting deep-sea creatures, catalyzing a reaction that yields the emission of blue light (known as bioluminescence). If the target antibody isn't present in the sample, the blue light is converted to green light through a physical process. On the other hand, if the target antibody is present, it binds with the sensor protein and cuts off the process that changes the light color, thereby emitting a blue light. In other words, a greener light emission indicates a lower presence of the antibody in the sample, while a bluer emission indicates a higher presence.

The blue-green light ratio is determined by the concentration of the antibody in the sample. A decrease of signal with time, a problem often faced by other biosensors, has also been resolved through the measurement of the light emission ratio. This research group built a prototype that successfully detected the presence of 3 types of antibodies (anti-HIV, anti-influenza, and anti-dengue fever) simultaneously. The group is aiming to commercialize the technology within a few years.

＜Details of Original Paper＞
Keisuke Tenda et al., *Paper-based Antibody Detection Devices Using Bioluminescent BRET-Switching Sensor Proteins*, Angewandte Chemie International Edition (2018).
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