Okayama University Medical Research Updates （OU-MRU） 2022.11 Vol.108

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Okayama University research: Track changes: A new test to study cancer progression

(Okayama, 18 November) **In a study recently published in *Frontiers in Oncology*, researchers from Okayama University develop a laboratory test to monitor the progression of cancer.**

The immune system fights cancer cells in various ways. Real time information about the 'fight-situation' in cancer could potentially be used as a prediction/evaluation tool in cancer care. When immune cells attack cancer cells, cancer cell-specific proteins (known as cancer antigens) are released from killed cancer cells, producing antibodies against cancer antigens. Thus, the antibodies in a patient's blood function as an indicator of the level of antitumor response. However, quantitatively measuring antibodies comprehensively has been challenging in laboratories because cancer antigens are unstable and aggregate. A research team led by Professor FUTAMI Junichiro and MIYAMOTO Ai (graduate student) at Okayama University has developed an assay that makes antibody testing more accessible.

Cancer/testis antigens (CTAs) are one of the main antigens expressed in cancer cells and show different expression patterns in cancer patients. A diagnostic test requires various CTAs array sets to detect antibodies related to antitumor immune reactions. The preparation of sets of aggregative and unstable CTAs and the construction of a validated assay system are needed for clinical applications.

To overcome this issue, the researchers used chemically modified CTA molecules. When CTA molecules were chemically modified with a cationic charge to sulfur-containing groups, they showed water-solubility and ensured all regions of the molecule were exposed. These modified CTA molecules were then conjugated onto chemical beads creating the 'MUSCAT' system.

The team first established the so-called MUSCAT's methodology for confirming the sensitivity, specificity, and accuracy using 'positive controls'. These control antibodies were produced in rabbits by the administration of modified CTAs. Antibodies were then purified from the rabbit blood and served to validate the MUSCAT system. These antibodies are also available for biochemical research to detect the endogenous CTAs expressed in cancer-derived cell-lines.

To clinically test the system, the researchers used samples from prostate cancer patients. The patients were enrolled in a successful clinical trial for an experimental gene therapy, resulting in complete tumor regression. When the antibodies from patient's blood were tested on the MUSCAT system, the quantities of antibodies found were closely related to the shrinkage of tumors. The MUSCAT system could therefore be used to monitor the effectiveness of cancer treatment.

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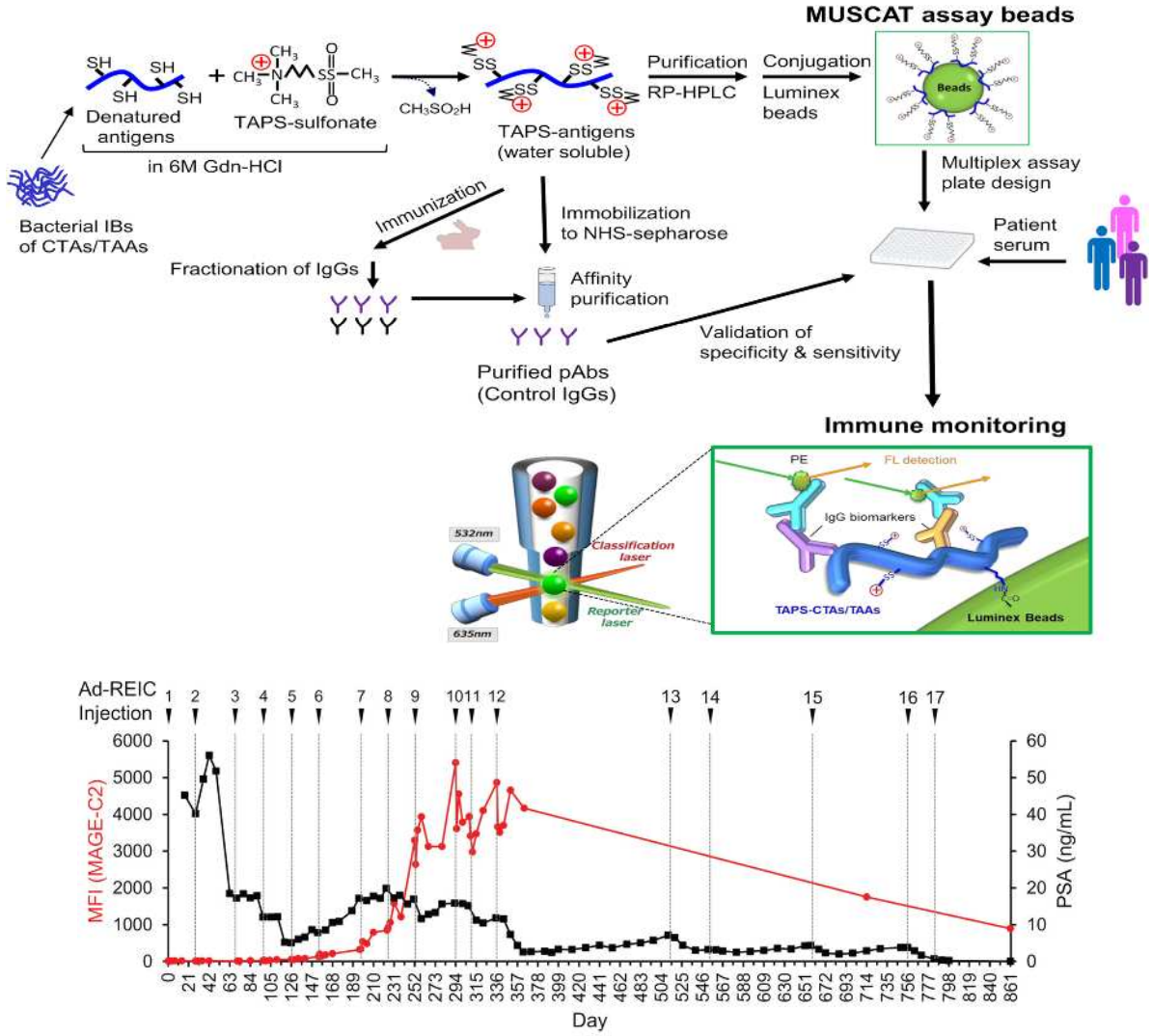
Background

Cancer/testis antigens: Cancer/testis antigens (CTAs) are the main class of antigens found on most types of tumors and restricted expression in normal tissues. During the immune system attacks on cancer cell, CTAs released from killed cancer cells stimulate anti-CTAs antibody production due to their immunogenicity. The level of anti-CTAs antibodies reflects the antitumor reaction and potential for immunotherapy.

With time, tumors develop techniques to evade the immune system. Immunotherapy, a form of cancer therapy, focuses on reigniting the immune system in such cases. Hence, measuring the reactivation of the immune response by means of antibody testing is an indispensable tool to check the effectiveness of immunotherapy. Assays that measure the antibody response are useful for monitoring the stages of cancer, repression of the immune system, or activation of the immune system after immunotherapy.



Figure

Top. A graphical representation of the process of synthesizing modified CTAs, introducing them in rabbits to induce positive controls, and subsequently using them to create the MUSCAT system.

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Bottom. Patterns of anti-CTA antibodies (MAGE-C2) versus cancer markers (PSA) observed on the MUSCAT over time during the clinical trial.

Reference

Ai Miyamoto, Tomoko Honjo, Mirei Masui, Rie Kinoshita, Hiromi Kumon, Kazuhiro Kakimi, Junichiro Futami. Engineering cancer/testis antigens with reversible S-cationization to evaluate antigen spreading. *Frontiers in Oncology*, 2022 May 4;12:869393.
DOI：10.3389/fonc.2022.869393.
https://www.frontiersin.org/articles/10.3389/fonc.2022.869393/full

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Okayama University Image Movie (2020):
https://www.youtube.com/watch?v=vQxeL0ztSLA
Okayama University supports the Sustainable Development Goals: https://sdgs.okayama-u.ac.jp/en/

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◆About Okayama University

Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index_e.html

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Hirofumi Makino, M.D., Ph.D.
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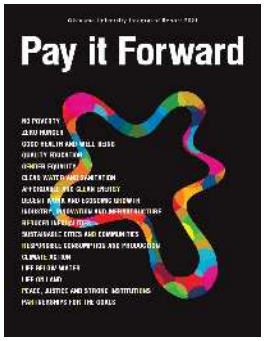

Okayama University Integrated Report => **click**

An integrated report is intended to explain how an organization creates value over time through an organic integration of the vision and the combination of financial information and other information. Through this report we hope to promote greater interest in Okayama University among readers everywhere. In order to help us make improvements in future editions, we encourage you to contact us with any comments and suggestions you may have.

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