

IMSUT Hospital

Department of Laboratory Medicine 検査部

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The Department of Laboratory Medicine comprises eight divisions: Clinical Hematology, Biochemistry/Serology, Microscopy, Pathology, Microbiology, Physiology, and a TR-Verification Laboratory. Clinical laboratory tests are essential for every step of clinical practice, including disease diagnosis, staging evaluation, treatment determination, and post-therapy assessment. Our department performs most of the clinical laboratory tests at our hospital under strict quality control, and collaborates with many other departments to provide investigative laboratory analysis. To facilitate translational research projects at this hospital, we established the TR Verification Laboratory division. This division contributes to evaluating the safety of experimental therapeutic approaches and biopharmaceutical products for clinical trials.

As a central medical division, we participate in numerous clinical trials and support many research studies conducted in our hospital.

1. Clinical Laboratory Operation and Quality Control

Nagai E and all medical technician members

The Department of Laboratory Medicine at the University of Tokyo Institute of Medical Science consists of eight laboratories: Hematology, Microscopy, Biochemistry and Immunology, Microbiology, Physiology, Emergency, Pathology, Genetic tests, and TR-Verification Laboratory rooms. Clinical tests are crucial for diagnosis, understanding disease states, and predicting prognosis. Reporting accurate test results with guaranteed quality is the mission of the Department of Laboratory Medicine. To keep the qualities of tests, we undergo both internal and external quality control (JAMTQC and CAPsurvey). Furthermore, on holidays, in the Emergency Laboratory, we

handles urgent testing, contributing to patient care in emergence.

2. Studies for improving clinical tests with high quality

Nagai E and all medical technician members, Ishigaki T, Ando S., Nagamura-Inoue T

In each laboratory we conducts research aimed at developing testing techniques and improving quality, based on questions arising during routine practice and accumulated data. In Hematology Laboratory, we report WBC differentiation counts even in nadir before and after hematopoietic stem cell transplantation (HSCT) and found the correlation of WBC counts and prognosis of HSCT by the collaboration with Hematology/Oncology department. We also studied to

improve the visual detection rate of ATL cells even in carrier stage. In Biochemistry and Immunology Laboratory, we studied the efficient detection of beta-thalassemia using the hemoglobin screening device ADAMS A1c by the joint collaboration with a company. In Biochemistry and Immunology Laboratory, we measured SARS-CoV-2 antibody titer and sorting patients' specimens of post-vaccination, collaborating with Department of Infection-Immunology. In Microbiology Laboratory and TR/Validation Laboratory, we have established a system for quality and safety tests including sterility testing, endotoxin and mycoplasma PCR testing, for gene and cell products (for clinical trials), as well as environmental microbial testing in cleanrooms, according to the request from internal and external researchers. These tests contribute to the quality assurances of the products. In Pathology Laboratory, we prepare histopathology specimens of not only for clinical pathology diagnoses but also animal species for basic researcher as the Pathology Core Laboratory 2. In Genetics Laboratory, we actively analyzed tests not only covered by health insurance, but also research level gene analysis (especially hematological malignancies) collaborating with Department of Hematology/Oncology.

3. Establishment of a new cytometric method to evaluate the immune function of chimeric anti-gen receptor T (CAR-T) cells and application for clinical testing

Tomohiro ISHIGAKI.

CAR-T cell therapy is a groundbreaking approach to treating hematological malignancies. However, relapses can occur due to the poor immune response or exhaustion of CAR-T cells after proliferation. In this study, we collaborated with joint researchers to de-

velop a new evaluation method using molecular imaging flow cytometry (MI-FCM). We obtained eight CAR-T clones by genetically modifying peripheral blood mononuclear cells (PBMCs) from eight healthy donors with lentivirus to express an anti-CD19 CAR. We assessed the clones' cytotoxicity in vitro using a luciferase assay and analyzed the intensity, area, and distribution of CAR expression (spot counts) using an imaging flow cytometer. We also evaluated the cytotoxicity of some clones in vivo using a xenotransplantation model with CAR-T cells and a B-cell leukemia cell line (NALM6) in NOG mice. We found that CAR antigens aggregate superficially in immune responses and that we could detect this as a decrease in CAR expression area. The percentage of CAR T-cells with a single-spot CAR concentration was significantly correlated with killing activity. Additionally, we confirmed that the clone with the lowest percentage of CAR T-cells could not prolong survival in xenotransplantation models. Additionally, we found that this method could be applied to remnants of CAR-T cell therapy products. In conclusion, quantifying the concentration of CAR on the surface of cells using MI-FCM could be useful for evaluating immune function.

4. Multicenter clinical and experimental studies of muscular dystrophy.

Kimura K., Aochi S., Kadoya M.

We performed multicenter clinical studies for patients with muscular dystrophy as well as several animal experiments using rats, dogs, pigs, and mice models with muscular dystrophy in collaboration with NHO (National Hospital Organization) hospitals and NCNP (National Center of Neurology and Psychiatry).