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General Summary

The main study was continuously accomplished by Welfare of Japan and the Practical Application of New Drugs for Hepatitis B provided by the Japan Agency for Medical Research and Development (AMED). We accomplished studies to connect experimental medicine with clinical medicine.

Research Activities

Clinical microbiology

Masaki T *et al.* conducted fundamental research and discovery research on hepatitis B virus (HBV) and hepatitis C virus (HCV). In the drug discovery research of HBV, the antiviral effect of a non-nucleic acid analog compound hit by high throughput screening was evaluated using a proprietary HBV sustained production cell line. In basic research on HCV, research was conducted to prevent HCV infection replication proliferation and pathogenicity development. They identified TGF- β -related molecules that increase in the blood at the early stage of liver fibrosis and examined the relationship with the pathology of chronic liver diseases.

Kono M *et al.* investigated characterization for differentiation at the strains level of *Helicobacter cinaedi* isolated from blood culture using multilocus sequence typing (MLST) method. They did try to perform an epidemiologic study of MRSA using a whole cell MALDI TOF MS. They investigated genetic characterization of extended-spectrum β -lactamase (ESBL)-producing Salmonella strain

Clinical chemistry

Yoshida H *et al.* demonstrated the association of adiponectin with HDL in non-diabetic subjects and the relevance of lipoproteins including Lp(a) to Framingham coronary risk score by our developed HPLC lipoprotein assay (*Ann Clin Biochem* 2018; 55: 165-71, *J Atheroscler Thromb* 2017; 24: 928-39). In the meantime, they reported that angiotensin-II (Ang-II) can enhance matrix metalloproteinase (MMP)-2 mainly through Ang-II receptor type 2 in endothelial cells (*J Cardiovasc Pharmacology* 2018; 71: 233-9).

Nakada K *et al.* studied gastric emptying and fat digestive and absorptive function after various types of gastrectomy by ^{13}C -breath tests. Function-preserving gastrectomy (FPV) attenuated rapid gastric emptying which is usually seen after conventional gastrectomy. This may, in part, explain the mechanism of ameliorating postgastrectomy syndrome such

as diarrhea and dumping.

Using a proteome analysis, Matsuura T *et al.* identified alpha-1 antichymotrypsin (ACT), which was increased in plasma samples from mini-pigs with hepatic encephalopathy (HE) and decreased in those after treatment with extracorporeal circulation by bioartificial liver. In *in vitro* experiments with human astrocytes, ACT showed growth-inhibitory and cytotoxic effects on astrocytes. In addition, the expression of water channel protein aquaporin-4, which is induced in injured astrocytes, was increased following ACT treatment. Interestingly, these effects of ACT were additively enhanced by adding arginine-vasopressin (AVP) and were canceled by adding an AVP receptor antagonist. These results suggest that ACT is involved in astrocyte injury and dysfunction in concert with AVP during the development of acute HE.

Clinical hematology

Kaito K had studied about thrombopoietin receptor agonist eltrombopag. Since thrombopoietin receptor agonist eltrombopag became usable not only for thrombocytopenia but also for aplastic anemia (AA), the effectiveness for refractory AA which could not obtain sufficient response by immunosuppressive therapy was investigated. Six patients (4 women and 2 men) included 2 cases of transfusion dependence were treated with eltrombopag. In 1 case, administration was discontinued due to hepatic injury, and 5 cases were administered for 3 to 6 months at a dose of 50 to 100 mg. Although it is still too early to evaluate the efficacy, 2 patients with increased platelet and 1 patient with increased hemoglobin were experienced. It is necessary to consider how much blood cells can be improved by long-term administration of the maximum dose of 100 mg in the future.

Ogasawara Y had studied the pathophysiology of bone marrow failure syndrome. To assess the optimal treatment for acquired AA, he analyzed the clinical and laboratory data of AA patients who received immunosuppressive therapy at our hospital and join a prospective randomized controlled study of rabbit antithymocyte globulin for AA.

Clinical physiology

Sugimoto K had continued research on arrhythmia diagnostic accuracy of the electrocardiogram automatic analysis. In the arrhythmic region, he also continued research related to catheter ablation of atrial fibrillation and reported it to Western magazines. In addition, he began research on the ECG waveform of premature contraction.

Clinical psychiatry

Taking the conception of the resilience into consideration, Sue H planned out a study on adult patients suffering from epilepsy, and he tried to reconsider the rational antiepileptic drugs polypharmacy. Furthermore, he planned to establish Epilepsy Center, which contribute toward the offering the comprehensive medical care and epilepsy research.

Basical Research

Mezaki Y had studied hepatic retinoid metabolism. Hepatic stellate cells (HSCs) play an important role in liver fibrogenesis, and are also known to be a site of retinoid storage. The enzyme that converts retinol to retinylesters in the liver is lecithin:retinol acyltrans-

ferase (LRAT). In order to analyze LRAT biochemically, a baculovirus-mediated expression system for LRAT was established.

Publications

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