Principal Investigator: Shigeo Horie (Professor)

The research topics in our department are diverse, ranging from cancer, men’s health, and geriatrics to hereditary kidney disease (Figure-1).

Research on urological cancer outcome

It is imperative to establish a patients’ database of urological cancer for appropriate evaluation and the further improvement of clinical outcomes in our department. Recently, we have completed a clinical database for bladder cancer based on more than 1000 patients at Juntendo University Hospital. Using this database, we are now attempting to identify the risk factors for progression of Japanese patients with bladder cancer. We also share this database with five prestigious Korean hospitals (Seoul National, Yonsei, Asan, Hyundai, and St. Mary) in order to achieve international collaboration in this field.

Molecular genetics of circulating tumor cells

Circulating tumor cells (CTCs) are cells that are shed into the vasculature from a primary tumor and circulate in the bloodstream. They play an important role in the formation of metastasis, which is, needless to say, the major cause of cancer-related death. Recently, some research showed that CTCs are not only a prognostic marker but can also be a treatment response marker. Reproducible practical methods to detect CTCs from a variety of cancers have not been established yet. We are now striving to devise methods to capture CTCs and analyze their genetic properties, so that we can unveil a yet-to-be-discovered mechanism of metastasis.

Comprehensive research of ADPKD

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disease. Numerous renal cysts appear bilaterally and their number increases in proportion to patient age. As a result, kidney function gradually deteriorates. We are currently performing the genotypic analysis of ADPKD patients in order to investigate whether there is any genetic mutation responsible for disease progression. We are also determined to find new
biomarkers for ADPKD from urine, such as urinary exosome.

**Group Leaders and Research Topics**

1) Akira Tsujimura (Senior Associate Professor) and Shin-ichi Hisasue (Associate Professor)

Our department is one of the main international research centers studying late-onset hypogonadism (LOH) and sexual dysfunction in elderly males. LOH is induced by the decrease in testosterone with aging. Recently, LOH has attracted tremendous interest as a factor deteriorating QOL among middle-aged males. We are investigating the influence of testosterone on QOL in males from various perspectives. We have revealed that testosterone decrease leads to low QOL, dry mouth, sleep disturbance, anxiety, and lower urinary tract symptoms.

Regarding erectile dysfunction (ED), we discovered the significant causal relationship between silent myocardial infarction and ED in diabetic patients. We assessed the degree of ED and diabetes in outpatients using multidetector computed tomography (MDCT).

2) Hiroaki Aoki (Assistant Professor)

Recently, the elderly population has been rising rapidly. Accordingly, the number of patients with urological symptoms has increased. Sarcopenia, which is defined as loss of muscle mass and strength with aging, and frailty, is a major geriatric syndrome. There is an urgent need for its definitive care and management.

We are now creating a protocol with regard to the management of invasive treatments such as operation and chemotherapy for elderly patients. For this purpose, we evaluated patients’ muscle mass before and after treatment. We could clearly demonstrate a significant inverse correlation between muscle mass and predisposition to postoperative sarcopenia after radical cystectomy. Preoperatively, we determine patients eligible for invasive surgery using the Comprehensive Geriatric Assessment (CGA). It enables us to assess patients with geriatric syndrome. We also evaluate the validity and usefulness of this measure, and hope to detect some biological markers for geriatric syndrome in the near future.

3) Haruna Kawano (Assistant Professor)

Newly developed molecular inversion probe (MIP) technology could allow us to obtain genomic profiles from formalin-fixed paraffin-embedded (FFPE) tissue even if such samples are old. This technique allows us to determine whole-genome copy number and loss of heterozygosity (LOH) and to analyze key somatic mutations of cancer.

There are some rare cancers in the urology field, such as urachal carcinoma, prostatic sarcoma, neuroendocrine-differentiated prostate cancer, adrenal carcinoma, and malignant pheochromocytoma. The mechanism of development of those tumors remains to be elucidated. Hence, there are no established standard treatments for them. To explore new treatment strategies for these rare cancers, we are attempting to detect genes responsible for the tumorigenesis of these rare cancers using MIP. To unveil the mechanism of development of renal cancer, we utilize an animal model in cooperation with the Department of Molecular Pathogenesis. The Eker rat is a model animal of renal cell carcinoma (RCC). This rat has a germline mutation in the tuberous sclerosis 2 gene ($Tsc2$). Heterozygous mutants develop RCCs within one year after birth due to LOH of the wild-type $Tsc2$ allele, whereas homozygous mutants die at the embryonic stage. We established embryonic stem cells (ESCs) from Eker rats to study the mechanism of $Tsc2$ mutation-associated carcinogenesis.