## The 645th Kitasato Medical Society Invitational Academic Lecture Series Abstract

(H26.11.13)

### Ureteral stenting -- a necessary evil

Dirk Lange
(Assistant Professor, Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada)

Since the introduction of the modern-day ureteral stent in 1978 by Finney et al., ureteral stenting has become one of the most commonly performed procedures across urology. Most commonly, they are used as an adjunct to stone therapy, to relieve benign and malignant obstruction, to promote ureteral healing and management of urinary leak, and pre-operative placement to aid in intra-operative ureteral identification. Despite their wide use throughout urology, ureteral stents are fraught with a wide array of complications, the most commonly being infection, encrustation and patient discomfort. As ureteral stents are a key tool in urology that we cannot do without, a sound understanding of common and uncommon complications is required to identify areas of improvement to stent design and to improve its use. This review will provide an overview of stent-associated complications, including the potential role for stent-induced ureteral aperistalsis. Furthermore it discusses novel ways currently being investigated and how these may be developed further to prevent complications and improve overall ureteral stent function.

## The 648th Kitasato Medical Society Invitational Academic Lecture Series Abstract

(H26.12.8)

### Development of cancer vaccines: strategies and translations

Masaki Terabe
(Vaccine Branch, Center for Cancer Research, National Cancer Institute, NIH, USA)

Cancer immunotherapy is a promising approach to treat cancer, as evidenced by the first US-FDA licensed therapeutic vaccine against prostate cancer (sipuleucel-T) and two checkpoint inhibitors (anti-CTLA-4, ipilimumab and anti-PD-1, pembrolizumab and nivolumab) that were recently approved for clinical use. However, there is still a long way to go to achieve true success for immunotherapy. Among approaches of cancer immunotherapy, a cancer vaccine may be the most cost-effective as it does not require continuous administration of expensive drugs to patients but instead utilizes the ability of a patient's own immune system to keep attacking cancer cells. However, distinct from prophylactic vaccines against infectious agents that we all received in childhood with a healthy immune system, therapeutic cancer vaccines in patients who already have cancer deal with dysregulated patients' immune system. To overcome road blocks existing in the immune system of cancer patients, our lab has proposed a "Push-Pull" approach where antigens are optimized in their amino acid sequences and combined with molecular adjuvants to accelerate immune responses as well as approaches to negate components suppressing immune responses, in order to optimize immune responses induced by therapeutic vaccines. In the presentation, I will discuss our data on the role of NKT cells in the regulation of tumor immunity as well as recent clinical trial data of our cancer vaccines.

## The 649th Kitasato Medical Society Invitational Academic Lecture Series Abstract

(H27.2.13)

### The family of secreted phospholipases A2: from toxic to therapeutic enzymes

Gerard Lambeau
(Professor, Institute of Molecular and Cellular Pharmacology, CNRS and University of Nice Sophia Antipolis, France)

Secreted phospholipases A2 (sPLA2s) are low molecular mass (14-19 kDa), Ca2+-dependent enzymes with a His-Asp catalytic dyad. These enzymes were first discovered in snake venoms where they usually exert digestive and toxic functions towards preys. More than two decades ago, we started to work on toxic venom sPLA2s and discovered specific sPLA2 protein receptors (M and N) including the so-called M-type receptor or PLA2R1, a 180 kDa C-type lectin membrane receptor.

Based on the large structural diversity of venom sPLA2s, we next hypothesized that there might be a similar diversity of sPLA2s in mammals, which would act as endogenous ligands of the above receptors identified with venom sPLA2s and would also exert enzymatic roles, bringing the concept of sPLA2s acting as both ligands and enzymes. This led us to clone a number of novel mammalian sPLA2s, bringing the total number of human and mouse sPLA2s to 11 and 12 members, respectively.

Since a decade or so, the major and still current challenge is to identify the respective biological roles of the different sPLA2s and their receptors in different tissues and settings. It is now known that the individual mammalian sPLA2 enzymes exhibit unique tissue and cellular localizations and enzymatic properties, suggesting distinct biological roles. Several of them also bind to specific proteins including PLA2R1, which may serve to inhibit or promote sPLA2 action in some specific tissues. It is now also clear that individual sPLA2s are involved in diverse biological events through enzymatic-dependent and -independent processes, act redundantly or non-redundantly in the context of physiopathology, and may represent potential drug targets or bioactive drugs in certain situations. Moreover, PLA2R1 may be a polymodal receptor with multiple ligands and functions, beyond its interaction with sPLA2s. In this talk, I will present novel biological roles of some sPLA2s and PLA2R1 in host defense, atherosclerosis, fertility, cancer and membranous nephropathy, a human auto-immune kidney disease.

## The 650th Kitasato Medical Society Invitational Academic Lecture Series Abstract

(H27.3.2)

### Novel protein trafficking and signaling pathways in kidney tubule cells

Michael J. Caplan
(Professor, Cellular & Molecular Physiology, Yale University School of Medicine, USA)

Autosomal Dominant Polycystic Kidney Disease (ADPKD) leads to end stage renal disease in ~50% of affected individuals. ADPKD is caused by mutations in the genes encoding polycystin-1 (PC1) and polycystin-2 (PC2). We find that the PC1-CTT interacts with and stimulates a co-activating protein that plays a critical role in controlling the activity of the transcription factor that mediates bone development. Thus, polycystin proteins signal from the cilium to the nucleus to modulate gene expression in a variety of cell types.

## The 651th Kitasato Medical Society Invitational Academic Lecture Series Abstract

(H27.3.2)

### Anion Transporters: Roles in Renal Salt and Oxalate Excretion

Peter S. Aronson
(Professor, Medicine and Cellular & Molecular Physiology, Yale University School of Medicine, USA)

Functional expression of SLC26A6 in Xenopus oocytes demonstrated that the transporter is capable of mediating Cl-formate exchange, Cl-oxalate exchange, Cl-OH exchange and Cl-HCO3 exchange. Comparison of wild-type and Slc26a6 null mice with respect to transport in renal brush border vesicles and microperfused tubules demonstrated that SLC26A6 primarily mediates Cl-oxalate exchange rather than Cl-formate exchange in the proximal tubule in vivo. We suggest that oxalate may be a pro-inflammatory factor contributing to CKD progression.