JDDW 2018 神戸　招待講演（消外）

11月2日（金）

14：00～14：40

神戸国際展示場2号館

Too Much, Too Little, or Just Right? Strategies to Optimize Immunosuppression for Patient and Graft Longevity

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この講演後に引き続き、ワークショップ１２（**消外・肝臓**）

肝移植待機患者の評価―適応と限界

14：40～17：00が予定されています。

Biography of Sandy Feng, MD, PhD

Dr. Feng is graduate of Harvard College, where she received the prestigious Marshall Scholarship. She utilized this fellowship to pursue graduate studies in Molecular Biology and received a doctorate from Trinity College, Cambridge University. Her medical training began at Stanford University School of Medicine, followed by general surgery residency at the Brigham and Women's Hospital, Harvard Medical School and Abdominal Transplant Surgery fellowship at the University of California, San Francisco. As Professor of Surgery, Dr. Feng performs liver, kidney and pancreas transplants. Her teaching and mentoring responsibilities include leading the Abdominal Transplant Surgery fellowship program and guiding medical students, residents, fellows, and junior attendings in clinical and translational research.

With respect to research, Dr. Feng's interests center on exploring mechanisms of spontaneous tolerance and approaches to induce tolerance in adult and pediatric liver transplant recipients. She is the overall principal investigator for numerous NIH-funded multi-center clinical trials and has consistently been among the highest NIH-funded surgeons in the United States. She serves in a leadership capacity on the Executive and Steering Committees of the Immune Tolerance Network with responsibility for overseeing the Transplant portfolio.

Within the transplantation community, Dr. Feng has served many years as one of eight worldwide Deputy Editors for the *American Journal of Transplantation* and remains a Consulting and Special Features Editor. She is currently a member of the *New England Journal of Medicine* Editorial Board. She has held numerous leadership roles for the American Society of Transplant Surgeons, American Society of Transplantation, and American Association for the Study of Liver Disease. Recently, she has spearheaded a successful effort engaging the National Academy of Medicine to conduct a study which was completed in October 2017 examining the ethical, regulatory, and logistical challenges that obstruct innovative research in deceased donors that can improve the quality and increase the quantity of organs available for transplantation.

Abstract

Too Much, Too Little, or Just Right?
Strategies to Optimize Immunosuppression for Patient and Graft Longevity
Sandy Feng, MD, PhD

Today, it is now well-known that patient and graft longevity are primary challenges for the liver transplant community. Over the past three decades, short-term outcomes have improved substantially while long-term outcomes have stagnated. Among adults, multiple issues have painted a somber landscape for patient longevity. First, the profile of transplant candidates has changed. Increasingly, older patients with multiple medical co-morbidities are accepted as transplant candidates. Second, more aggressive organ utilization practices have resulted in heightened ischemia/reperfusion injury that leads to tumultuous peri-transplant courses with lasting consequences. Third, our standard armamentarium of immunosuppression incurs cumulative toxicities. Moreover, the common side effects of hypertension, hyperglycemia, hyperlipidemia and nephrotoxicity often exacerbate pre-existing conditions, catapulting the risk of cardiovascular disease. Finally, loss of immunosurveillance predisposes to malignancy that is another major mortality risk, yet another example of how immunosuppression amplifies the vulnerabilities of an aged population.

The issues that plague adult liver transplant recipients as delineated above are arguably less damaging to pediatric liver transplant recipients. However, two streams of data suggest that the standard of care management of chronic immunosuppression is sub-optimal and may shorten graft or patient longevity. First, within the rigorous context of prospective, multi-center clinical trials, immunosuppression has been successfully discontinued without evidence of allograft injury in the short and mid-term. Second, multiple single center, cross-sectional, typically retrospective reports have shown that, for pediatric liver transplant recipients with normal liver tests maintained on immunosuppression, inflammation and/or fibrosis appears increase in both prevalence and severity, over time. The frequent presence of silent allograft injury has been confirmed by biopsies performed as an eligibility assessment to enter an immunosuppression withdrawal trial – arguably a cohort of “clinically ideal” patients. Moreover, emerging data suggests that biopsies with portal inflammation and interface activity express the transcriptional program of subclinical rejection. These intriguing reports of operational tolerance juxtaposed against silent chronic allograft injury suggest that, among pediatric liver transplant recipients with normal liver tests, some are maintained on too much while others are maintained on too little immunosuppression. The optimal management of immunosuppression – a personalized approach aiming at not too much or too little but just enough – is critical to simultaneously maximize both patient and allograft longevity.