

# JPS-ASPET Lecture

3月9日（水）8:45~9:45（第95回日本薬理学会年会 A会場）

Neurovascular Interactions: Mechanisms, Imaging, Therapeutics

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日本薬理学会と米国薬理学会（ASPET）の講師交換プログラムは今回5回目となります。Akassoglou教授は、ギリシャのアテネ大学でPhD（神経免疫学）を取得され、ロックフェラー大学でのポストドクを経てUCSDでPIとなり、2008年にグラッドストーン研究所/UCSFへ移り、2012年に神経学の教授に就任されています。脳、免疫、血管系間のコミュニケーションを制御するメカニズム、特に多発性硬化症、アルツハイマー病などの幅広い神経疾患における共通の糸としての血液凝固因子フィブリノーゲンの役割に関する研究を開拓され、神経血管界面を解析する最先端イメージングツールを開発し、脳を神経炎症から保護する新しいフィブリン標的免疫療法と小分子化合物を発見されています。ASPETから交換プログラム講師としてご推薦いただき、薬理学会年会にお招きすることになりました。多数の会員のご参加をお願いします。

The communication between the brain, immune and vascular systems is a key contributor to the onset and progression of neurological diseases. We discovered the coagulation factor fibrinogen as a blood-derived driver for neuroinflammation and inhibitor of repair in a wide range of neurologic diseases, such as multiple sclerosis, Alzheimer's disease and brain trauma. We showed that fibrinogen is necessary and sufficient for neurodegeneration and a new culprit for microglia-mediated oxidative stress-dependent spine elimination and cognitive impairment. By developing Tox-Seq, we reported the oxidative stress innate immune cell atlas in neuroinflammation. We developed cutting-edge imaging tools to study brain network synchronization and the neurovascular interface. We discovered a first-in-class fibrin-targeting immunotherapy to selectively target inflammatory functions of fibrin without interference with clotting with potent therapeutic effects in autoimmune- and amyloid-driven neurotoxicity. High throughput drug screens identified small molecule compounds to block fibrin-induced activation of microglia with therapeutic effects in neuroinflammatory disease. These findings could be a common thread for the understanding of the etiology, progression, and new treatments for neurologic diseases with neuroimmune and cerebrovascular dysfunction. As fibrin is a global activator of toxic innate immune responses in the brain and periphery, these studies could provide the basis for the development of a new class of therapeutics for autoimmune and inflammatory diseases<sup>1</sup>.

1. Akassoglou, K. The immunology of blood: Connecting the dots at the neurovascular interface. *Nat Immunol* 2020, 21:710-712.