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Biography

Kun Ping Lu, MD, PhD, received his medical training from Fujian Medical University and passed The United States Medical Licensing Examinations, as well as obtained PhD degree from Duke University, followed by postdoctoral training in the Tony Hunter’s laboratory at Salk Institute, where he cloned human NIMA-interacting proteins, Pin1 and Pin2/TRF1. He became an independent investigator at Harvard Medical School in 1996, rising through the ranks to become a full Professor at Harvard Medical School, the Founding Chief of Division of Translational Therapeutics at Beth Israel Deaconess Medical Center and Associate Member of Broad Institute of MIT and Harvard.

Abstract

“Pin1-Regulated Phosphorylation Signaling and -Targeted Therapy in Alzheimer and Cancer”

Proline-directed Ser/Thr phosphorylation is a central signaling mechanism presumably by inducing protein conformational changes, but the significance and regulation of such conformational changes were unknown until the discovery of Pin1. In collaboration with Dr. Xiao Zhen Zhou, Dr. Lu identifies Pin1 as the only enzyme that catalyzes proline cis-trans isomerization after phosphorylation, leading the discovery of post-phosphorylation conformational regulation as a unique signaling mechanism. Dr. Lu/Zhou lab shows that Pin1 is highly regulated physiologically and its deregulation has the pivotal but opposite impact on the development of cancer and Alzheimer’s disease, two major age-related diseases that had rarely been studied together, but have now widely been shown to be the two-side of the same coin. Notably, in cancer, Pin1 overexpression promotes cancer and cancer stem cells by acting as a master regulator of over 60 oncogenes and over 30 tumor suppressors. Importantly, their recent Pin1 drug screens have unexpectedly identified Pin1 as the long-sought-after drug target for all-trans retinoic acid and arsenic trioxide to treat acute promyelocytic leukemia, breast and liver cancers. These results not only elucidate how ATRA and arsenic trioxide cure most patients with acute promyelocytic leukemia, but also demonstrate the potential role of Pin1 inhibitors in treating many other cancers. In Alzheimer’s disease, Dr. Lu/Zhou lab find that Pin1 helps protect against neurodegeneration in AD by converting the phosphorylated Thr231-Pro motif in tau (P-tau) from the pathogenic cis conformation to the physiologic trans. To detect Pin1-catalyzed conformational changes, Dr. Lu/Zhou lab has recently developed innovative technology to create antibodies able to distinguish cis from trans phosphorylated proteins, such as P-tau. These new antibodies have led the discovery that cis P-tau is a common early driver of disease development, and to develop Pin1-targeted therapies, notably Pin1 inhibitors to simultaneously stop multiple cancer-driving pathways in cancer and cancer stem cells for overcoming drug-resistance in cancers, and cis P-tau antibody for early diagnosis and treatment of Alzheimer’s disease, brain injury and other dementia.