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

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Secreted phospholipases A_2 (sPLA$_2$s) are low molecular mass, Ca^{2+}-requiring enzymes with a His-Asp catalytic dyad. These enzymes were first discovered in animal venoms where they usually exert digestive and toxic functions towards preys. Over the years, 10 different mammalian sPLA2 isoforms homologous to the venom sPLA2s have been cloned. These enzymes exhibit unique tissue and cellular localizations and enzymatic properties, suggesting distinct biological roles. They also bind to specific proteins including PLA2R1, a C-type lectin receptor.
It is now clear that mammalian sPLA$_2$s are involved in diverse biological events through enzymatic-dependent and -independent processes, act redundantly or non-redundantly in pathophysiology, and may represent potential drug targets or bioactive drugs in several diseases. Over the years, several sPLA2 inhibitors have been developed by pharmaceutical companies and clinically tested, but none of them are currently used in the clinic. In this talk, I will present novel biological roles of sPLA$_2$s and PLA2R1 in atherosclerosis, host defense, fertility, cancer and membranous nephropathy, a human auto-immune kidney disease.

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