Secreted phospholipase A_2 enzymes and diseases

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Phospholipase A_2 (PLA_2) hydrolyzes glycerophospholipid to yield fatty acid and lysophospholipid. More than 20 PLA_2 enzymes have been identified in mammals. Although the crucial contribution of $cPLA_2\alpha$, a cytosolic PLA_2 with *sn*-2 arachidonate preference and μM Ca^{2+} sensitivity, to lipid mediator production has been well documented, the pathophysiological functions of most other enzymes, secreted PLA_2s ($sPLA_2$s) in particular, have remained elusive. Two prototypic $sPLA_2$s, namely pancreatic group IB and inflammatory group IIA, have been shown to participate in dietary phospholipids digestion and anti-bacterial defense, respectively. In this talk, I will discuss the unexplored roles of group III, V and X $sPLA_2$ enzymes in biology on the bases of the analyses of their transgenic and knockout mice. Individual $sPLA_2$s, by acting on distinct target membranes, appear to participate in various pathological events, such as inflammation, allergy, tissue damage and metabolic syndromes, as well as in physiological events, such as reproduction and skin homeostasis. Thus, each $sPLA_2$ may represent an attractive novel target for therapeutic and diagnostic intervention for patients with various diseases.