東京医学会

東京医学会　第 2451 回集会

日時：平成 20 年 5 月 26 日（月）　17：00～18：30
場所：医学部教育研究棟　6 階　細胞情報学セミナー室

演者：**Professor John A. Oates**

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演題：**Inherited Human Deficiency of Cytosolic Phospholipase $A_2\alpha$**

紹介：Cytosolic phospholipase $A_2\alpha$ ($cPLA_2\alpha$) hydrolyzes arachidonic acid from cellular membrane phospholipids, thereby providing enzymatic substrates for the synthesis of eicosanoids, such as prostaglandins and leukotrienes. Considerable understanding of $cPLA_2\alpha$ function has been derived from investigations of the enzyme and from $cPLA_2\alpha$-null mice, but knowledge of discrete roles for this enzyme in humans is limited. We investigated a patient hypothesized to have an inherited prostanoid biosynthesis deficiency due to his multiple, complicated small intestinal ulcers despite no use of cyclooxygenase inhibitors. Levels of thromboxane B_2 and 12-hydroxyeicosatetraenoic acid produced by platelets and leukotriene B_4 released from calcium ionophore-activated blood were markedly reduced, indicating defective enzymatic release of the arachidonic acid substrate for the corresponding cyclooxygenase and lipoxygenases. Platelet aggregation and degranulation induced by adenosine diphosphate or collagen were diminished but were normal in response to arachidonic acid. Two heterozygous single base pair mutations and a known SNP were found in the coding regions of the patient's $cPLA_2\alpha$ genes (p.[Ser111Pro]+[Arg485His; Lys651Arg]). The total PLA_2 activity in sonicated platelets was diminished, and the urinary metabolites of prostacyclin, prostaglandin E_2, prostaglandin D_2, and thromboxane A_2 were also reduced. These findings characterize what we believe is a novel inherited deficiency of $cPLA_2$.

主催：東京医学会
共催：細胞情報学（清水研究室）
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