

## O2: THE MOLECULAR MECHANISM OF HEMIN

### INDUCE PLATELET AGGREGATION AND SECRETION

Jaroen Sarasumcuji, Noppawan Phumala Morales, Udom Chantharaksri, Nuttawut Sibmoo and Supeenun Unchern

*Department of Pharmacology, Faculty of Science, Mahidol University, Bangkok 10400, Thailand*

#### ABSTRACT

It was previously demonstrated that the response of platelets in splenectomized- $\beta$ -Thalassemia/Hemoglobin E (Sp- $\beta$ -thal/ Hb E) patients were increased both to mechanical and chemical stimulation. However, the precise cause of platelet hyperactivity in these patients has not been elucidated. Recently, our group demonstrated the presence of high concentration of hemin (a degradative product of hemoglobin) in serum of  $\beta$ -thal/Hb E patients and found that hemin readily catalyzed free radical reaction. Hemin, however, has not been detected in the serum of non-thalassemia subjects. It was previously demonstrated that hemoglobin released from RBCs modulated platelet functions through the free radical reaction; therefore, we performed the study to evaluate whether hemin (iron (III) protoporphyrin IX), was responsible for platelet hyperfunction in the splenectomized  $\beta$ -thal/Hb E patients. The effects of hemin on platelet aggregation of normal volunteer's blood were performed using both whole blood (impedance aggregation) and platelet rich plasma (optical aggregation). Platelet ATP release was also monitored. The results showed that hemin was dose dependent induced platelet aggregation and secretion. The platelet aggregation and secretion induced by hemin was shown to be inhibited by COX-inhibitor (indomethacin), and an adenosine-uptake inhibitor (dipyridamole). However, mannitol (an OH<sup>•</sup> radical scavenger) did not inhibit hemin's effects. In addition, deferoxamine (an iron chelator) partially inhibit hemin-induced platelet aggregation and secretion. It is likely that cyclooxygenase pathway and / or increase the production of cyclic nucleotides are involved in hemin-induced platelet aggregation and secretion.

**Keywords:** hemin, platelet aggregation, platelet secretion, indomethacin, and dipyridamole