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The role of different aggregating agents in the inhibition of nitric oxide synthesis in platelet aggregation

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The aggregation of platelets is by the activation of cyclooxygenase (COX) that catalyzed the conversion of arachidonic acid to prostaglandins and to thromboxane A2 (TXA2). No mechanism of release of arachidonic acid from the platelet membrane is currently available. The candidate for the first time ever reported that the inhibition of nitric oxide (NO) synthesis ultimately resulted in increased aggregation of platelets that has been reported to result in the development of acute coronary syndrome (ACS). NO was measured by methhemoglobin method. The purified nitric oxide synthase (NOS) was prepared by repeated gel electrophoresis using of the platelet cytosolic fraction by SDS-PAGE and the amino acid sequence of the purified protein was determined by mass spectrometry. Incubation of platelet rich plasma (PRP) with 8.0μ M ADP resulted in increased platelet aggregation (~90%) with simultaneous reduction of basal NO level to 0nmol/108 platelets, P<0.0001, n=10). It was found that different aggregating agents reduced the basal NO synthesis in platelets by ~50%. This reduction resulted in the appearance of Ca2+ in the platelet cytosol and in the release of arachidonic acid from the platelet membrane for TXA2 synthesis. This novel NOS was identified to be α -1 anti trypsin (AAT), a 47kDa protease inhibitor as determined by amino acid sequence. The results demonstrated that the reduction of NO level in platelets is a priori event in the activation of COX leading to the aggregation of platelets. The identification of the NOS as the AAT can be a therapeutic target for the treatment of ACS.

Biography

Debipriya Banerjee is a PhD student recently submitted her thesis under Department of Physiology, University of Calcutta, India. Her work focuses on understanding the interplay between nitric oxide and the increased occurrences of acute coronary syndromes. She is a Master degree topper with a gold medal. She has received financial support from Government of India to present her findings in the conference.

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