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Von Willebrand Factor and GPIbα regulates proplatelets formation by human megakaryocytes

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A key step in thrombopoiesis is the reorganization of the mature megakaryocytes (Mks) cytoplasm into pseudopodes called proplatelets, that release platelets into the bone marrow sinusoids. In this study we have investigated the biochemical mechanisms that control and regulate this process.

Human umbilical cord blood $CD34^+$ cells derived Mks extended, spontaneously, proplatelets in suspension after 8 hours of incubation. When plated on fibrinogen (FNG) or von Willebrand factor (VWF), that are supposed to be components of extracellular matrix, Mks extended proplatelets only after 4 h; in contrast type I collagen was unable to support proplatelet formation, indicating that matrices regulate proplatelet formation (1-2). Spontaneous proplatelet formation in suspension appeared to be significantly affected by the selective Src kinases inhibitor (PP2), PI3-K inhibitor (Wortmannin), protein kinase C inhibitor (Ro-31-8220) and the intracellular Ca^{2+} chelator (BAPTA-AM), patways involved in the crosstalk between the GPIbα and $\alpha_{IIb}\beta_3$ integrin. When Mks were allowed to adhere to FNG or VWF, only protein kinase C played an essential role in proplatelet formation; Src kinases, PI3-K and intracellular level of Ca^{2+} only minimally reduced this process.

The $\alpha_{IIb}\beta_3$ antagonists anti-CD61 antibody and RGDS peptide didn't cause reduction of proplatelet formation by both non adherent and adherent Mks, while anti GPIbα antibodies totally suppressed this process.

These results indicate that proplatelet formaton is regulated through GPIbα rather than $\alpha_{IIb}\beta_3$.

References

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