SUMMARY:

Megakaryocytes and platelets, which are their progeny, are highly specialized cells that participate in hemostatic and inflammatory functions. The most recognized model of platelet formation provides that it occurs in the bone marrow environment where megakaryocytes extend long filaments, called proplatelets, that protrude through the vascular endothelium into the sinusoid lumen, where the platelets are released.

To date many aspects regarding the mechanisms underlying proplatelet extension and platelet release remain unsolved. Consequently, insight into the pathogenesis of megakaryocyte related diseases as well as treatment options are missing; among the diseases, myeloproliferative neoplasms (MPNs), which include polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF), represent one of the most severe clinical picture that is still incurable.

Recent studies pointed to a key role of abnormal megakaryocytopenesis in the pathogenesis of MPNs; however, little is known about the latter stage of megakaryocyte development and proplatelet formation in these diseases. In this study the authors analyzed the in vitro megakaryocyte differentiation and proplatelet formation in 30 PMF, 8 ET, 8 PV patients, and 17 healthy subjects with the aim of establishing to what extent the observed abnormalities are attributable to intrinsic cellular defects.

The results demonstrated that each MPN category displayed peculiar alterations of megakaryocyte differentiation and function in vitro, suggesting that, besides the potential deregulation of bone marrow microenvironment, intrinsic defects of megakaryocyte function contribute to the pathogenesis of MPNs.

In conclusion, this study provides important new elements in the understanding of the biology of megakaryocyte and proplatelet formation in MPN, and opens a new perspective into the understanding of the pathophysiology of platelet production in these disorders. These results suggest that this experimental model may be useful for dissecting the pathogenesis of MPN, for identifying lesions responsible for disease evolution and for testing therapeutic agents. The long-term goal is to utilize the model to elucidate new clinical options for disease management.