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Correlation between Protein Kinase Cε expression and thrombotic risk in Primary Myelofibrosis (PMFs)

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Myelofibrosis (MF) - either primary (PMF) or arising from a previous PV or ET - is a Philadelphia-negative MPNs characterized by aberrant platelet production and consequent variable platelet count with altered hemostatic function (1). It has already been demonstrated that the risk of thrombotic events is one of the most common co-morbidities associated with PV and ET (2-5). However, risk of thrombotic events in PMF has not been investigated yet. We previously demonstrated that PKCepsilon (PKCε) is over-expressed in platelets from patients with acute myocardial infarction and accounts for their increased reactivity (6). Additionally, we recently showed that PKCε overexpression plays a crucial role in PMF MK impaired differentiation and that its levels correlated with the disease severity (expressed by the IPSS/DIPPS risk category) (7,8). On these bases, we analyzed PKCε expression in platelets from PMF patients, investigating a potential correlation with thrombotic risk and the aggressiveness of the disease. For this study, peripheral blood samples from 6 PMF patients and 3 healthy donors (HD) were collected in Na-citrate tubes. PKCε mRNA and protein levels were determined in platelets purified as described by Carubbi C, 2012. Finally, patients are stratified according to the history of cardio-vascular events and the IPSS/DIPSS risk category. PMF platelets showed significantly higher mRNA levels of PKCε as compared to HD. Protein analysis confirm PKCε over-expression in PMF platelets, almost reaching statistical significance. We then found that platelet from PMF patients who suffered from cardiovascular events display significantly higher levels of PKCε as compared to the one with a negative history. Finally, similarly to what observed in PMF magakaryocytes, we showed a positive correlation between PKCε platelets levels and IPSS/DIPSS risk category, with the lowest levels in low-risk patients and higher levels in high-risk patients. Collectively, our preliminary results indicate that PMF platelets show an aberrant expression of PKCε which correlates with the disease burden and a history of cardiovascular events. This suggests that the over-expression of PKCε may account for PMF platelet altered reactivity and function.

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