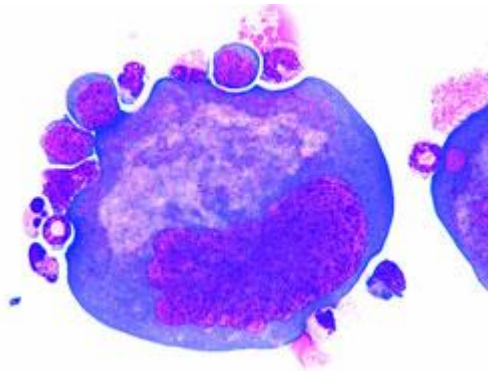


## Modified platelets with enhanced function for vascular targeting

### Project Leader: Prof Dr Dr Modlich

Platelets are anuclear blood cells of only 2µm size with an irrecoverable role in hemostasis, but also important functions in inflammation, angiogenesis, tumor growth and innate immunity. Furthermore, platelets play crucial roles in life threatening diseases such as thromboembolic events. Platelets are produced by megakaryocytes in the bone marrow, circulate through the blood stream within the blood vessels and maintain inactive (resting) until activated by environmental signals such as endothelial damage.



Murine Megakaryocyte. Source: PEI

Platelets transport numerous proteins within their granules, which can be released after platelet activation, therefore act as "natural carriers". These natural characteristic of platelets make these cells an interesting target for cell therapy. We are proposing to develop modified platelets that would carry therapeutic proteins in their granules, which can be released after activation of platelets. This will create local milieus of therapeutic factors and will terminate with the end of the platelet life time. Because platelets will not persist long term, side effects induced by long term ectopic expression are not likely.

The modification of platelets has to be performed at earlier step of differentiation, the megakaryocyte, hematopoietic progenitor, HSC or even the pluripotent stem cell. For the genetic modification we use lentiviral vectors with transcriptional control that targets expression to megakaryocytes, or by the use of inducible vectors. By protein modifications we can supply synthetic growth factors, dominant-active or dominant-negative proteins and specifically target these proteins into the secretory platelet granules or to the cell surface. Furthermore, we envisage that platelets can be generated that respond to pharmaceutical inducers. Finally, we are interested in the in vitro production of platelets from ES/iPS cells.