to reticulocytes. Correlation of the TER119/CD71 expression phenotype with erythroid differentiation allowed development of an in vitro culture system that more closely recapitulated the in vivo pattern of differentiation. Using this system, oncogenic H-ras but not dominant-negative H-ras was found to partially block CFU-E colony formation.

The authors then evaluated the TER119/CD71 expression profile observed following transfection with H-ras. Infected cells accumulated at the CFU-E and proerythroblast stages, suggesting H-ras exerts its effects by blocking differentiation and enhancing abnormal proliferation at that level. No effects on apoptosis were seen.

Apart from the new information they provide, these elegant studies remind us that better definitions of the phenotype of hematopoietic progenitors and further improvements in culture techniques retain the capacity to enhance the molecular investigation of hematopoietic regulation.

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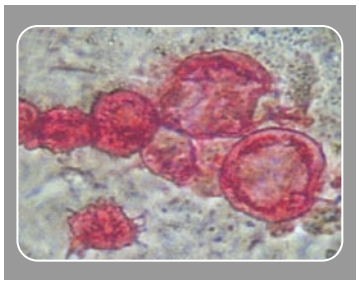
Platelets made to order

Given their abundance and importance in thrombosis and hemostasis, platelets have been the target of intense scientific inquisition for decades. While the study of physiologic platelet functions such as aggregation and granule secretion have been well characterized, platelets remain a difficult target of study from the perspective of signal transduction. Nucleated cells can be genetically manipulated via a variety of rapid techniques to map out detailed signaling pathways, whereas the study of platelet signaling has largely been limited to the use of soluble agonists or inhibitors, knockout mice, or platelet precursor cells such as megakaryocytes. Although these techniques have provided invaluable insights into platelet signaling pathways, they are hindered by issues of specificity and/or time.

In this issue of *Blood*, Fujimoto and colleagues (page 4044) describe a detailed and efficient technique by which functional platelets derived from embryonic stem (ES) cells can be genetically transfected. Recent studies have shown that the nucleated megakaryocytes can be manipulated by viral



infection[1] or by RNA interference.[2] Additionally, physiologically active platelets can be produced from megakaryocytes in vitro.[3] However, Fujimoto and colleagues bring together the concepts of exogenous gene expression in megakaryocytes and platelet differentiation. The authors first confirmed the presence of functional platelets from their differentiated megakaryocyte cultures through both subcellular imaging and agonist-induced fluorescent fibrinogen binding. Next, they transfected the differentiated megakaryocytes with either green fluorescent protein (GFP) or a β_3 integrin construct (Tac-β_3) that has been shown in nonplatelet systems to inhibit agonist-induced $\alpha_{IIb}\beta_3$ activation. The transfections were demonstrated to carry over from the megakaryocytes to the platelets, since GFP-transfected megakaryocytes produced GFP-positive platelets, and Tac-β_3–transfected megakaryocytes produced platelets that were significantly impaired in their ability to bind fibrinogen in response to protease-activated receptor 4 (PAR4)–activating peptide.

Along with demonstrating the ability to "transfect" platelets, another important feature of this study is the utility it provides for other platelet researchers. In addition to employing a system using cultured and renewable ES cells, the authors show that this system can generate levels of platelets that are comparable to platelet numbers obtained from murine blood (1×10^4 ES cells yielding up to 1.8×10^8 platelets). The article also goes into great detail to document the processes of megakaryocyte differentiation and platelet production, demonstrating the transition of ES cells to undefined colonies of cells to individual megakaryocytes positive for α_{IIb}, and finally the presence of proplatelet structures leading to platelet release. This flow chart of cellular maturation is a useful tool for interpreting the results from a culture that contains a heterogeneous mix of cells types that are constantly changing. Studies such as these should pave the way for further exploration of intracellular platelet processes by allowing for rapid platelet production and manipulation. As the authors also point out, platelets produced similarly with human ES cells may provide a therapeutic benefit for patients with platelet disorders.

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Where have all the T cells gone?

The majority of cutaneous T-cell lymphomas (CTCLs) consist of clonal proliferations of skin-trafficking T cells that are usually $CD4^+/CD45RO^+/CCR4^+/CLA^+/CD26^-$. The malignant T cells frequently exhibit a Th2 cytokine profile with up-regulation of glutamate acetyltransferase 3 (GATA-3), enhanced interleukin-4 production, and depressed interferon-gamma production. Furthermore, signal transducers and activators of transcription 4 (Stat 4) expression by the malignant T cells appears to be markedly diminished. Progressive disease is