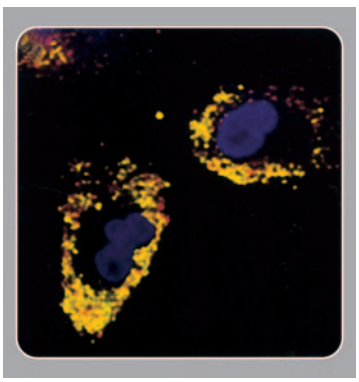
Magnetic cells show the way home

Recent progress in stem cell biology has made cell-based therapies for the treatment of tissue damage a realistic prospect. The ability to track noninvasively the migration of these cells after implantation could aid the development of this therapeutic approach. In this issue Hinds and colleagues (page 867) describe a cell-labeling method that will allow cell tracking using an imaging modality, magnetic resonance imaging (MRI), that is widely used in the clinic.

The idea of labeling cells with MRI-detectable paramagnetic complexes is not new (Hawrylak et al, Exp Neurol. 1993;121: 181-192). Studies over the last 10 years have defined the requirements of such labels. They should be very sensitive to MRI detection, cell uptake should be rapid and uniform, there should be even distribution to daughter cells, and they should have no effect on cell viability, proliferation, or function. The agent described by Hinds et al fits the bill on all counts. An important attribute, which is shared by some other particles of this type, is that it permits detection of single cells (Dodd et al, Biophys J. 1999; 76:103-109). This is possible since, although MR image resolutions are rarely comparable with cell dimensions, the particles distort the magnetic field far beyond the cell. Thus water molecules moving within the vicinity of a cell are affected, and the effect of the label is amplified enormously. A distinguishing feature of the agent described by Hinds et al is that it is relatively large, and this should allow detection of single cells at the lower image resolutions that can be achieved in vivo.



MRI detection of labeled cells is one of a growing number of noninvasive methods for investigating biologic processes in vivo (Weissleder and Mahmood, Radiology. 2001;219:316-333). These techniques are a valuable tool in the laboratory, but perhaps more importantly, they can also be used to help translate our understanding of these processes into new treatments in the clinic.

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ESCs and hematopoietic fate: mixing the perfect "cocktail"

The relatively recent availability of human embryonic stem cell (ESC) lines holds tremendous potential for a variety of therapeutic applications. ESCs are self-renewing and pluripotent, capable of generating cells of all tissue types. The ability to coax ESCs in vitro toward lineage-specific differentiation by varying culture conditions has been demonstrated in several mammalian species. But detailed characterization of the culture conditions required for differentiation of human ESCs has not been elucidated. Comparison of undifferentiated mouse and human ESCs has revealed important differences in morphology, marker gene expression, and culture conditions, further emphasizing the need for the precise characterization of human ESCs.

In this issue, Chadwick and colleagues (page 906) report that BMP-4, together with a specific combination of cytokines, can reproducibly induce multilineage hematopoietic fate from human ESCs under embroid body (EB) culture conditions. These results are consistent with the early role of BMP-4 in inducing ventral mesoderm, the tissue that gives rise to all embryonic blood lineages. Chadwick and colleagues further demonstrate that BMP-4, either alone or in combination with cytokines, promotes an increase in self-renewal of hESC-derived hematopoietic precursors, without significantly affecting their differentiation.

The detailed characterization presented here extends previous findings and represents an important step in defining a "cocktail" of factors capable of efficiently inducing hematopoietic differentiation from human ESCs. Recent studies have shown that the Wnt (Reya et al, Nature. 2003;423: 409-414) and FGF (de Haan et al, Dev Cell. 2003;4:241-251) signaling pathways can promote expansion and self-renewal of murine HSCs. Do these signaling pathways interact or synergize with the BMP-4 pathway to enhance multilineage hematopoietic differentiation from human ESCs? Future studies addressing the identification of the precise target populations acted upon under specific culture conditions and the further assessment of the long-term repopulating ability of these cells will be critical. Such studies lead the way toward a better understanding of the early development of human ESCs and provide a basis for tapping into their tremendous clinical potential.

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Antithrombotic thrombocytes

The Quebec platelet disorder (QPD) is a rare, autosomal dominant bleeding disorder that was characterized initially by a deficiency of platelet-associated factor V (Tracy et al, J Clin Invest. 1984;74:1221-1228). Subsequent studies revealed that QPD is associated with proteolytic degradation of multiple platelet alpha-granule proteins (Janeway et al, Blood. 1996;87:3571-3578) and that urinary-type plasminogen activator (u-PA) levels within platelet alpha-granules are markedly elevated in QPD patients compared to normal controls (Kahr et al, Blood. 2001;98:257-265). In addition to compromising hemostasis by catalyzing degradation of factor V and other alpha-granule proteins, such as von Willebrand factor (vWF), overexpression of platelet u-PA could cause