Chapter 8

Erythroid – Megakaryocytic Cell Lines

Hans G. Drexler

DSMZ-German Collection of Microorganisms and Cell Cultures, Department of Human and Animal Cell Cultures, Braunschweig, Germany; Tel: +49-531-2616-160; Fax: +49-531-2616-150; E-mail: hdr@dsrz.de

1. INTRODUCTION

For reasons outlined below, leukemia cell lines derived from erythroid or megakaryocytic cells are combined in this chapter. These cell lines represent in vitro models of immature erythroid and megakaryocytic cells and their distinct or common precursors.

Morphologically, the erythrocytic series consists of a succession of cells which begins with a pronormoblast and ends with the erythrocyte (or red blood cell) [1]. These circulating red cells and their precursors may be considered as a functional unit which has been designated as the erythron. The cells of this unit are not restricted to those recognizable morphologically in the bone marrow and in the peripheral blood, but also include elements which are not morphologically identifiable, namely the committed precursors of the erythroid line, the existence of which has been demonstrated by functional assays [2].

The thrombocyctic series is a succession of cells which starts with the basophilic megakaryoblast in the bone marrow and ends with the circulating thrombocyte or platelet [1]. In normal human bone marrow, the megakaryocyte is the largest cell, measuring 20–150 µm in diameter. The cells are polyploid, but not multinucleated, in contrast to the other giant bone marrow-derived cells, the osteoclasts. Normal megakaryopoiesis is maintained by morphologically unidentifiable precursors which are capable of differentiating into morphologically recognizable megakaryoblasts or of reproducing themselves [3].

As both erythrocytes and thrombocytes are terminally differentiated, anucleated end-stage cells, immature progenitor and precursor cells are considered to be the targets in the leukemogenic process. The acute myeloid leukemias originating in these cell lineages have been termed AML M6
(erythroid) and AML M7 (megakaryocytic) [4,5]. Erythroid and/or megakaryocytic cells can also represent a subpopulation of the main leukemic population in the myeloid blast crisis of CML [6].

Over the last two decades, a large panel of erythroid-megakaryocytic leukemia cell lines has been established from patients with AML, CML in blast crisis or rare hematological disorders [7–9]. The features displayed by a cell line assigned to this category are not single lineage-specific, but in most instances extend to both lineages. Indeed, data from both normal and malignant cells support this notion. Multiple lines of evidence underscore the concept of a close relationship between erythroid and megakaryocytic lineages [10]. The two share a number of transcription factors (including NF-E2, GATA-1, GATA-2, SCL) [11–13]. Furthermore, erythroid and megakaryocytic cell surface markers (including GlyA, CD41, CD42, CD61) are found on both types of leukemia cell and this dual expression is found on the same cell [14–17]. The cytokines EPO and TPO, originally considered to be cell lineage-specific, also have stimulatory effects on the megakaryocytic cell system and the erythron, respectively [18–20]. The receptor for EPO, which is the principal growth factor regulating the production of erythrocytes, has also been detected on megakaryocytes [21]. A bipotent normal erythroid-megakaryocytic progenitor could be isolated from human bone marrow [22]. Finally, most of the “erythroid” cell lines available display, or can be induced to display, features of megakaryocytic differentiation. The converse is true for cell lines initially thought to be exclusively megakaryocytic.

While a given cell line may show a preponderance of erythroid or megakaryocytic features, the notion of a close lineage relationship, extended here to the assignment of such cell lines to a common category, is borne out by the extensive published data, summarized here in Tables 1–6. Most erythroid-megakaryocytic cell lines were established in the 1980s (49%) and 1990s (47%), with K-562 being the oldest cell line [45].

2. CLINICAL CHARACTERIZATION

Forty-nine cell lines with erythroid and megakaryocytic characteristics are listed in Table 1. These cell lines were derived mainly from patients with CML in blast crisis (41%), de novo or secondary AML M6 (14%) or AML M7 (33%). It is of note that 4/7 AML M6 and 8/16 AML M7 cases were either secondary to or accompanied by other hematological disorders or (pre)malignancies. The ages of the patients ranged from 0.5 to 73 years with 3 infants (<1 year) and 10 other children. Specimens were obtained at diagnosis (n = 12), at relapse (n = 11) or in blast crisis (n = 20). Taking CML blast crisis as an indicator of relapse, then 63% of these cell lines were