Influence of the Localization of Erythroid Cell Death on Erythropoiesis Kinetics

V. V. Svishchenko and E. D. Gol'dberg*

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 121, № 3, pp. 359-360, March, 1996
Original article submitted November 10, 1995

The fundamental patterns of influence of the localization of erythroid cell death on cell kinetics are defined with the aid of mathematical modeling. It is established that the kinetic picture is mainly dictated by the region where the death is localized.

Key Words: *erythropoiesis; kinetics; cell death*

It is well known that the death of erythroid cells has a profound influence on cell kinetics [1]. We were interested in finding the laws of behavior of cell kinetics when the localization of cell death changes during differentiation. Mathematical modeling was used [2] to solve this problem.

MATERIALS AND METHODS

Using a mathematical model [2] for a pool of proliferating cells of some stage of differentiation, the following expression may be obtained:

$$\mu=\sum_{i=1}^{m}\mu_i;\quad g=\sum_{i=1}^{m}g_i;\quad g^{out}=\sum_{i=1}^{m}g_i^{out},$$

$$\mu_i=P\gamma_i\sum_{l=1}^{k_i}2^{l-1}\exp\left\{-\sum_{j=1}^{l}\lambda_{j,i}a_iB_{j,i}T\right\},$$

$$g_i=P\gamma_i\sum_{l=1}^{k_i}2^{l-1}\exp\left\{-\sum_{j=1}^{l-1}\lambda_{j,i}a_iB_{j,i}T\right\}\times$$

$$\times[1-\exp\{-\lambda_{l,i}a_iB_{l,i}T\}],$$

$$g_i^{out}=P\gamma_i2^{k_i}\exp\left\{-\sum_{l=1}^{k_i}\lambda_{l,i}a_iB_{l,i}T\right\},\qquad(1)$$

where μ is the number of cells forming per unit time due to divisions at the stage; $\mu(0)$ is the value of μ if death is absent; g is the number of cells dying per unit time; g^{out} is the number of cells leaving the given stage and passing to the next stage per unit time; $g^{out}(0)$ is the value of this parameter without death; γ_i is defined as the fraction of cells in the flow at input P which go through k_i divisions at the stage; m is the number of flows; $B_{j,i}T$ are the generation times; $\lambda_{j,i}a_i$ define the magnitude of the fraction of cell death in the flow with a number i of the generation with a number j; $\lambda_{j,i}$ and $B_{j,i}$ are dimensionless quantities. The following relations are in force:

$$\mu^n=\mu(0)-\mu\qquad(2)$$

$$\mu^{n,d}=\mu^n+g=g(0)-g^{out},\qquad(3)$$

where μ^n denotes the number of cells which do not appear due to death at the differentiation stage in question per unit time; and $\mu^{n,d}$ is the number of cells which die and hence do not reach the given stage per unit time.

RESULTS

For convenience, let us impose the following condition on $l_{j,i}$:

$$\sum_{j=1}^{k_i}\lambda_{j,i}B_{j,i}=k_i.\qquad(4)$$

When P, γ_i, a_i, and k_i are unchanged and for any $\lambda_{j,i}$ satisfying (4), g^{out} and $\mu^{n,d}$ will be unchanged, as follows from (1) and (3). If (4) is fulfilled and P, γ_i, a_i, and k_i are unchanged, two limiting cases may be considered: 1) when the whole fraction of death in each

---

Siberian State Medical University; *Institute of Pharmacology, Russian Academy of Medical Sciences, Tomsk

0007-4888/96/0003-0329$15.00

flow $P\gamma_i$ falls within the first generation and $\lambda_{1,i}B_{1,i}=k_i$, $\lambda_{2,i}=\lambda_{3,i}=\ldots=\lambda_{k_i,i}=0$; 2) when the whole fraction of death in each flow $P\gamma_i$ is localized in the last generation and $\lambda_{1,i}=\lambda_{2,i}=\ldots=\lambda_{k_i-1,i}=0$, $\lambda_{k_i,i}B_{k_i,i}=k_i$. Using these fractions of death and expressions (1), we get: $g^{(1)} \leq g \leq g^{(2)}$; $\mu^{(1)} \leq \leq \mu \leq \mu^{(2)}$; $\mu^{n(2)} \leq \mu^n \leq \mu^{n(1)}$, where $g^{(1)}$, $\mu^{(1)}$, and $\mu^{n(1)}$ are the characteristics if the fraction of death in each flow $P\gamma_i$ is localizes in the first generation and $g^{(2)}$, $\mu^{(2)}$, $\mu^{n(2)}$ are the characteristics if it is localized in the last generation. The magnitude of the difference between these limiting cases can be judged from the following relations:

$$g_i^{(2)}(a_iT)/g_i^{(1)}(a_iT)=2^{k_i-1};$$

$$\mu_i^{n(1)}(a_iT)/\mu_i^{n(2)}(a_iT)=2-2^{-k_i+1};$$

$$\mu_i^{(2)}/\mu_i^{(1)}=[\exp\{k_ia_iT\}(2^{k_i-1}-1)+2^{k_i-1}]/[2^{k_i}-1].$$

The last expression rapidly increases as the fraction of death a_i and k_i and rises can markedly exceed 1. Consequently, for the same cell flow P at the differentiation stage examined and the same flow of cells g^{out} from this stage, the characteristics of cell kinetics change markedly depending on the localization of death, and the kinetic picture changes too.

All behavioral tendencies found for the different characteristics are preserved if in each cell flow $P\gamma_i$ the maturation pool is substituted for the last generation. Such a case actually holds true for a pool of morphologically identifiable cells.

The laws of behavior for cell kinetics described here must be taken into account in various studies involving data on the status of bone marrow.

REFERENCES

1. G. I. Kozinets, I. A. Bykova, and T. G. Sukiasova, in: *Kinetic Aspects of Hemopoiesis* [in Russian], Eds. G. I. Kozinets *et al.*, Tomsk (1982), pp. 79-148.
2. V. V. Svishchenko and E. D. Gol'dberg, *Mathematical Modeling of Erythropoiesis Kinetics* [in Russian], Tomsk (1995).