Fractal Analysis in epigenetic differentiation of leukemic cells

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1. Introduction

This communication describes the application of fractal analysis to epigenetic suppression of malignancy as a potential tool for diagnostic and prognostic purposes. Using the fractal dimension, we found that the complexity of malignant cells is lower in comparison with non-malignant ones.

Usually, the structure of an object can be described utilizing tools of common geometry. A square, for example, can be described by the measure of its sides. However, "complicated" objects, particularly naturally occurring objects such as clouds, mountains, and coastlines, do not apparently appear as a sum of triangles and lines. Such objects are better described using fractal geometry. Fractal geometry has been known as a mathematical concept for many years and was introduced by B. Mandelbrot [1]. Its tools were applied successfully to characterize irregularly shaped and complex figures by a mathematical value wherever Euclidean geometry fails. One of the advantages of fractal analysis is the ability to quantify the irregularity and complexity of objects with a measurable value, which is called the fractal dimension. The fractal dimension can be determined using the box-counting method [2]. Fractal analysis techniques are common tools in physics and image processing.

Fractal geometric analysis, using such tools as fractal dimensions, is thus a more valid method of quantification and is more likely to provide discrimination between different types of fractal objects. In the field of pathology [3], fractal geometry has proved its utility in particular in cancer research [4], such as in endometrial carcinoma [5], in breast cancer [6] and tumour growth [7]. In view of the amazing growth in the understanding of the fractal complexity of the cancer mechanisms, most researches are carried out by measuring the fractal dimension (FD) of different cancer cells or tumour growth. But nothing has been said in relation to the reverse processes, the epigenetic suppression of malignancy. Recently, Lotem and [8] have found that there are Myeloid leukemic cells that can be induced by adding different cytokines including IL-6 to differentiate to non-dividing mature granulocytes and/or macrophages.

2. Results

We applied a fractal dimension analysis, in particular box-counting dimension [9] to epigenetic differentiation of leukemic cells. We found that a significantly higher architecture complexity was noted for non-malignant cells during different stages in differentiation to granulocytes (FD = 1,332; 1,260; 1.209, *Figures 1b,c,d*) in comparison with myeloid leukemic cell, (FD = 1.018, *Figure 1a*).

As it is shown, the complexity of the non-malignant cells is higher than in the malignant one in epigenetic suppression of malignancy by inducing differentiation bypasses the genetic abnormalities in tumour cells. As a fact, this finding corresponds to a general regularity in the biological systems [10].

In summary, fractal analysis applied to epigenetic differentiation of leukemic cells show promise as useful measure of these complex processes. Furthermore, it may provide an additional tool to prognostic information as well as to shed light on the evolution of tumour cells toward the epigenetically reprogrammed to a non-malignant phenotype cells.

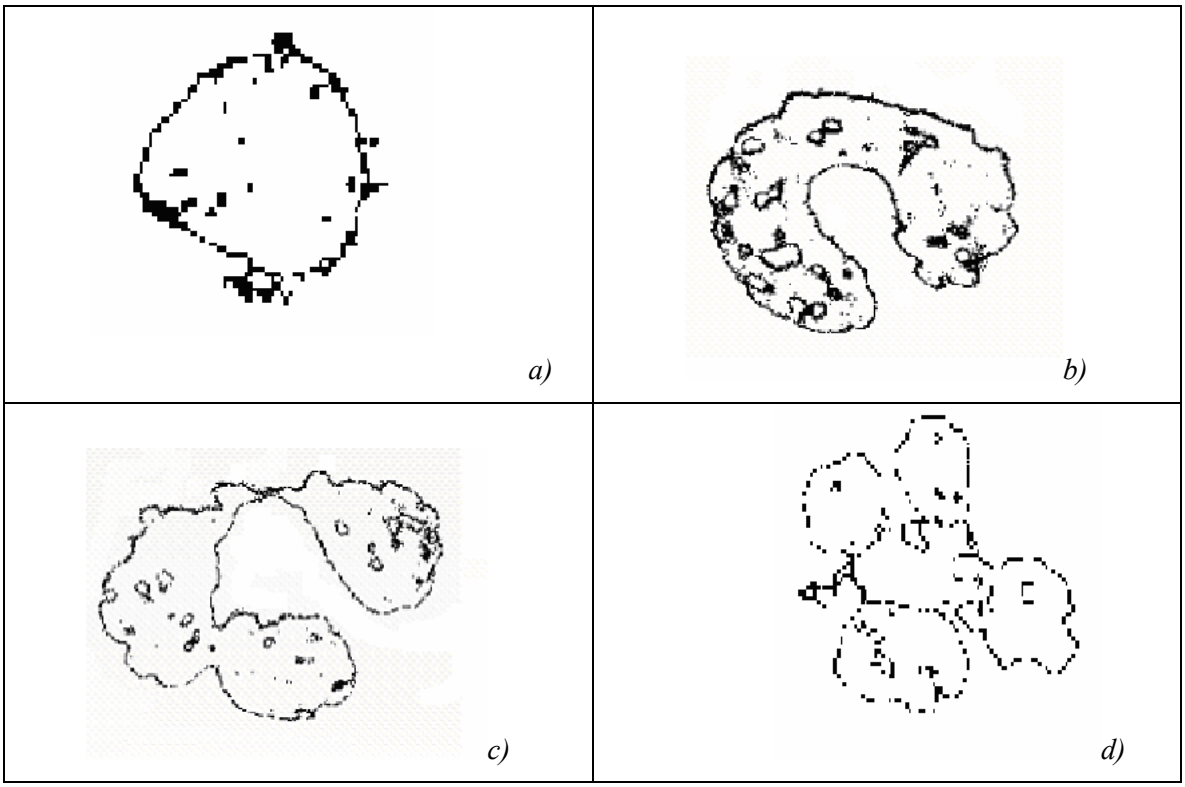

Figure 1 Epigenetic differentiation of genetically abnormal myeloid leukemic cells to non-malignant granulocytes by IL-6: Black/white representation of with a grey level threshold set at: (a) leukemic cell (50-100); stages in differentiation to granulocytes b (100-150), c (94-136), d (50-100).

3. Financial Disclosure

The authors have no connection to any companies or products mentioned in this letter.

4. References

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