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Motility, Shape and Fibrillar Organelles of Leukemia Cells

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LOCOMOTIVE behavior, cellular shape and the distribution pattern of fibrillar organelles in rat and human acute leukemia cells were studied by means of microcinematography (MCM), scanning (SEM) and transmission electron microscopy (TEM). Microcinematographic observations were performed under *in vitro* conditons. The combination of MCM and SEM offers the possibility to correlate surface architecture and cell shape of fixed cells with the behavior of living cells [1, 2].

During locomotion, leukemia cells assume a polarized configuration which is characteristic for the different cell classes: blast cells irrespective of their origin move in a handmirror shape with a tail-like posterior protrusion and a roundish anterior part, promyelocytes are elongated with prominent extensions at the anterior part, and myelocytes have a round body with especially well developed cytoplasmic veils. At rest, leukemia cells are spherical [3, 4]. The various configurations of leukemia cells at rest and during locomotion cannot only be recorded by MCM and SEM but can also be seen in TE micrographs. The possibility to recognize the different cellular shapes in thin sections therefore allows to study occurrence and distribution pattern of fibrillar organelles in leukemia cells fixed at rest and during locomotion [5, 6]. A correlation between the fibrillar structures and cellular shape and activity can be thus established. Microfilaments and microtubules have a similar distribution pattern in polarized locomotive and spherical resting cells of the diffrent classes of leukemia cells. Intermediate filaments (IF), on the other hand, occur in two main patterns, as thin and thick bundles. In a transplantable, unclassifiable rat leukemia and in 9 out of 12 cases of acute human myeloid leukemias, the two cell configurations, spherical and polarized, were found to coincide with a different pattern of IF. While in most of the spherical myeloblasts, IF are arranged in large bundles, polarized myeloblasts have small groups or single filaments. Only a minority of spherical myeoblasts in each of the leukemic populations shows small bundles of IF.

With regard to the role of IF in leukemic myeloblasts two alternative interpretations are presented. The first possibility requires a disaggregation–reaggregation cycle of IF bundles accompanying the cycle of cell shape changes. This can occur either through a transitory stage of spherical cells with small bundles, or directly. The alternative assumes that the transition from spherical to polarized cells, and back, occurs exclusively among cells with small bundles of IF. Cells with thick bundles of IF would then represent a functional impasse. Our own observations provide some arguments in favour of a disaggregation–reaggregation cycle of thick IF bundles whereas a 'pathological' significance of these IF aggregates seems less likely.

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To what extent can these various aspects of cell motility be integrated into an exploitable concept, particularly with regard to cell locomotion? In the following contribution, the two basic elements of such a concept—the generation of motive force and the latter's transformation to locomotion—are evaluated.

Conformance Versus Divergence: A General Consideration

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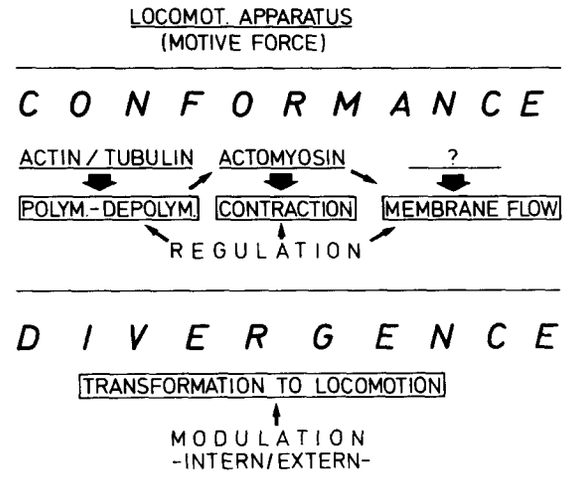
FOR THE initiation and maintenance of cell locomotion, two main prerequisites must be fulfilled: a motive force must be generated and this force must be transformed to actual translocation of the cell. During the last decade, chemo-mechanical energy transformation in unicellular organisms and in tissue cells has been associated with two protein systems: the cytoplasmic actomyosins and the tubulin–dynein system. While it is an established fact that actomyosin plays a major role in motive force generation, the extent to which cytoplasmic microtubules participate in this step is still unclear. Polymerization processes have been considered, especially since it was shown that cytoplasmic actin can produce motive force by undergoing polymerization without involvement of an ATP-ase. In addition to polymerization $\leftrightharpoons$ depolymerization and to contraction, it cannot be ruled out that membrane movement phenomena (membrane flow) also contribute to locomotion by means of unknown force-developing processes within the membrane itself.

In the following diagram, the mechanisms definitely or possibly involved in the generation of motive force are presented.

The diagram emphasizes the concept that on the molecular level of motive force generation, there exists a certain *Conformance* of phenomena, while the translation of the molecular events to actual locomotion shows a considerable *Divergence* in the different cell types. It is evident that the mechanisms leading to motive force generation must be controlled by regulation mechanisms, some of which have become apparent during the past years.



Obviously, contraction phenomena of cytoplasmic actomyosin, polymerization processes of tubulin or actin and membrane flow phenomena are not sufficient to explain the complicated patterns of cytoplasmic streaming involved in cell locomotion. Contraction can only result in a linear approximation of two cytoplasmic areas or, as a continuous sliding (shearing movement), in unidirectional streaming movements. Polymerization processes of actin and tubulin, on the other hand, have primarily morphogenetic functions which result in unidirectional translocation of cytoplasmic material but cannot, by themselves, explain the complicated patterns of cell locomotion.

For this reason, the processes leading to primary force generation, while operating in a certain conformance, need translation mechanisms by which the motive force is converted to locomotion. According to our experience with different objects, such as free-living amoebe, acellular slime molds and tissue culture cells, we have to consider that the transformation processes show a great divergence in different cell types. Therefore, they have to be studied separately for each cell type, and no prediction can be made from one cell type to another. Furthermore, the divergent transformation processes are modu-