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The Cytoskeleton of Mouse Neuroblastoma Cells

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The oriented cell shape of cultured neuroblastoma cells with their long dendritic processes, each ending in a highly motile growth cone, requires mechanisms for the maintenance of stability and for control of motility. The filamentous proteins are believed to serve these functions by providing a cytoskeleton and the structural basis for force-generating phenomena.

Immunofluorescent techniques show that the distribution of tubulin and actin in neuroblastoma cells is strinkingly different [1]. Whereas microtubules are found to arise near the cytocenter and to radiate over long distances to the cell periphery, actin is localized beneath the plasma membrane and, especially accumulated, in the outer tips of the neurites. Improved methods for the visualization of the cytoskeleton of whole cells, using Triton-extracted, negatively stained cell monolayers [2, 3], have shown that actin filaments are the only filamentous components in the leading edge and at the tips of the neurites. Actin filaments have at least two supramolecular aggregation states: a planar filament meshwork and paracristalline-like filament bundles, partly corresponding to microspikes. In addition, decoration with myosin subfragment-1 (S-1) revealed that the actin filaments in this area are singly polarized towards the cell body. This unipolar organization of actin is a general feature of advancing lamellae of cultured cells, and is not only found in microspikes but also in the interconnecting filament meshwork [3, 4].

Since the polymerization of F-actin occurs in a direction opposite to that of the arrowhead complex, it is suggested that unidirectional polymerization of actin may constitute the primary force producing mechanism for the advancement of growth cones and leading edges. The direct correlation between actin polymerization and arising leading edges is especially prominent when neuroblastoma cells are treated with concanavalin A. This induces the formation of broad and extensive lamellae regions which are formed nearly around the whole perimeter and contain a filamentous actin meshwork as well as abundant paracrystalline-like actin bundles [5]. Membrane ruffling may also be explained by the same polymerization and depolymerization process. It occurs when the terminal filament meshwork locally binds to and detaches from the substrate via the plasma membrane. Depolymerization of actin results in the disappearance of the ruffles into the cell body.

While microtubules and 100 Å filaments (neurofilaments) are found in the core of cell extensions, actin filaments obviously are lacking in this region. The interaction of microtubules and 10nm filaments and their possible involvement in intracellular transport phenomena and locomotion remains to be clarified.

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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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