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Review

# Controlling cell length

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ABSTRACT

Control of cell dimensions is an important but poorly understood aspect of morphogenesis. In this review, our primary focus is on control of cell length in different types of cells and cytoskeletal regulation of this parameter. Cell length is not a constant characteristic of certain cell type but of cells of fibroblastic morphology. Since cytoskeleton organization can change during different processes of morphogenesis changes in length control during cell spreading, epithelio-mesenchymal transformation and also in neoplastic transformation are discussed.



**Contents**



## 1. Introduction

Controlling cell and organelle size is an important aspect of morphogenesis. Control of cell morphology is critical for cell differentiation and for tissue and organ development. Cell size is dependent on type of cell, stage of cell cycle, and ploidy. For instance alteration of cell shape and cell size is observed during neurogenesis and cardiac development in animal cells [1,2], in the genesis of root hairs, pollen tubes, and vascular elements in plants [3]. In culture changes of cell area, number and size of processes take place during cell spreading, movement and also in tumor transformation [4]. Cell shape is controlled by cytoskeleton structures on the inside and adhesion structures attaching the cell to the substrate and to other cells [5,6].

There are many ways to study mechanisms controlling cell dimensions and cell shape. Some of them involve use of drugs that affect cytoskeleton structures and regulatory proteins. Another method is use of substrate with different degree of adhesiveness and different distribution of adhesive and non-adhesive regions. Such substrates can be prepared by evaporation of metal, by coating glass or plastic surface by non-adhesive agents [7–9].

## 2. Control of cell length in fibroblasts and epitheliocytes

One of the ways to study regulation of cell dimensions is to use substrates with different adhesive properties. To study experimentally one of the parameters of cell shape and size and cell length we [10] used the following method. The glass substrate was covered with a thin non-adhesive layer of biocompatible hydrogel, poly-2-hydroxyethilmethacrilate (poly-HEMA) [11,12]. Then narrow cuts were made in this layer by razor blade. Cell on this substrate can form adhesive contacts only within the strip therefore spreading of cell lengthwise is not restricted. Width of the cell is strictly limited by boundary of poly-HEMA. Therefore it is possible to talk about “unidimensional” spreading. The cells were seeded on this substrate and spreads for 24 h. Coverslips were used as control substrate. Measurements of morphometric parameters of non-transformed fibroblasts of different types had shown that

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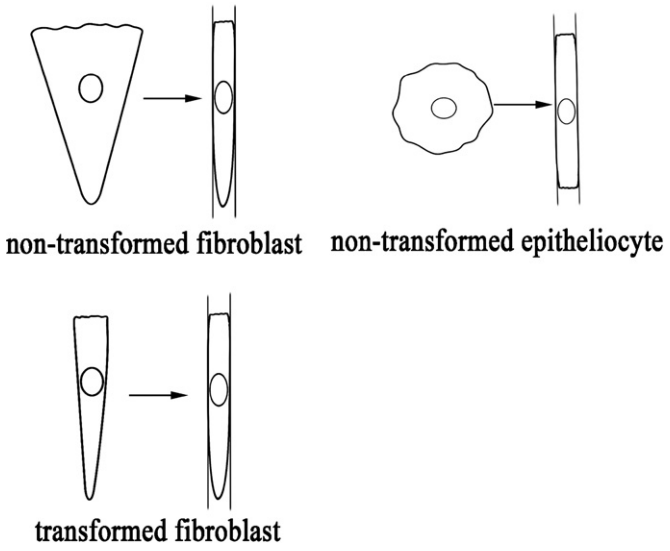


**Fig. 1.** Comparison of cell length of non-transformed fibroblasts, epitheliocytes and transformed fibroblasts on control substrate and on strip. Area of non-transformed fibroblast is much smaller on strip than on the control substrate but length of the cell on strip is not decreased. Length of epitheliocyte on strip is considerably higher than the diameter of discoid cell on planar substrate. Length of transformed fibroblast on strip does not exceed length on control substrate. Difference between areas of transformed and non-transformed fibroblasts on the strip is much less pronounced than on the control substrate.

length of cells on the strips, that is, on the substrate favoring "unidimensional" spreading, does not exceed the average length of the cells spreading 'bidimensionally' on the standard substrate – glass or plastic [10] (Fig. 1). Cell length was defined as the length of straight line between two points at the maximal distance on a cell outline. This constancy of cell length was observed in the experiments with three types of fibroblastic cells independently obtained from different sources: in two different permanent lines of human fibroblasts and in culture of mouse embryo fibroblasts. It is interesting to note that all three types of cells had different average cell lengths but all the same demonstrated similar reactions.

Thus, constant length may be a general characteristic of cells with fibroblastic morphology.

Experiments with epitheliocytes show that mechanisms controlling the shape of single discoid cells of this tissue type are significantly different from those of fibroblasts. Squeezed on the linear strip epitheliocytes acquired an ellipsoid shape with a length considerably higher than the diameter of discoid cell on the planar substrate (Fig. 1). Obviously epitheliocytes have no control of their length [10].

Probably, differences in control of cell length between epitheliocytes and fibroblasts are due to differences in cytoskeletal organization. Fibroblasts, being fully spread, usually have straight bundles of actin–myosin microfilaments (stress fibers) running through the cell body approximately parallel to the body axis and microtubules running from perinuclear part toward the cell periphery forward and backward (Fig. 2). Epitheliocytes have circular actin bundles at the cell periphery with adherent junctions that are aligned tangentially along cell boundaries (Fig. 3).

The shape of substrate-spread polarized fibroblasts has two distinct components: longitudinal spreading along the main cell axis and transversal spreading in the direction perpendicular to that axis. When fibroblasts are forced to spread on the narrow strips of adhesive substrate, their width is drastically decreased but their length did not change compared to the same cells spreading bidirectionally on the plane. These results show that longitudinal and transverse spreading have distinct and possibly independent

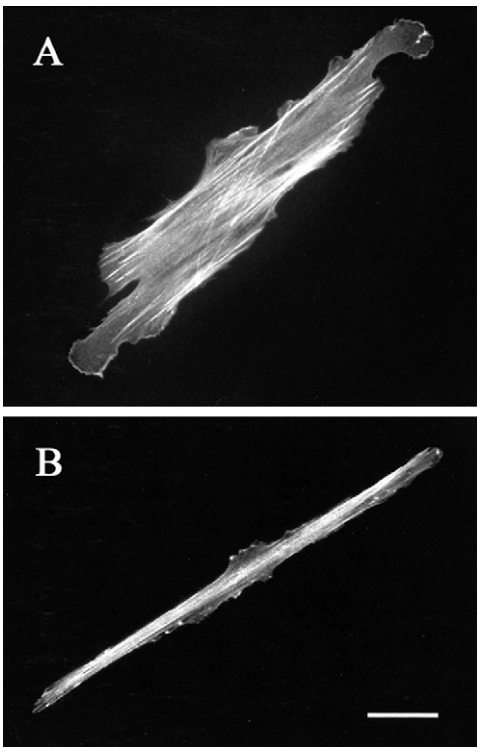


**Fig. 2.** Shape and cytoskeleton organization of non-transformed M19 fibroblasts on control substrate (A) and on the strip (B). Area of M19 fibroblast is much smaller on strip than on the control substrate but length of the cell is not decreased. Fluorescent microscopy after staining for actin. Scale bar, 20 μm.

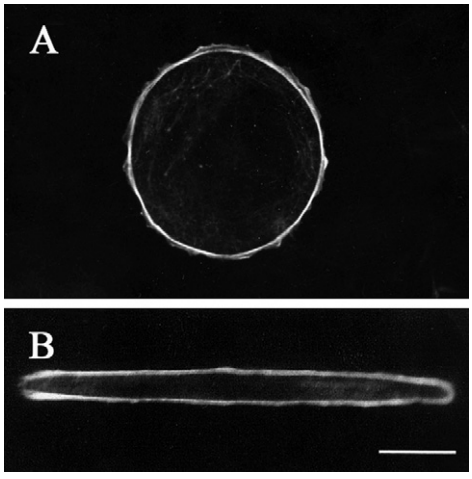


**Fig. 3.** Shape and cytoskeleton organization of IAR2 epitheliocytes on control substrate (A) and on the strip (B). Length of epitheliocyte on strip exceeds length on control substrate. Fluorescent microscopy after staining for actin. Scale bar, 20 μm.

mechanisms. During spreading of epitheliocytes, longitudinal and transverse directions are not distinguished. Most probably, these cells form and attach lamellipods in all possible radial directions.

## 3. Length control is determined by cell present shape

Cytoskeleton organization can change during different processes of morphogenesis, particularly during cell spreading. In the course of spreading on planar isomorphic substrate fibroblasts usually pass through several morphological stages. The first is discoid or radial stage, when spheroidal cells parachuting onto the sub-