【Grant-in-Aid for Transformative Research Areas（B）】

Cell behavior control and morphological design via nanostructures of rod-shaped materials

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Project Information	Project Number : 26B308　Project Period (FY) : 2026-2028 Keywords : Rod-like materials, Collagen fiber, Nanoscale patterning, Coordinated cell behavior, Cellular cytoskeleton, Tissue morphogenesis

Purpose and Background of the Research

● Outline of the Research

Multicellular organisms are composed of soft cells, yet their bodies possess rigid and stable structures such as bones, tendons, fins, and other appendages. These shapes and mechanical properties are supported not by the cells themselves, but by stiff, rod-like extracellular materials, including collagen fibers. Cells produce, transport, align, and assemble these fibrous materials, acting much like construction workers who build the body's architecture. However, how cells manipulate these rod-like materials with such precision has remained largely unknown. This research area aims to uncover the molecular and cellular mechanisms underlying the coordinated interactions between cells and extracellular fibrous materials, and to explain how these interactions generate tissue morphology. A central hypothesis of this project is that the nanoscale patterns inherent to the fibrous materials themselves—such as periodic surface ridges or alignment—play a decisive role in guiding cell behavior. This perspective has been largely absent from traditional developmental biology and offers a new paradigm for understanding morphogenesis during later developmental stages.

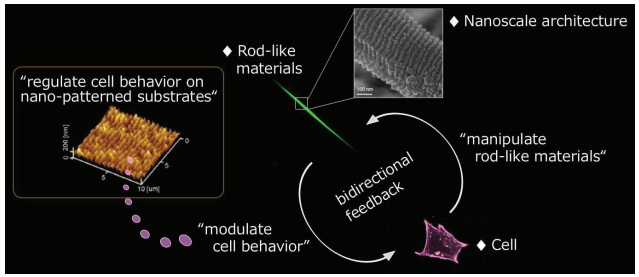

Fig 1. Conceptual diagram of the research in this project

● Research Framework

This research area integrates biology and materials science, combining three complementary approaches to uncover common principles:

• Sponges (A01): Sponge cells manufacture, transport, position, and connect glassy spicules—rigid rod-like skeletal elements—demonstrating a literal "construction process" carried out by cells.

• Zebrafish fins (A02): Cells manipulate collagenous rods called actinotrichia to shape the fin. Recent findings suggest that regular nanoscale surface patterns on these fibers influence how cells attach and operate on them.

• Engineered nano-patterned substrates (A03): In vitro systems using substrates with nanoscale grooves show dramatic switches in collagen fiber alignment, indicating that nanoscale patterns can reprogram cell behavior.

Together, these studies suggest that the nanoscale architecture of fibrous materials actively regulates cell dynamics, and that tissue morphology emerges from the coordinated interplay between cells and extracellular rods. This research area aims to elucidate this mechanism from multiple angles.

Expected Research Achievements

Three planned research projects (A01, A02, A03) work together to establish a new morphogenetic principle: Cells interpret the nanoscale patterns of rod-like materials and cooperatively organize them into functional tissue structures.

● A01 (Funayama): Deciphering the behavior of "cellular workers" in sponge skeletal construction

Sponge cells handle glassy spicules through four steps:
1)production, 2) transport, 3) positioning, and 4) connection.
A01 will analyze the cells responsible for transport and connection, identifying the molecular mechanisms enabling:
♦adhesion to spicules
♦alignment and angle adjustment between spicules
♦collagen-mediated bonding of spicules

By comparing these mechanisms with those in zebrafish (A02), A01 aims to identify conserved gene sets for rod-handling behaviors across species.

● A02 (Kuroda): Revealing how cells manipulate collagen rods in zebrafish fins

At the fin tip, cells interact with actinotrichia (AT), rod-like collagen fibers essential for fin shape. A02 will test the hypothesis that:
♦periodic nanoscale surface structures on AT
♦micron-scale spacing between AT fibers
determine the direction of cell protrusions and adhesion patterns.

A02 also examines how collagen fiber alignment patterns (parallel vs. orthogonal) are controlled, using genetic factors that regulate AT orientation. By altering collagen alignment in the developing limbs of non-fish vertebrates, A02 will test whether changes in fiber orientation contributed to the evolution of appendage morphology.

● A03 (Matsugaki): Reconstructing the mechanism using artificial nano-structures

A03 uses engineered substrates with nanoscale grooves or ridges to manipulate collagen fiber alignment in vitro. This project will determine:
♦how groove spacing and depth alter focal adhesions and cytoskeletal organization
♦how these cellular responses generate parallel or orthogonal collagen alignment

A03 will also identify molecular factors that induce orthogonal alignment and will reconstruct the morphogenetic mechanism in an artificial system, providing causal validation of principles discovered in A01 and A02.

● Originality and Expected Impact

This research area seeks to establish a new principle of morphogenesis:
cells actively manipulate rod-like extracellular materials, reading their nanoscale architecture to construct tissues.
If successful, this work will:
1. Introduce a new paradigm in developmental biology, shifting focus from cell–cell interactions to cell–material coordination.
2. Enable control of collagen fiber orientation and bonding, opening possibilities for reshaping tissues and organs.
3. Drive innovation in regenerative medicine, biomaterials, and artificial tissue engineering.

Understanding how cells coordinate with extracellular rods addresses a fundamental question in biology and provides a foundation for future biomedical applications.

Website(s)	https://www.brh.co.jp/research/lab06/