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

Mechanical self-transformation of living systems

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Research Area Information	Number of Research Area : 22A302 Keywords: Force, Development, Transformation, Morphogenesis, Self-organization	Project Period (FY) : 2022-2026

Purpose and Background of the Research

●Outline of the Research

Background: Elucidating the design principles of multicellular organisms is a fundamental challenge for life science. Global order of an organism generally develops from local interactions among molecules and cells. Collectively, these interactions—referred to as self-organization—give rise to the emergent properties of fate, form, and function of cells, ultimately leading to morphogenesis of tissues and organs. During morphogenesis, cells exert mechanical forces mainly by contraction of the cellular cytoskeletons. These forces are transmitted to neighbouring cells and external environment, thereby causing changes in size, shape, and position of cells (Fig. 1). Notably, recent studies have highlighted the potential for forces to modulate cellular fate and function, suggesting the existence of a complex feedback between forces and cellular physiology (Fig. 2). It, however, remains largely unknown how cells sense forces in their environment and coordinate the collective behaviours of cells during self-organizing morphogenesis.

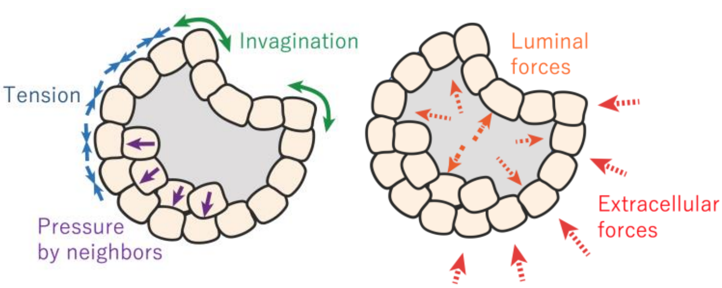

Fig. 1. Mechanical forces exerted by neighboring cells (left) and extracellular spaces (right) during development of multicellular organisms

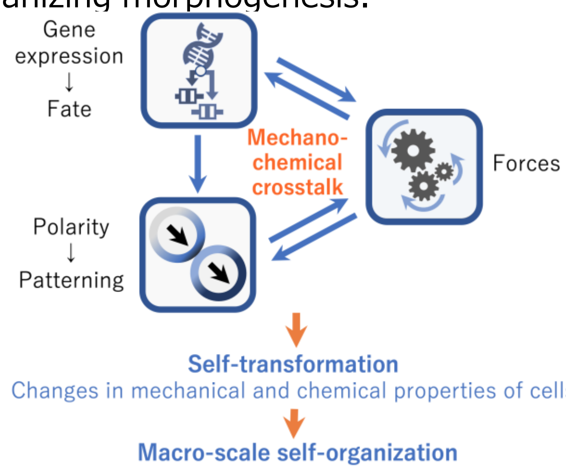

Fig. 2. A concept of mechanical self-transformation

Purpose: The project in the Grant-in-Aid for Transformative Research Areas (A) aims to develop new paradigms of morphogenesis through quantitative and holistic evaluation of how mechanical forces control emergent properties of self-organizing feedback in developing organisms. We will develop cutting-edge technologies to investigate mechanical processes and determine the magnitude and distribution of forces within cells and extracellular spaces. With this insight, we will understand how mechanical forces elicit self-organizing feedback, leading to progressive self-tuning transformation of multicellular systems over longer timescales (Fig. 2). This outcome will shed light on the design principles underlying the integration of tissue mechanics with gene expression, how these principles arise during development, and their mal-adaption in aging and disease conditions.

Expected Research Achievements

●Aim of the research program

An embryo produces cells with specific fates, forms, and functions during development. This fascinating process requires collective interactions of biological components, which give rise to an ordered state in space and time. The concept of "self-organization" is widely recognized as a core principle in pattern formation, but the mechanisms underlying multicellular morphogenesis are only beginning to be elucidated. We aim to develop new paradigms for morphogenesis through quantitative and holistic evaluation of how mechanical forces of cells and tissues control the emergent properties governing self-organizing feedback.

Our team is composed of three sub-groups: A01 and A02 will elucidate the mechanical self-organization in a diverse array of multicellular systems including embryos, tubular organs, and neural systems; B01 will develop new techniques for the measurement and manipulation of mechanical forces, as well as theoretical methods for modelling and simulating self-organization (Fig. 3). With cutting-edge technologies needed to interrogate the mechanical processes, we will establish a unique multi-disciplinary research that harnesses expertise from the diverse fields, such as biomedical sciences, engineering, mathematics, physics, and chemistry.

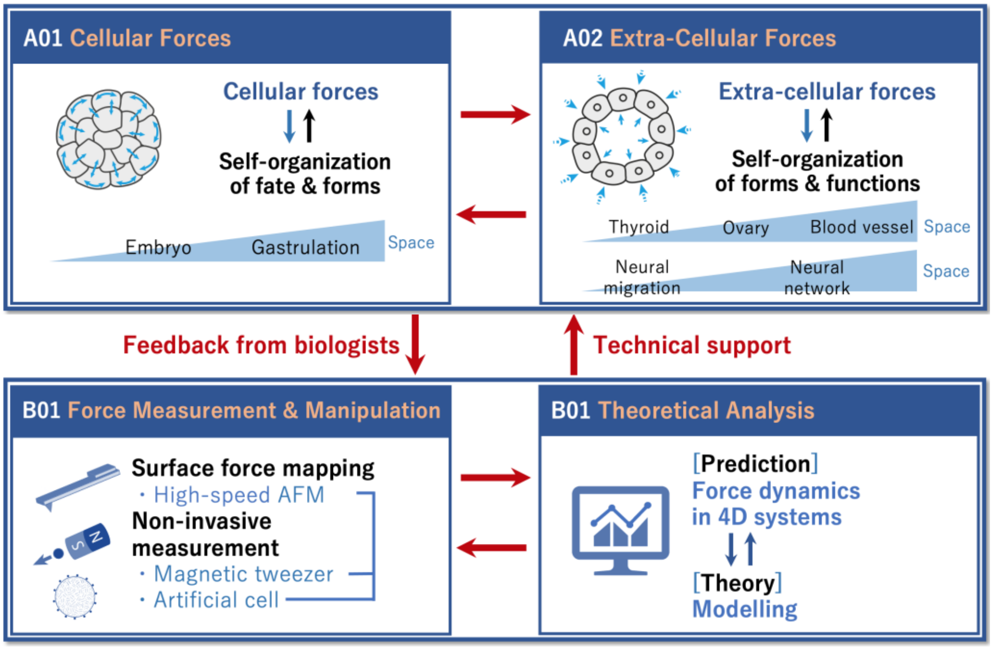

Fig. 3. A strategy to uncover the principles in mechanical self-transformation during development

●Potential contribution to society

By introducing the role of forces into a paradigm that cannot be explained by existing concepts, this research area will make a broad ripple effect on the understanding of diverse biological phenomena. Given that potent effects of mechanical forces are related to many physiological events such including tumorigenesis, we expect that this research area promotes not only basic biology but also development of tissue regeneration technologies and biomedical applications. Therefore, this research area will connect the life sciences with the medical and engineering fields, strengthening the link between academia and society. The outstanding internationality of this research team will promote collaborative research through international research networks and serve as a foundation for fostering international competitiveness.

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