Emergence of Traveling Waves in the Segmentation Clock

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***Short Abstract* —Spatial and temporal periodicity of somite formation is controlled by the segmentation clock, where numerous cells cyclically exhibit *her1* expression with a posterior-to-anterior phase delay, forming 'traveling waves'. Here we demonstrate the mechanism underlying the emergence of the traveling wave.**

***Keywords* — Segmentation Clock, Traveling Wave, Bifurcation, Period gradient.**

I. Background

The somite, the origin of the segmental body structure (e.g. spines), is generated with a strict temporal/spatial periodicity; segmentation occurs at the equal-spaced interval at a fixed time-interval, budding off from a somite-precursor tissue (presomitic mesoderm; PSM). This periodicity is controlled by the segmentation clock functioning in the PSM, a congregation of cells oscillating *hairy*-related transcriptional repressors (*her1*) driven by its negative-feedback, i.e. Her1 protein represses its own transcription. In zebrafish, each somite is formed every 30 min, and the segmentation clock cyclically exhibits a dynamic spatial pattern of *her1* expression in the PSM with the same periodicity. Previous studies demonstrated that the oscillation phases of cellular oscillation are spatially highly coordinated, displaying traveling waves, which sweep toward the anterior and arrest at the future segmentation points [1]. Although many studies have been done on the steady state of the segmentation clock [2], little is known about the early segmentation clock. At the emergence of traveling wave, mode transition from a stable state to wave propagation occurs in the early segmentation clock. In the present study, we address the bifurcation mechanism of this mode transition using in vivo and in silico analysis.

II. Summary of the Results

Our results consist of the following three parts.

A. Traveling wave is created in the oscillatory system

We demonstrate by in vivo experiments that the traveling wave requires neither pulse-generator nor intercellular coupling when it appears, indicating that the traveling wave is created in the oscillatory system although both excitable and oscillatory systems can be generated in our mathematical simulation based on the known molecular network.

B. Fgf controls both the bifurcation and the oscillation period

The oscillatory state of each cell was found to be regulated by Fgf, a secreted growth factor. Expansion of Fgf activity was found to induce the bifurcation of cellular oscillators and to kick off the traveling wave. Also, by combining in vivo and in silico analyses, we demonstrated that Fgfs are also responsible for the formation of a period gradient, which is crucial for the observed spatial pattern of the traveling wave [3].

C. The reaction step responsible for the emergence of the traveling wave

Finally, we discuss which reaction step in *her1* negative-feedback, such as transcription or transcriptional repression, is responsible for the emergence of the traveling wave, i.e. the target of Fgf signaling. Using a specific model for the segmentation clock [4], we predict that reaction steps sensitive to Fgf would be degradation rate of RNA/protein or repression efficiency of Her1 protein.

III. Conclusion

We demonstrate the basic mechanism underlying the emergence of the traveling wave that the bifurcation and the establishment period gradient occur at the same time, both of which are controlled by Fgf.

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