【Biological Sciences（Biology）】

Role of PIP3 Transport in Regulation of Cell Polarity

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【Outline of survey】

PIP3 is involved in diverse cell biological phenomena such as proliferation and differentiation. Recent studies have revealed that PIP3 accumulates at the leading edges of migrating cells and at the growth cones of axons, where it plays crucial roles in the regulation of cell polarity. However, the molecular mechanism of how PIP3, which constitutes the membrane, accumulates at such specialized areas remains largely unknown. I identified a microtubule-based motor protein as a novel substrate for a polarity-regulating kinase. It was found that this motor protein accumulates at the growth cones as does PIP3. A foreign research group has suggested that a motor protein associates with and transports PIP3-containing lipid vesicles.
These new findings raise the possibility that the PIP3 accumulation occurs via the transport on the cytoskeleton. In this project, I am going to investigate the regulatory and functional mechanisms of motor proteins and clarify the importance of the PIP3 transport in cell polarity.

【Expected results】

Since the discovery of PIP3, most researchers have focused on the enzymes that generate or degrade PIP3. In this point, the idea that PIP3 is recruited by the transport on the cytoskeleton is a very interesting one and this study will certainly produce valuable results with a strong impact on cell biology. Malfunction of PIP3 regulation is known to be responsible for several human diseases such as cancers and diabetes, and thus this study may clarify the link of the cytoskeleton and the motor protein with human diseases.

【References by the principal investigator】

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- Yamazaki et al. (2003) WAVE2 is required for directed cell migration and cardiovascular development. ***Nature*** 424, 452-456.
- Funato et al. (2006) The thioredoxin-related redox-regulating protein nucleoredoxin inhibits Wnt-β-catenin signaling through Dishevelled. ***Nat. Cell Biol.*** 8, 501-508.

【Term of project】 FY2008-2012

【Budget allocation】
70,200,000 yen (direct cost)

【Homepage address】 http://www.protein.osaka-u.ac.jp/intra_signal/index.html