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Tracking of Single Microvilli to Study Regulation of the Intestinal Phosphate Transporters

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Intestinal phosphate (Pi) uptake is one of the key mechanisms of systemic Pi homeostasis. Modulation of intestinal Pi transport has been recently recognized as an important target in prevention of hyperphosphatemia and the associated cardiovascular complications in Chronic Kidney Disease. Intestinal Pi absorption is mainly mediated by the type IIb sodium-phosphate co-transporter NaPi2b which is expressed in the intestinal apical microvilli. Recent evidences show that agonists of the LXR nuclear hormone receptor inhibit intestinal NaPi transport activity, NaPi2b protein and mRNA abundance, and decrease serum Pi level [1]. However, the detailed mechanisms of how LXR decreases intestinal NaPi transport activity, including the role of changes in membrane cholesterol or PDZ interacting proteins, remain to be determined.

In order to study these processes at the molecular level we apply the Modulation Tracking nanoimaging method [2] to microvilli of live cells expressing fluorescently tagged NaPi2b. This technique generalizes the principles of Single Particle Tracking to allow the imaging of extended subcellular structures. Tracking the single microvilli we directly measure their motion, while we also image NaPi2b distribution along the membrane and perform Fluorescence Correlation Spectroscopy techniques (RICS, N&B) in steady state, even if the microvilli are moving. Different dynamic properties, including motility of the microvilli and protein diffusion and clustering, are monitored under stimulation to get insights into the process of intestinal transporters regulation.

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