Modeling of T-Cell polarization

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Cytotoxic T lymphocytes (T) eliminate pathogen-infected or tumorigenic cells (target cells). Once T-cell identifies a target cell, a tight contact, the immunological synapse (IS), is formed. Subsequently, one observes repolarization of the cell involving the rotation of the microtubule (MT) spindle and the movement of the microtubule organizing center (MTOC) to a position that is just underneath the plasma membrane at the center of the IS. Concomitantly, a massive relocation of organelles attached to MTs is observed, including the Golgi apparatus, lytic granules and mitochondria. Subsequently, T-cell releases lytic granules containing perforin/granzyme and cytokine containing vesicles. Although the polarization was observed experimentally, its inner mechanism remains poorly understood. We devised a theoretical model for the molecular motor driven motion of the MT half-spindle confined between the plasma membrane and nucleus. Multiple scenarios currently discussed in the literature, including capture-shrinkage and cortical sliding mechanisms, are analyzed. We compared quantitative predictions about the spatio-temporal evolution of MTOC position and spindle morphology with experimental observations. The case of two IS including the oscillations of MTOC is examined. We propose that our model opens a way to infer details of the molecular motor distribution from the experimentally observed features of the MT half-spindle dynamics.