



Distinguished Lecture Series

Action of Microtubule Drugs via Systemic Immune Modulation in Cancer and Inflammatory Disease

-  25 May 2021 (Tuesday)
9:30-10:30 a.m. GMT+8 (Hong Kong Time)
-  Online via Zoom
(Meeting ID: 971 5634 1506)



ABSTRACT

Microtubules are dynamic protein fibers that transport vesicles in non-dividing cells and chromosomes during mitosis. Small-molecule drugs that target microtubules, which are mostly plant-derived toxins, are important medicines for cancer and inflammatory diseases. We know how they work at the molecular level, but not how they act therapeutically in the human body. Taxanes stabilize microtubules and are used to treat adult solid cancers. They block mitosis in cancer cells, but so do more recent drug candidates that failed in the clinic, so taxanes must have additional actions. We found that taxanes, alone among anti-mitotics tested in the clinic, cause chromatin bridges in post-mitotic cells. These activate the viral DNA sensor cGAS which triggers interferon secretion. We hypothesize this immune-activating signal contributes to successful tumor regression. The ancient drug colchicine destabilizes microtubules and is used at low doses to treat gout and other inflammatory diseases. Using mouse disease models, we found that colchicine acts selectively in the liver to trigger release of anti-inflammatory hepatokines. These act on circulating myeloid cells to inhibit inflammation. Our unexpected findings that both taxanes and colchicine modulate inflammatory signaling illustrates the importance of these pathways in disease and therapy and has interesting implications for drug discovery and plant-derived traditional medicines.

Professor Timothy Mitchison

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Professor Timothy Mitchison is the Hasib Sabbagh Professor of Systems Biology at the Department of Systems Biology, Harvard Medical School. Professor Mitchison's research group has long been interested in fundamental mechanisms by which cells use for physical organization and movement, and more recently exploring and developing small molecules that can perturb these processes in cancer and inflammatory disease. Professor Mitchison is a Fellow of the Royal Society in the United Kingdom and a member of the National Academy of Sciences in the United States.