Dying Cells "Speed Up" Intracellular Transport

In the human body, the number of cells is tightly regulated. When cells are no longer needed, they commit suicide through a programmed cell death, called apoptosis. Massive amount of cell apoptosis takes place in developing tissues and even adult bodies. For example, billions of cells die in the bone marrow every hour.

Over the past 40 years, although the biological aspects of apoptosis such as the molecular signaling pathway have been intensively studied, still we have little knowledge in the physical aspects such as intracellular dynamics.

A team led by Dr. LI Hui, Associate Professor at the Institute of Physics (IOP), Chinese Academy of Sciences (CAS) discovered that the intracellular transport with both directed and non-directed motions is accelerated in early apoptotic cells.

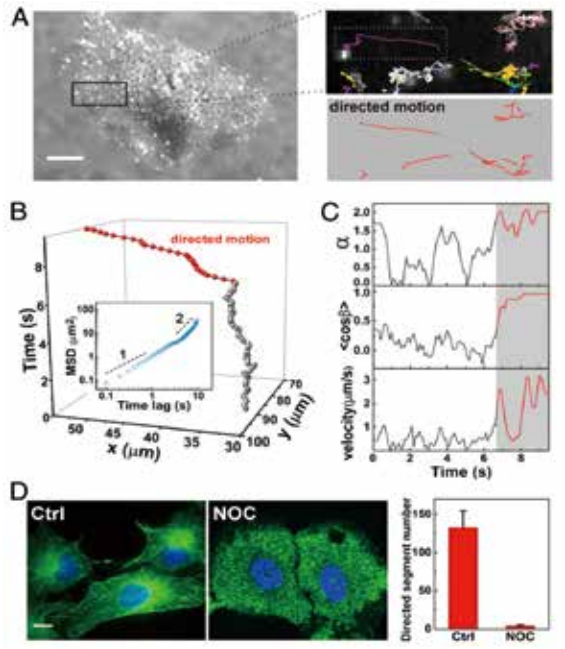
LI and his colleagues carried out experiments on living human lung cancer cells, of which they labelled transmembrane proteins with quantum dots – a newly semiconductor fluorescence probe. They then used the single-particle tracking method to directly observe and quantify the proteins' endocytic transport.

"In contrast with the general concept that apoptosis is programmed with the shutdown of normal physiological activities," LI says, "for the first time, we find the increased intracellular dynamics in cells undergoing programmed cell death."

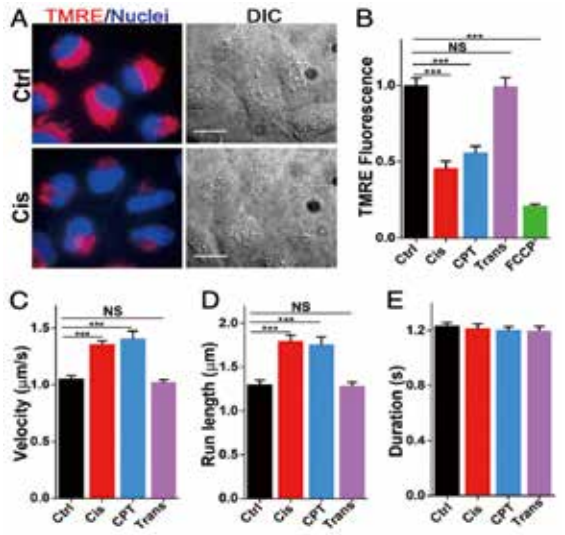
After examining several factors involved in intracellular transport, the investigators further found that its acceleration is likely resulted from the elevated ATP level, in early apoptotic cells.

Since intracellular transport is the basis for molecule translocation and signal transduction, LI wondered whether the enhanced intracellular transport is indispensable for apoptosis.

To do this, they used osmotic pressure to compress the cells and reduce the intracellular transport dynamics. Interestingly, the apoptotic progress was significantly



Dynamic analysis of intracellular transport by tracking endocytic vesicles labeled by quantum dots. (Image from the published article)



Directed motion is accelerated in the detected early apoptotic cells. (Image from the published article)

delayed when the accelerated intracellular transport was regulated back to the normal level.

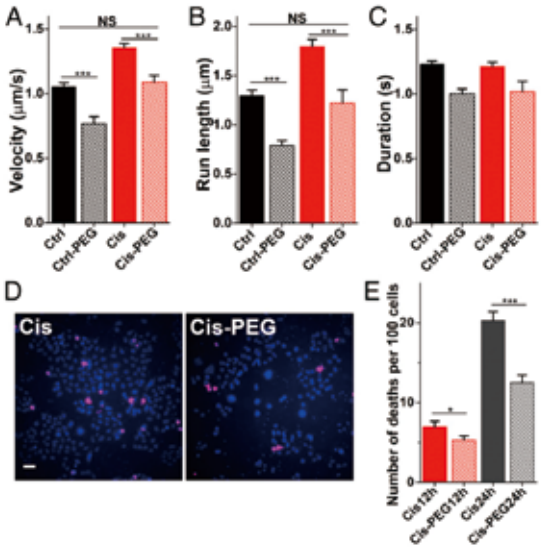
These results have revealed a direct correlation between the intracellular transport dynamics and the cell apoptotic process, and highlighted the importance of intracellular dynamics in maintaining the cellular physiological functions.

"The accelerated intracellular transport could offer an essential physical environment to support the initiation and proceeding of apoptosis," LI says. "For example, not only molecule signaling cascades take place, but the organelle mitochondria undergo fragmentation, aggregation and rearrangement in a brief period."

Deregulation of apoptosis is associated with an accumulation of unwanted cells and development of tumors. The intracellular transport dynamics may serve as an approach to regulate the cell apoptosis, which could be exploited to control the apoptosis ratio of cancer cells.

"We provide a new physical perspective to understand apoptosis in live cells, and offer the physical approach of osmotic compaction to control apoptosis," LI says. "We hope our work is helpful for developing new therapy strategies in the treatment of cancer in the future."

This study entitled "Intracellular transport is accelerated in early apoptotic cells" was published in *Proceedings of the National Academy of Sciences*.



Dead cells under apoptosis stimuli being reduced when intracellular transport dynamics is regulated back to the normal level. (Image from the published article)

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