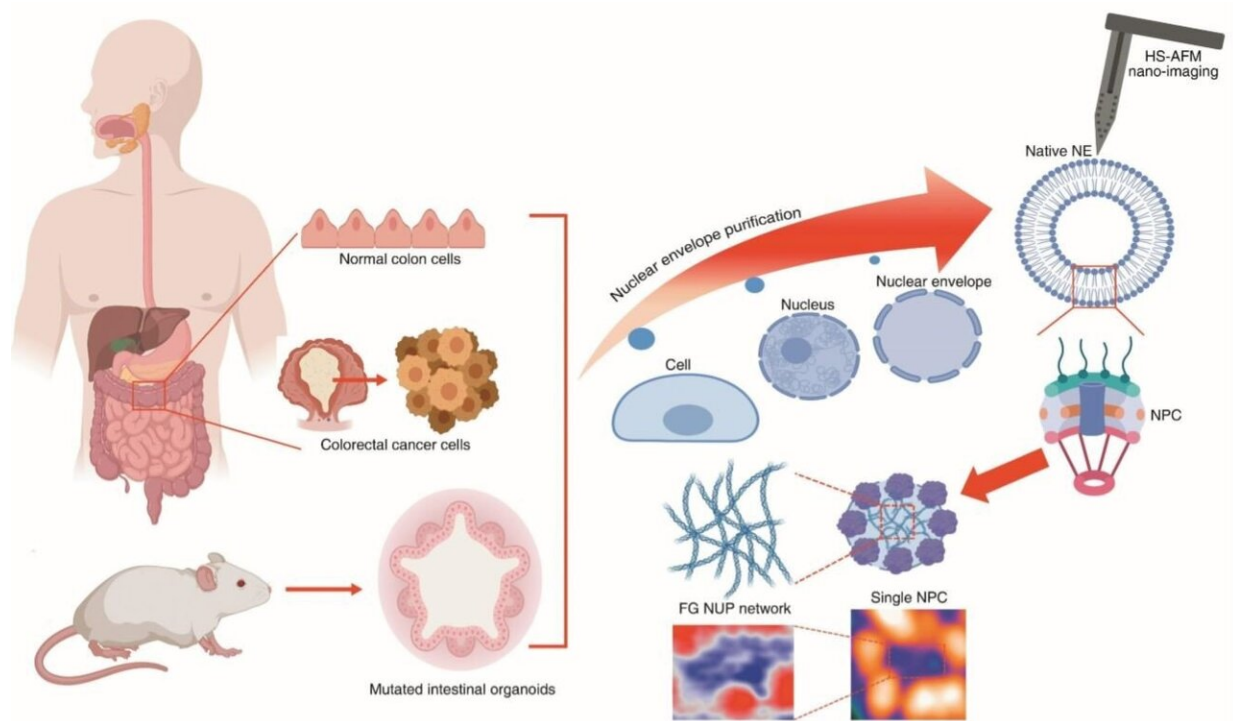


# Real-time monitoring of proteins in the nuclear pore complex

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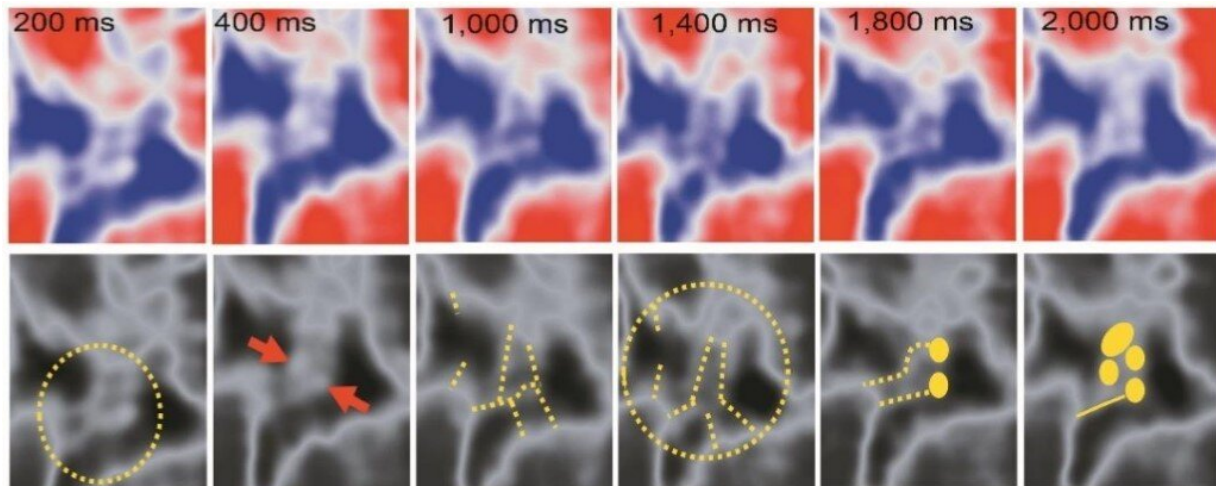
Schematic illustration of manipulation and tracking of native nuclear nano-pores from colon cancer cells and mouse organoids. Live tracking of single bio-filament conformations inside the nuclear pore presented as a nano diagnosis tool for the colorectal cancer. Credit: Kanazawa University

In human cells, the nucleus is enclosed by a structure called the nuclear pore complex (NPC). It acts as a 'gatekeeper' controlling the transport of

molecules between the nucleus and the surrounding cytoplasm (the protein-containing solution in the inside of a cell). The NPC consists of proteins known as nucleoporins; some of these, the so-called FG-NUPs, belong to the class of intrinsically disordered proteins (IDPs) and capable of forming liquid-liquid phase separation (LLPS), lacking a well-defined tertiary structure (that is, a particular 3-D shape). Although a lot is known about FG-NUPs, a thorough understanding of how their structure varies in time and space has been missing. But now, by applying high-speed atomic force microscopy (HS-AFM), Richard Wong from Kanazawa University and colleagues provide much-needed insights into the spatiotemporal structure of FG-NUPs.

The technique used by the researchers, HS-AFM, is typically used for imaging surfaces. A tiny cantilever is made to move over the surface; at any given time, the force experienced by the cantilever probe can be converted into a height measure. A scan of the whole surface then results in a height map of the sample. By repeatedly scanning the surface rapidly, a video of its evolving structure is obtained. Applying HS-AFM to FG-NUPs, Wong and colleagues were able to measure several of the molecules' properties, including the extension velocity of FG-NUP filaments (thread-like protruding structures), their bending angles and how they form knots.

The scientists studied FG-NUPs in normal colon cells and in colorectal cancer cells and organoids. They found that the former displayed less conformational dynamics. A particularly interesting conclusion is that in colon cancer cells, the structure of the so-called central plug is smaller, and cannot develop filamentous features as easily as in normal cells, a finding with high clinical relevance.



HS-AFM enables dynamically studying filament structures in FG-NUP LLPS proteins, including twisting and knot formation. Credit: Kanazawa University

The results of Wong and colleagues regarding the central plug are very important and timely, as its morphology and function have been the subject of debate. The researchers now provide strong evidence that the central plug at least partially consists of FG-NUPs.

Apart from demonstrating that HS-AFM is a tool capable of visualizing FG-NUP filament motion in real time, another implication of the work of the scientists is "that bio-recycled nanomaterials [like NPC nanopores] ... have biocompatible advantages ... directly derived from cells and organoids, rather than other engineered nanomaterials [like e.g. carbon nanotubes, which may induce tumors and related pathologies] opening a new avenue for nano-tissue engineering."

**More information:** Mahmoud Shaaban Mohamed et al, Spatiotemporally tracking of nano-biofilaments inside the nuclear pore complex core, *Biomaterials* (2020). [DOI: 10.1016/j.biomaterials.2020.120198](https://doi.org/10.1016/j.biomaterials.2020.120198)

Provided by Kanazawa University

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