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Winner 2022

Thi Hoang Duong Nguyen

Cambridge, UK

2022 Winner of the Eppendorf Award for Young European Investigators

»I feel humbled and honoured to receive the 2022 Eppendorf Award. I am very grateful to my laboratory, past and present colleagues, mentors, collaborators and family, without whom this would not have been possible. The award recognises our contribution to the elucidation of the molecular mechanisms of important processes through visualisation of the three-dimensional structures of the biological molecules involved. Our current research focuses on cellular pathways that maintain the essential chromosome caps to preserve genomic information. Defects in these pathways result in numerous human diseases. We hope that the insights gained from our work will facilitate therapeutic developments to treat these diseases.«

Dr. Thi Hoang Duong Nguyen

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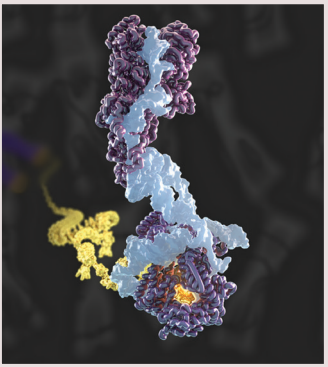
Award-Winning Research

Unravelling molecular mechanisms of ribonucleoproteins through structural biology



The atomic structure of human telomerase bound to DNA (in cartoon) shows how telomerase engages with the chromosome end (gold) for DNA extension. Extension of the chromosome end by telomerase is important for maintaining genome stability.

The ends of eukaryotic chromosomes are protected by specialised caps, called telomeres. Unlike bacteria whose chromosomes are circular, eukaryotic chromosomes are linear, and therefore they have ends, which cannot be fully copied by the conventional DNA replication machinery. This results a gradual erosion of the protective telomere caps. Cells that lose too much of their telomeres will stop dividing and eventually die.

To overcome this cellular aging problem, an enzyme, called telomerase, is employed to add the lost DNA back to the chromosome ends. Most adult cells, however, do not have sufficient telomerase to avoid the cellular aging process. In contrast, stem cells, germlines and cancers switch telomerase on to extend their lifespans. In addition, mutations that disrupt telomerase function lead to numerous premature aging diseases. Therefore, since its discovery, telomerase has been considered as a prime anti-cancer and anti-aging drug target.

For decades, the lack of our knowledge on the three-dimensional shape of telomerase hindered progress towards its manipulation for therapeutic purposes. We have recently filled in this knowledge gap by providing the first three-dimensional visualisation of human telomerase in unprecedented detail. We discovered that most premature aging disease mutations cluster around one hotspot, which explained how these mutations lead to telomerase deficiency and may provide avenues towards treating these diseases.

We also identified entirely new telomerase components. These findings open up exciting future opportunities to study telomerase mechanism and regulation at a molecular level. A deep understanding of how this fascinating enzyme functions will greatly accelerate the development of telomerase-based therapeutics.

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Read more about our Award winner Dr. Nguyen.

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