A novel technology for lighting up NAD^+ metabolism in live cells and *in vivo*

With the support by the National Natural Science Foundation of China, the research teams led by Prof. Zhao YuZheng (赵玉政) and Prof. Yang Yi (杨弋) at the East China University of Science and Technology cooperated to develop a genetically encoded fluorescent sensor for monitoring nicotinamide adenine dinucleotide (NAD^+), which was published in *Developmental Cell* (2020, 53(2): 240—252).

NAD^+ plays central roles in energy metabolism, redox reactions and many regulatory enzymes, and is involved in diverse biological processes such as development, aging, immune response, cancer, and neurodegenerative diseases. An increasing number of studies have shown that cellular NAD^+ levels decline with age, and its supplement can alleviate the aging process. Monitoring the NAD^+ level in living cells and *in vivo* is thus of great interest for various research fields in life science; however, it can hardly be realized by traditional biochemical methods.

To meet this challenge, Zhao's and Yang's groups develop FiNad, a highly responsive, specific and ratiometric genetically encoded fluorescent sensor for NAD^+, and established the *in-situ* monitoring technology for NAD^+ dynamics in a variety of organisms, including bacteria, cell lines, mice, zebrafish, and human-derived stem cells. They utilized FiNad to study the NAD^+ biosynthetic pathways in different species in the presence of common NAD^+ precursors, and found that increased NAD^+ synthesis controls morphofunctional changes of activated macrophages. In addition, FiNad allows them to visualize the decline of NAD^+ in cell senescence, in the aging mouse, and in human urine-derived stem cells at different ages. This technology tackles a bottleneck of metabolic analysis and supports the visible investigation of cell metabolism and the development of NAD^+-targeting anti-aging strategies.

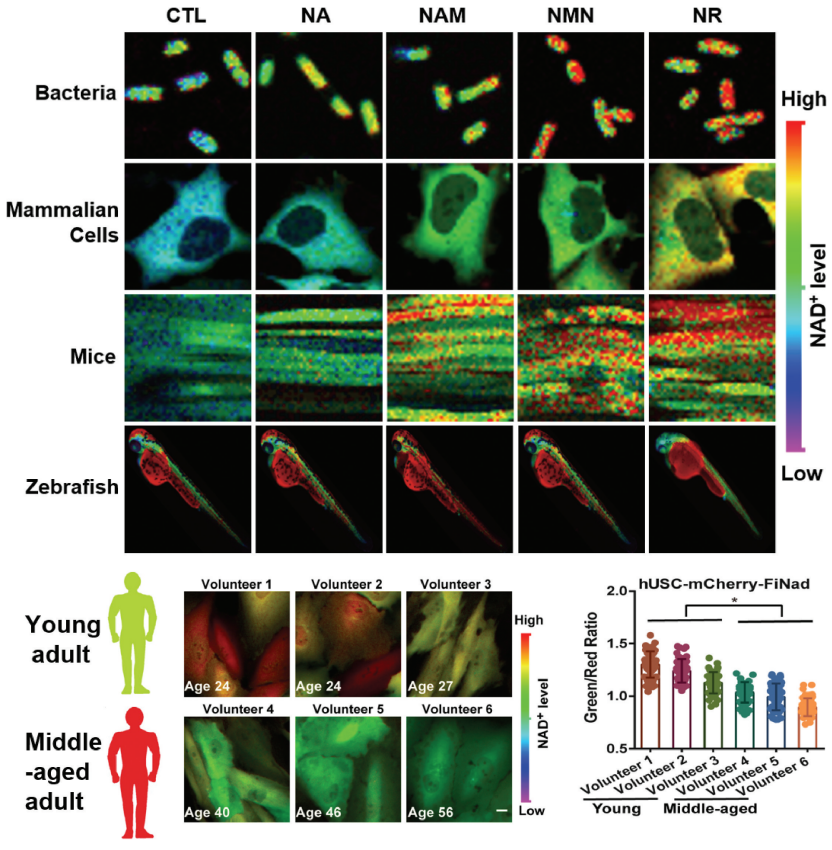

Figure Mapping the different roles of NAD^+ precursors in various organisms (top), and imaging NAD^+ decline during aging *in situ* (bottom).