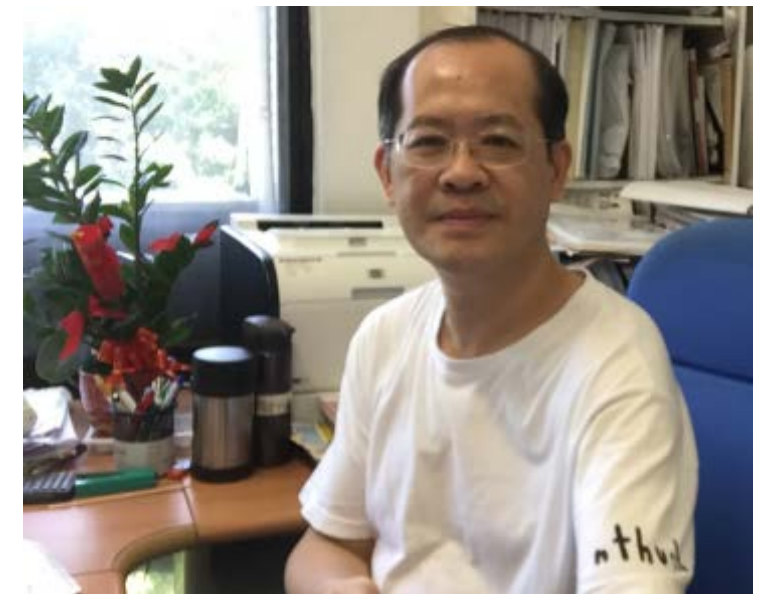




國立清華大學分子醫學研究所

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Functions and pathophysiology of human mitochondrial complex I

Introduction:

Among the five enzyme complexes in the oxidative phosphorylation system (OXPHOS), human complex I is the most intricate membrane-bound enzyme known to date. Dysfunction in this enzyme complex has been linked to a wide variety of mitochondrial and neurodegenerative diseases (including Parkinson's disease), and is also involved in aging process. The underlying genetic defect may either be at the mtDNA or at the nuclear DNA level. Because of the complexity of the enzyme and its dual genetic origins, the majority of complex I defects still lack an identified pathogenic mechanism, and no effective remedies have been established for complex I deficiencies.

Specific Aims:

- Understanding the functional mechanisms of human mitochondrial complex I
- Revealing the functional and structural roles of component subunits in complex I
- Developing new approaches to treat the diseases caused by the defects of complex I
 - Allotopic expression of mitochondrial-encoded subunits of complex I
 - Xenotopic expression of mitochondrial-encoded subunits of complex I
 - The strategy of organelle-targeted delivery of mitochondrial proteins using the protein transduction domain (PTD)
 - Gene therapy of nuclear-encoded subunits of complex I

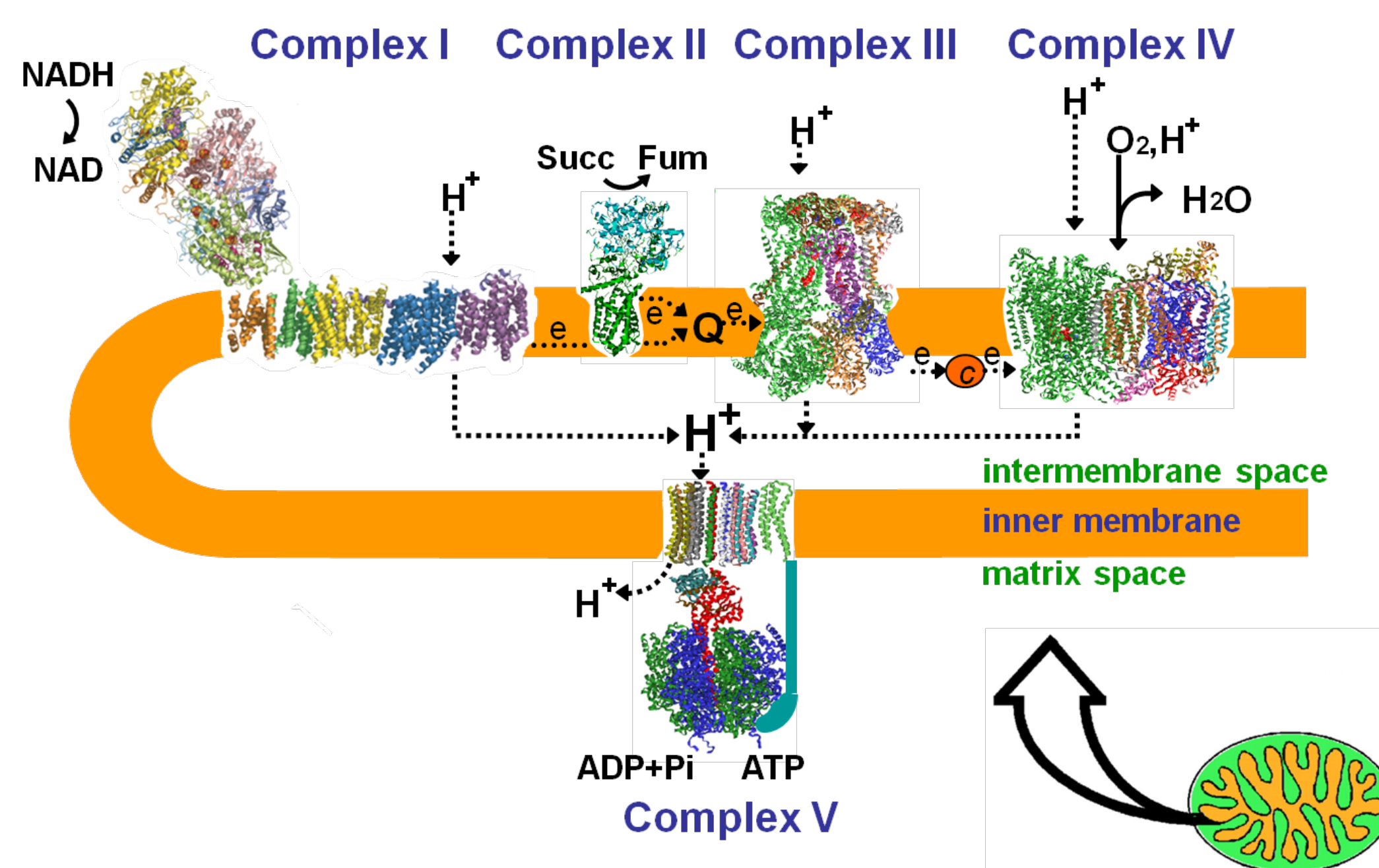


Figure 1: Overview of the mammalian mitochondrial oxidative phosphorylation system.

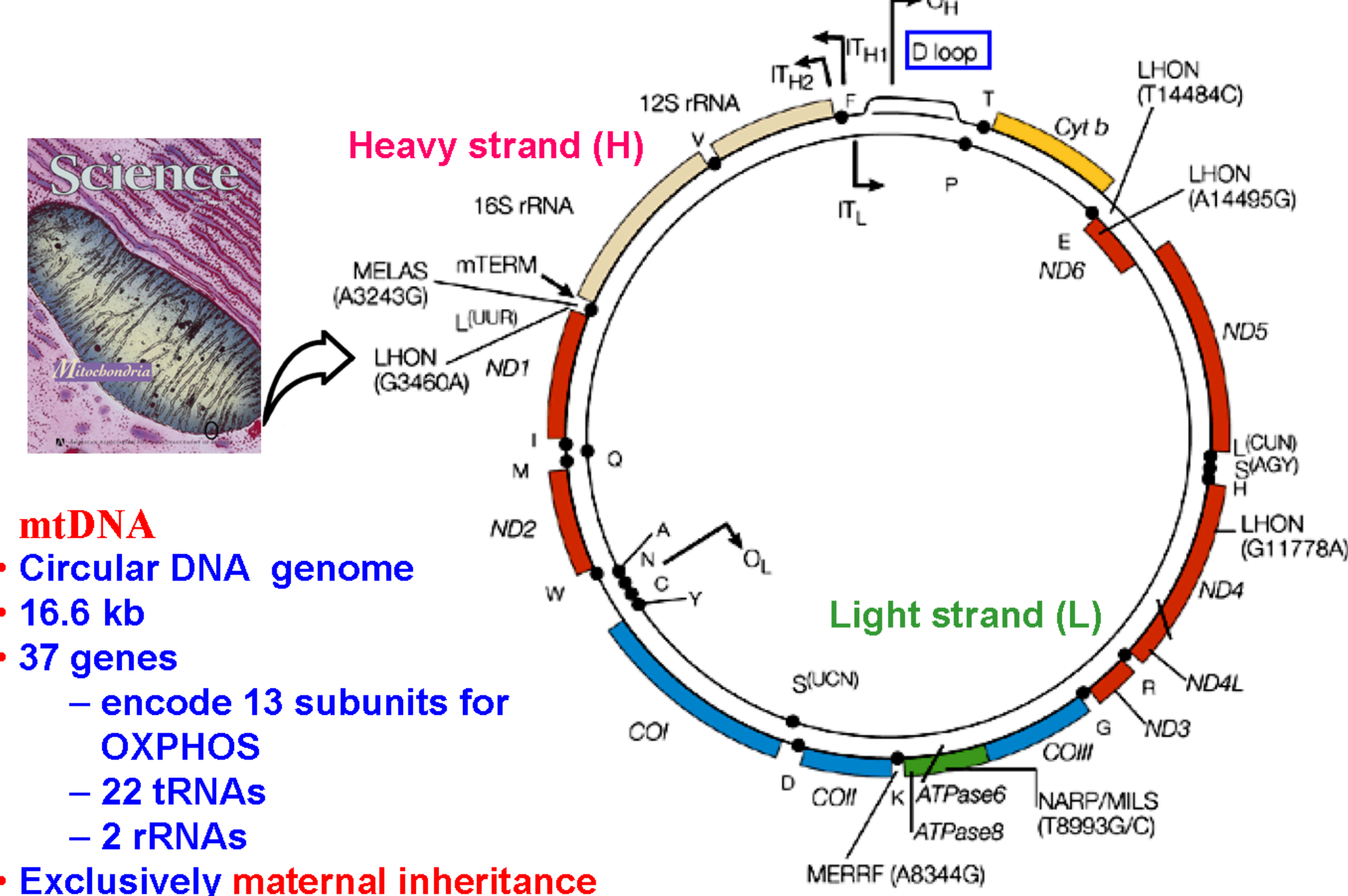


Figure 2: Human mitochondrial genome.

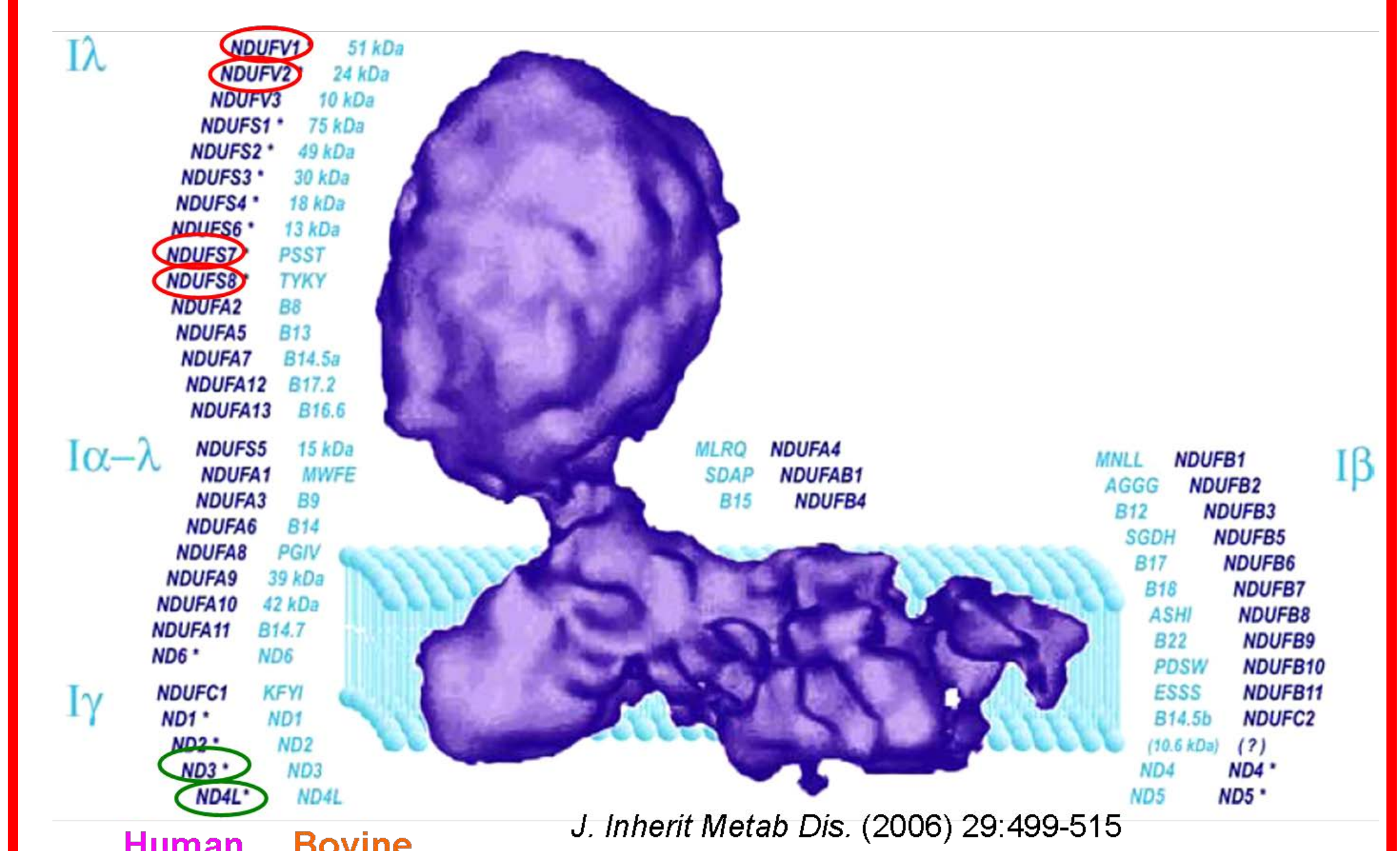


Figure 3: Subunit composition of mammalian complex I.

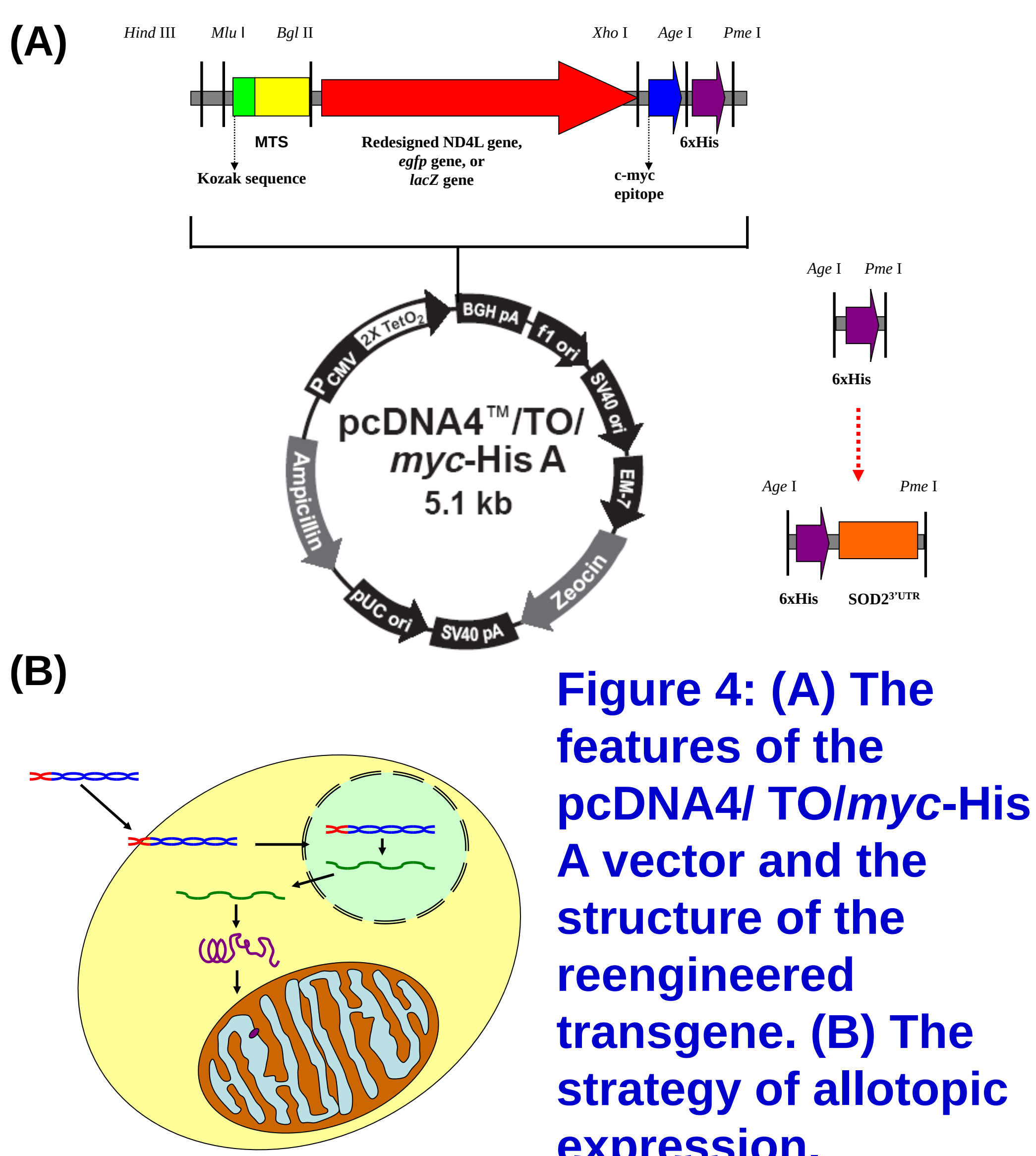


Figure 4: (A) The features of the pcDNA4/TO/myc-His A vector and the structure of the reengineered transgene. (B) The strategy of allotopic expression.

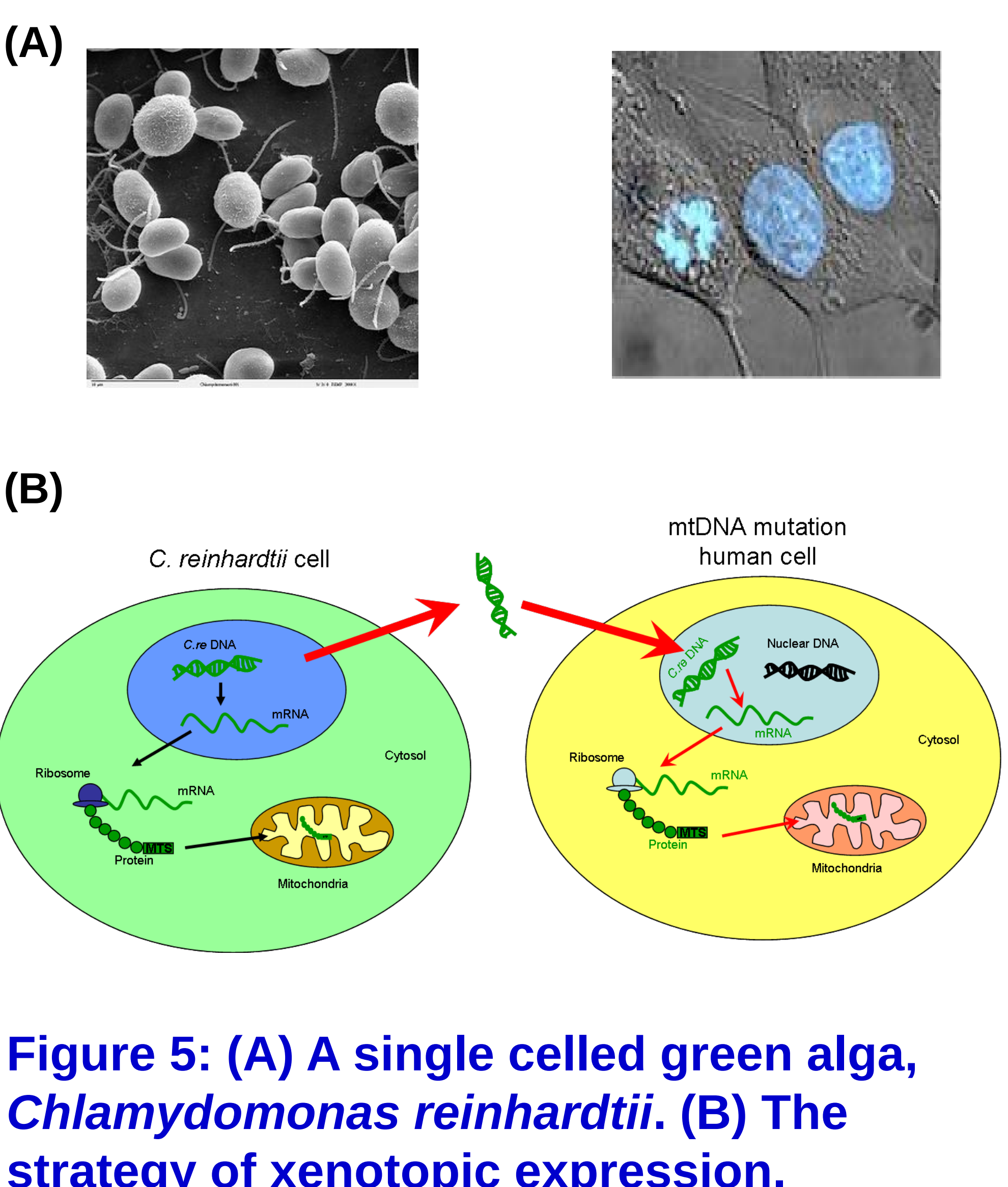


Figure 5: (A) A single celled green alga, *Chlamydomonas reinhardtii*. (B) The strategy of xenotopic expression.

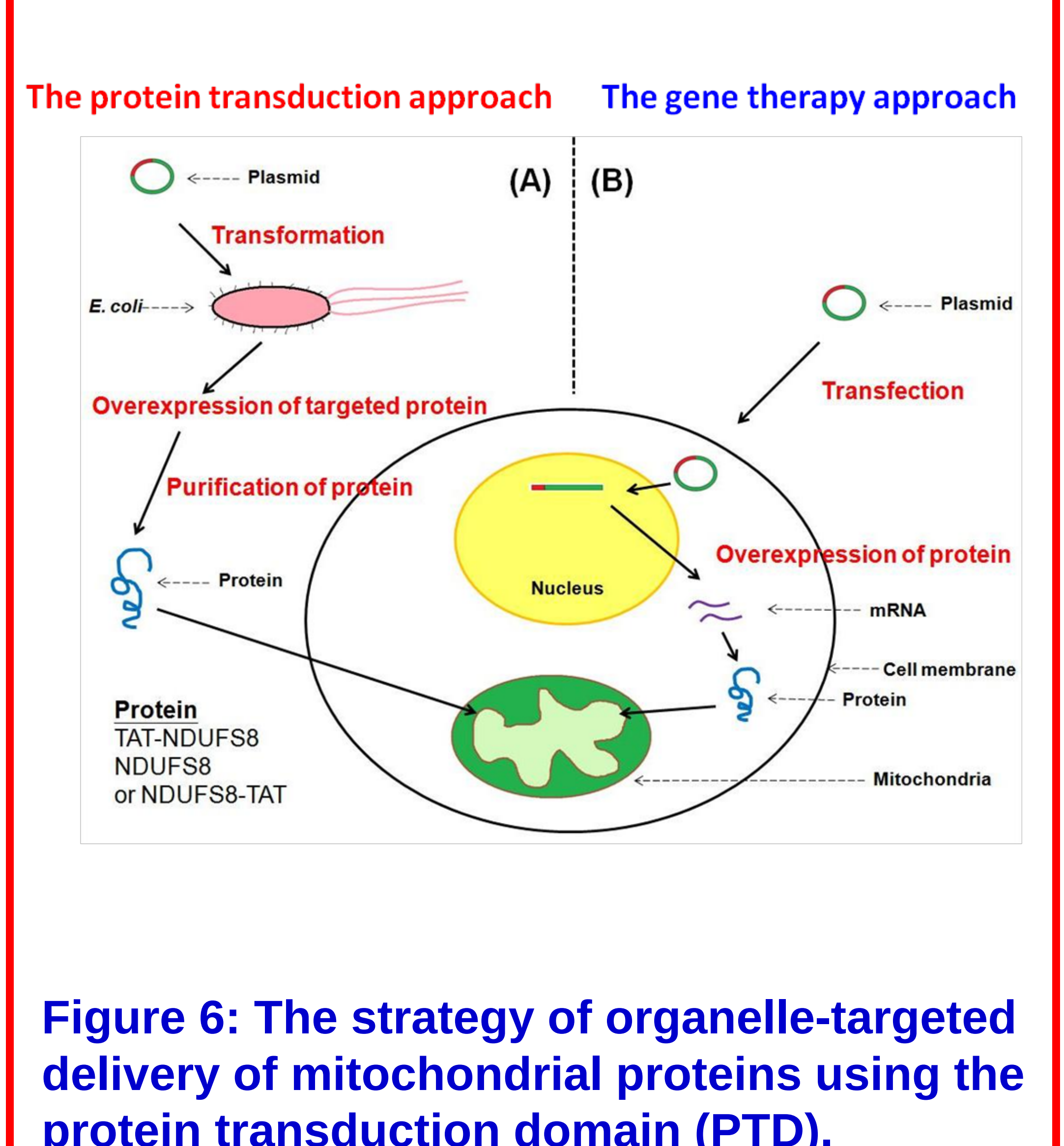


Figure 6: The strategy of organelle-targeted delivery of mitochondrial proteins using the protein transduction domain (PTD).