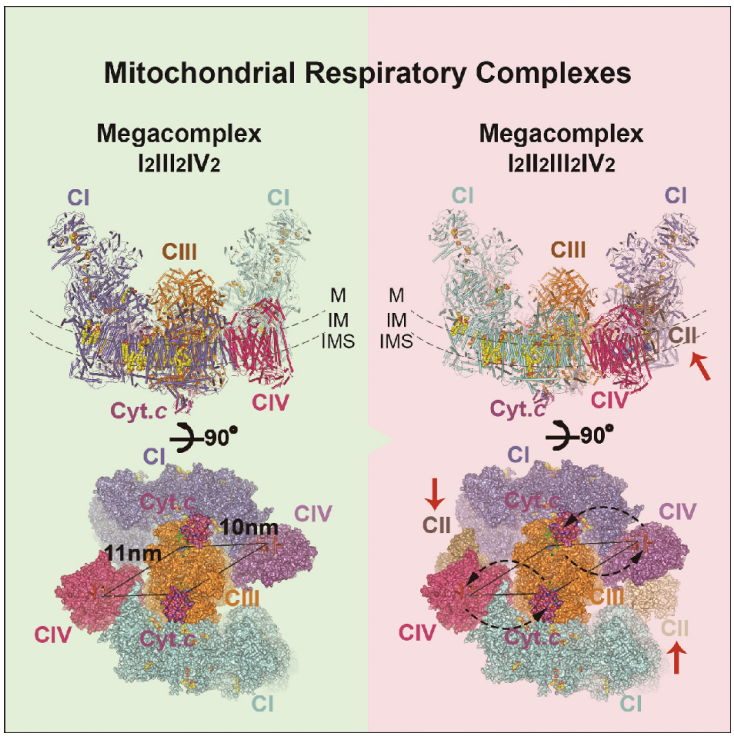
Cryo-EM structure of human respiratory megacomplex

With the support by the National Natural Science Foundation of China, the group of Yang Maojun (**杨茂君**) firstly solved the medium resolution structure of human respiratory megacomplex $I_2III_2IV_2$ and the atomic structure of the supercomplex $I_1III_2IV_1$ in the world. The results were published in *Cell* (2017, 170: 1247－1257).

The respiratory megacomplex represents the highest-order assembly of respiratory chain complexes, and it allows mitochondria to respond to energy requiring conditions. To understand its architecture, they examined the human respiratory chain megacomplex-$I_2III_2IV_2$ ($MCI_2III_2IV_2$) containing 140 subunits and a subset of associated cofactors using cryo-electron microscopy.

The overall structure is ~ 220 Å in height, ~280 Å in width, and ~300 Å in length, containing 140 subunits with 238 transmembrane helices (TMHs). All the TMHs are aligned to form a slightly bent plane. Two complex I (CI) molecules encircle the whole structure centrosymmetrically with the complex III (CIII) dimer located at the center of the huge machine. Two complex IV(CIV) molecules are anchored by the distal end of two CI membrane arms at each side, with a clear gap between CIV and the other CI. Meanwhile, the two protomers of the CIII dimer both have intensive interactions with CI and CIV at the same side, so both monomers could receive QH_2 from one CI and pass reduced Cyt. *c* to one adjacent CIV to transform energy most efficiently. The interfaces between the CI-CIII and CI-CIV cover areas of 2,616 Å^2 and 946 Å^2, respectively. The structure not only reveals the precise assignment of individual subunits of human CI and CIII, but also enables future in-depth analysis of the electron transport chain as a whole.



Analyses also indicate that complex II could insert into the gaps between CI and CIV to form a closed ring.