adoption, and propagation of corrupted biomedical terms. Such slips, even if harmless in themselves, are a sign that errors, even when misquoted, can apparently go unnoticed at various stages of the publication process, which favours their further dissemination in the scientific literature.

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We 1 Respiratory complexes and supercomplexes I

We 1 K-1
The rotary mechanism of ATP synthase; how it is regulated and influences the assembly of the enzyme

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The ATP synthase in the mitochondria of each human being generates about 50 kg of ATP daily, maintaining a steady state level of about 10 g to sustain life. The enzyme has a rotary mechanism to transmit energy from a transmembrane proton motive force across the inner membrane of the organelle (derived by respiration) to the catalytic sites where ATP is formed from ADP and phosphate. The bovine enzyme is made of 29 protein subunits of 18 types, including the inhibitor protein IF_1 [1,2]. They are organised into a rotor and a stator. The rotor consists of a membrane bound c_8-ring attached to a central stalk (subunits γ, δ and ε) that protrudes into the mitochondrial matrix, and penetrates into the spherical catalytic domain ($\alpha_3\beta_3$) of the stator. The stator is completed by a peripheral stalk (PS; subunits OSCP, F_6, b and d), bound to the external surface of the catalytic domain and extending into the membrane domain (subunits ATP6 and ATP8 plus three small membrane subunits e, f and g, which form a wedge encapsulating lipid molecules). ATP6 is intimately associated with the c_8-ring and provides two proton half channels involved in the generation of rotation. The wedges in two ATP synthases interact to form the characteristic dimers that sit on the tips of the cristae and subunit k links dimers together. The assembly of the human enzyme involves the formation of intermediate modules representing (i) the catalytic domain ($\alpha_3\beta_3\gamma\delta\varepsilon$, or F_1, plus IF_1), (ii) the PS plus the membrane "wedge". [3,4], and (iii) the membrane bound c_8-rotor ring [5]. They form the key intermediate F_1-IF_1-c_8-PS [5] into which subunits ATP6 and ATP8 are inserted between the c_8-ring and the wedge with subunit j bound to ATP6, forming the proton pathway. Two protein assembly factors are required to build the c_8-ring and three others to assemble the catalytic domain. IF_1 is another key assembly factor that intervenes to prevent partially formed complexes that are capable of ATP hydrolysis (but not synthesis) from doing so. The assembly pathway reflects the probable modular path of evolution of the enzyme. Finally, I will comment on the lack of involvement of ATP synthase in the permeability transition.

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We 1 K-2
High resolution cryoEM structures of terminal oxidases

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The membrane integrated terminal oxidases comprise the evolutionary unrelated oxygen reductases of the heme-copper type and the bd oxidases. We are interested to understand their mechanisms of action based on accurately determined atomic structures including those of intermediates of their catalytic cycles. In the past we have determined the structures of intermediates of the catalytic cycle of the cytochrome c oxidase from the soil bacterium Paracoccus denitrificans yielding surprising results suggesting a novel catalytic cycle [1] (Kolbe et al., Nature communications 12, article number: 6903 (2021)). Now we have determined the structures of intermediates of the catalytic cycle at resolutions of up to 1.7 Å leading to novel insights.

In addition we have determined the structures of a number of bd oxidases. These enzymes oxidize quinones. Surprisingly, they are mechanistically and structurally quite diverse including a rearrangement of high-spin hemes and conformational adaption of a transmembrane helix to generate a distinct oxygen-binding site. The bd oxidases from pathogenic bacteria like Mycobacterium tuberculosis are potential drug targets to fight infectious diseases like tuberculosis.

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We 1 K-3
SCAF1 drives the compositional diversity of mammalian respirasomes

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The mitochondrial respiratory chain (MRC) is a central component of mammalian metabolism and is composed of four membrane-embedded protein complexes (complex I -CI-, complex II -CII-, complex III -$CIII_2$-, complex IV -CIV-) working in a chain to generate the electrochemical gradient necessary for the ATP synthase-driven ATP production. The MRC complexes are functional in isolation but associate in the membrane in high-order structures named supercomplexes. Important open questions regarding the assembly and composition of supercomplexes need to be addressed to elucidate the physiological role of supercomplexes in metabolism. Our cryo-EM work tackled the role that the supercomplex associated factor SCAF1 plays in supercomplexes assembly using murine mitochondria as a model for mammalian species. SCAF1 is required for the assembly of supercomplex $CIII_2CIV$, while its role in the formation of

respirasome (supercomplex $ClCIII_2CIV$), featuring $CIII_2CIV$ alongside CI, is unclear. SCAF1 expression has been linked to differential fitness in humans and mice and to cancer, making it a relevant target for human health. Our structures [1] showed that SCAF1 N-terminus inserts into $CIII_2$, while the C-terminus binds CIV, keeping $CIII_2$ and CIV together during the $CIII_2CIV$ assembly and in the mature form. Furthermore, biochemical assays proved that $CIII_2$ and CIV gain catalytic advantage when assembled in the supercomplex. Our structural analysis also confirmed that SCAF1 is not present in the respirasome, in agreement with previously solved structures, but in disagreement with biochemical data, which detected SCAF1 alongside the respirasome components. We thus set to structurally investigate the high-molecular-weight murine supercomplexes [2] and found SCAF1 bound to a newly identified respirasome (named the CS-respirasome), compositionally different from the previously observed canonical respirasome (the C-respirasome). Our structures finally explain why SCAF1 is biochemically detected in respirasome-like species, but not present in the canonical respirasome. In addition to the CS- and the C-respirasomes, we were also able to identify an alternative conformation of the canonical respirasome (named the A-respirasome), with CIV bound to the "back" of complex I as opposed to the "heel". This body of work reveals the SCAF1-driven compositional landscape of mammalian supercomplexes and form a basis to hypothesize how conformationally and compositionally diverse supercomplexes can fine-tune mammalian metabolism.

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Th 1 Organelle dynamics

Th 1 K-3
The role of MICOS in respiratory chain assembly

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The inner mitochondrial membrane has an intricate architecture that is important for efficient respiration and oxidative phosphorylation, but that also poses challenges for the multi-step biogenesis of respiratory chain complexes. The respiratory chain is asymmetrically localized in cristae membranes, whereas many of its assembly steps take place preferentially in the inner boundary membrane. MICOS, the mitochondrial contact site and cristae organizing system, is required for the stability of crista junctions that connect these inner membrane subdomains, and consequently for native cristae architecture and dynamics. We find that MICOS deletion mutants display delays in the assembly of specific respiratory chain subunits rather than generalized defects resulting from an aberrant cristae architecture. Our results show that MICOS recruits intermediates and assembly factors to crista junctions, thereby facilitating specific assembly steps of the respiratory chain. Thus, going beyond a passive scaffolding function, MICOS plays a direct role in the spatial and kinetic coordination of respiratory chain assembly.

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Sa 1 Respiratory complexes and supercomplexes III

Sa 1 K-1
Structure and mechanism of the energy-coupled nicotinamide nucleotide transhydrogenase from *E. Coli*

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The nicotinamide nucleotide transhydrogenase catalyzes reversible hydride transfer between NADH and $NADP^+$ and couples this reaction to the proton motive force to promote the generation of NADPH. This transhydrogenase is present in the mitochondrial inner membrane and in the cytoplasmic membranes of many bacteria including E. coli. The enzyme consists of three domains: domain I binds NAD(H); domain II contains multiple transmembrane helices and a proton channel; domain III binds NADP(H). Large conformational changes of the enzyme isolated from ovine mitochondria were previously observed in the presence of $NADP^+$ or NADPH [Kampjut and Sazanov, Nature**573**, 291-295(2019], but none of the conformations are compatible with hydride transfer from NADH to $NADP^+$. In this work, the structure of the transhydrogenase from E. coli has been determined by cryo-electron microscopy, capturing multiple conformations in the presence of pairs of substrates/products: NAD^+ & $NADP^+$ and NADPH & $NADP^+$. Most important is a conformation observed in the presence of a mixture of NADPH and $NADP^+$ in which the binding sites for NADH (domain I) and $NADP^+$ (domain III) are adjacent and compatible with direct hydride transfer. The structures, along with previous data, suggest a plausible mechanism for coupling the proton motive force to hydride transfer between NADH and $NADP^+$.

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Sa 1 K-2
Deciphering the molecular mechanism of proton-electron coupling in the Complex I machinery

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Complex I is a gigantic redox-driven proton pump that catalyzes an NADH-driven reduction of quinones transducing the free energy into proton pumping across a biological membrane, >200 Å away from the active site.[1,2] Yet, despite major advances, its energy transduction mechanism remains poorly understood and much debated. Here we integrate biophysical, computational, and structural experiments to derive a unified molecular understanding of the long-range proton pumping mechanism in the Complex I machinery.[3-8] We show how the quinone chemistry triggers conformational and hydration changes in the membrane domain of Complex I activating the proton pump. Moreover, we dissect and engineer the minimal proton transport elements of the pumping machinery, and show how the proton translocation activity is achieved by electric field effects. Finally, we discuss how mutations,