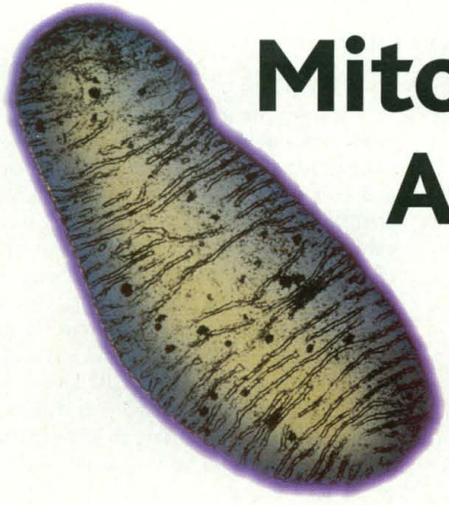

Mitochondria Make A Comeback

It was more than 50 years ago that mitochondria first captured the attention of cell physiologists. Abundant, easy to purify, and a rich source of vital enzymes, these organelles were pivotal in the Nobel Prize–winning research that defined the fundamental principles of cellular energy metabolism. But over the years, as technological advances in molecular biology made nuclear functions more accessible to researchers, interest in mitochondria began to wane.

It appears that this lapse was only temporary. Our special section illustrates that mitochondria are once again at the forefront of research—this time in fields as diverse as cell death, evolutionary biology, molecular medicine, and even forensic science.

One of the most important developments has been the recognition that mitochondria play a central role in the regulation of programmed cell death, or apoptosis. As reviewed in a recent issue of *Science* (28 August 1998, p. 1309), mitochondria can trigger cell death in a number of ways: by disrupting electron transport and energy metabolism, by releasing/activating proteins that mediate apoptosis, and by altering cellular redox potential. Any or all of these mechanisms may help to explain how mitochondrial defects contribute to the pathogenesis of human degenerative diseases, aging, and cancer. This theme is developed further by Wallace, who reviews the genetics of mitochondrial disease, a field that has witnessed phenomenal growth in the past 10 years. Also discussed are new mouse models of mitochondrial disease, which should greatly enhance our understanding of pathogenetic mechanisms and allow development and testing of new therapies.

Mitochondria feature prominently in evolutionary biology in at least two important ways. The question of how the mitochondrion itself originated is addressed by Gray *et al.*, who discuss recent comparative sequence analyses of primitive mitochondrial and eubacterial genomes—results that seem to challenge certain aspects of popular endosymbiotic models. A News story by E. Strauss (p. 1435) examines new developments in the use of mitochondrial DNA as a "clock" to gauge the relatedness and origin of various species. Because the mitochondrial clock does not tick steadily, some researchers question its reliability for dating evolutionary events, while others argue that with careful use, the clock can produce accurate results.

Mitochondria produce most of the cell's energy by oxidative phosphorylation, a process that requires the orchestrated actions of five respiratory enzyme complexes located in the mitochondrial inner membrane. Atomic resolution structures are now available for key components of three of these complexes: cytochrome bc_1, cytochrome c oxidase, and ATP synthase. Saraste discusses how this new information has both substantiated earlier ideas about enzyme mechanisms and yielded some surprises.

Finally, because mitochondria are essential for cell viability, mechanisms must exist to ensure their distribution to daughter cells during cell division. Mitochondrial inheritance/movement is no longer thought to be a passive process but one that requires the action of an elaborate cytoskeletal machinery. Yaffe reviews the components of this machinery, just now beginning to be identified by genetic and biochemical approaches.

All this leaves no doubt that mitochondria will retain a captive audience for some time to come.

—PAULA A. KIBERSTIS

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