
PREFACE

Cilia and flagella have long been the subject of intense study and a previous volume of *Methods in Cell Biology* dedicated to this organelle was published in 1995. However, in the 15 years since that publication, interest in the organelle has dramatically increased as it has come to be appreciated that these tiny structures play fundamental roles in the development and health of mammals and are vital for vertebrates to perceive their environment and respond to it. In humans the list of ciliary diseases, or ciliopathies, has grown tremendously since the publication of the previous volume. In 1995 the field recognized that cilia and flagella played critical roles in male fertility and respiratory disease and were recognized as being important in the determination of left-right asymmetry of vertebrates but the mechanism was not known. In addition, it was known that the senses of vision and smell depended on receptors localized to modified cilia. It is now appreciated that ciliary defects underlie a wide range of human diseases. These include polycystic kidney disease (PKD), nephronophthisis, Bardet-Biedl syndrome (BBS), Meckel-Gruber syndrome, Joubert syndrome, Jeune syndrome, and short rib-polydactyly syndrome that are thought to result from defects in primary cilia. Other diseases such as male infertility, hydrocephaly, juvenile myoclonic epilepsy, primary ciliary dyskinesia, Kartagener's syndrome, and left-right asymmetry defects of the heart are thought to result from defects in motile cilia. In addition, anosmia and blindness can derive from dysfunction of the highly specialized sensory cilia of the olfactory epithelium and retina. It is clear from studies in mouse that this collection of diseases is just the tip of the iceberg for ciliary disorders of man.

Eukaryotic cilia and flagella are complex organelles composed of hundreds of different proteins. This complexity likely reflects the diverse motility and sensory roles played by these organelles. The motility functions of cilia have long been recognized and in mammals these are important for moving mucus in the lungs, moving cerebrospinal fluid in the brain, and propelling the male gametes. The sensory functions are less well known but include roles in olfaction in the nose and light detection in the eye. In addition, nearly every cell type in vertebrate organisms is ciliated by nonmotile primary cilia that are thought to sense the extracellular environment. The proteins of the cilium are organized around a microtubule-based cytoskeleton termed the axoneme and a specialized domain of the plasma membrane that covers the axoneme. The ciliary membrane is contiguous with the plasma membrane of the cell but is a separate domain containing a unique set of proteins, many of which play roles in sensory perception. The axonemes of motile cilia typically have a 9 + 2 arrangement of microtubules while nonmotile sensory and primary cilia typically have a 9 + 0 arrangement. These microtubules serve as scaffolding to bind and organize the multitude of proteins needed to carry out the motility and sensory functions of cilia. The microtubules of the axoneme are templated from a centriole at

the center of the centrosome. When the cell is ciliated, the centriole (which is now called a basal body) and centrosome remain at the base of the cilium. The centrosome is best known for its role in organizing the cytoskeleton and also is postulated to be an important control center of the cell, integrating signals that regulate morphology, migration, and proliferation.

With the explosion of interest in cilia, the model organisms available to study cilia and flagella have grown much more diverse, and the techniques available for assessing cilia structure and function have become more sophisticated. In these three volumes, we have asked top researchers in the field to provide methods used in their laboratories to study cilia and flagella. *Cilia: Structure and Motility*, Volume 91, focuses on general methods to study these organelles covering microscopic techniques for both structural analysis and detailing motility parameters, as well as biochemical approaches to define protein-protein associations and complexes. *Cilia: Motors and Regulation*, Volume 92, focuses on techniques for studying dynein structure and function and the varied mechanisms by which these motor complexes are regulated. *Cilia: Model Organisms and Intraflagellar Transport*, Volume 93, focuses on the methods for studying intraflagellar transport which is required for assembly of the organelle and provides general approaches for studying this and other cilia-related phenomena in all of the major model organisms that are currently being used to study cilia and flagella.