Beating Cilia and Whipping Flagella: More Than Meets the Eye
Ronald C. Gentile, MD; Carlo Iomini, PhD

The terms “cilia” and “flagella” are the Latin words for “eyelash” and “whip,” and refer to a hair-like structure found protruding from the surface of a cell. Cilia are found in some of the most primitive unicellular organisms, as well as on almost all vertebrate cells, including man. Cilia can be motile or non-motile. Motile cilia beat and generate forces. Non-motile cilia, also called primary cilia, are single cilia and function as sensors or transporters. Despite a large variety of functional and morphological adaptations, ciliary architecture and composition has been preserved during evolution for more than 3 billion years.

The internal structure of the cilium includes a central shaft or axoneme originating from a modified centriole (basal body). The axoneme has nine microtubule doublets arranged in a circular pattern. In addition to a structural role, the axoneme also acts as a track for molecular motors that power a bidirectional transport of protein particles involved in cilia assembly and signaling called intraflagellar transport. A ciliary membrane, continuous with the plasma membrane, surrounds the axoneme and contains specialized receptors and signaling molecules.

Defects affecting cilia can lead to a group of genetic diseases called ciliopathies that are often syndromic. More than 100 genes causing ciliopathies have been identified, and uncovering the functions of cilia help us understand the diverse clinical findings in these diseases. Defects affecting ciliary motility cause primary ciliary dyskinesia, a disorder that affects the respiratory system (infections), fallopian

Figure. Cilia (red brackets) allow for primitive animals to move and humans to see. Ax = axoneme; bb = basal body; cc = connecting cilium (Reprinted with permission from Hogan MJ, ed. Histology of the Human Eye. Philadelphia: W.B. Saunders; 1971.)

From the Department of Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York (RCG); Winthrop University Hospital, Mineola, New York (RCG); and the Departments of Ophthalmology and Developmental and Regenerative Biology, Icahn Medical School at Mount Sinai, New York, New York (CI).

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Correspondence: Ronald C. Gentile, MD, New York Eye and Ear Infirmary of Mount Sinai, 310 East 14th Street, New York, NY 10003. doi: 10.3928/01913913-20150427-03
tubes and sperm (sterility), and the mammalian node, all of which use motile cilia to function. Ciliopathies affecting the non-motile functions can impair their ability to detect external stimuli. In the kidney, cilia detect fluid flow in the renal tubules through calcium channels in their membrane. Defects affecting these channels result in cystic kidney diseases.

Ciliopathies can also affect transport function. Retinal photoreceptors contain a modified cilium called a connecting cilium that connects the inner segment of the photoreceptor to its outer segment. The connecting cilium mediates the transport of proteins and phospholipids needed for proper function and maintenance of the photoreceptors. Impairment in the connecting cilium or in proteins mediating ciliary transport has been found in approximately 11% of patients with retinitis pigmentosa. This includes 70% of X-linked retinitis pigmentosa, 25% of male retinitis pigmentosa simplex, and 6% of patients with Leber's congenital amaurosis.

Primary cilia also mediate important morphogenetic pathways; therefore, defects in cilia can be associated with multiple developmental abnormalities. This appears to explain the associated degenerative retinopathy seen in combination with neurological, hepatic, and renal disease, including mental retardation, obesity, polydactyly, situs inversus, skeletal dysplasia, and cleft palate. Ciliopathy syndromes include Senior–Løken (Retinal–Renal), Bardet–Biedl, Joubert, Kartagener, Meckel–Gruber, Alström, and orofaciiodigital.

Cilia and flagella have been crucial to the survival of both unicellular organisms and humans. Cilia, both motile and primary, are vital cellular organelles and understanding their function can help us understand the different ophthalmic ciliopathies and their associated syndromes.

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