Abstract

Primary ciliary dyskinesia (PCD) is a rare but underdiagnosed genetic disease. This innate disorder of motile cilia causes a non-functional mucociliary clearance which is the main reason for a clinical picture of recurrent or chronic upper and lower respiratory tract infections. Fertility disorders or abnormal organ situs can also be found in some patients. The diagnosis of PCD is extremely complicated and complex. A combination of several diagnostic procedures as well as skilled personnel and special technical equipment are usually needed for the PCD diagnostics. Although significant progress has been made in understanding the PCD etiopathogenesis and the advanced diagnostics has become available, therapeutic possibilities are rather limited and the treatment efficiency still remains to be confirmed by the evidence base medicine.

The dissertation thesis assembles several publications in which different aspects of primary ciliary dyskinesia were addressed. The most extensive part of our research addressed rapidly evolving possibilities of PCD genetic diagnostics. We studied possibility of priority sequencing of several segments of the genes *DNAH5* and *DNAI1* which were known to be the most frequently mutated genes in the PCD patients at the time of the study. We proved this method being able to identify most of the patients carrying mutations in these genes. The most recent part of our work focused on the next generation sequencing methods in combination with the classic Sanger sequencing. Using this method, we were able to establish the genetic diagnosis in the two thirds of the Czech patients achieving the same diagnostic rate as the best scientific groups worldwide. About a third of the Czech PCD cases were predictably caused by the mutations in the *DNAH5* gene. Surprisingly, another quarter of the PCD patients carried ancestral mutations in the *SPAG1* gene. Other genes found to be mutated only in individual families were *DNAI1*, *LRRC6* and *CCDC40*. We also suggested a cost-effective genetic diagnostic pipeline.

Secondly, in collaboration with British researchers, we designed an image processing software method capable of automatic ciliary beat frequency assessment with a high accuracy. In another study, we proved that the PCD patients are at risk of the growth failure at childhood. In the last study, we developed easy-to-use validated clinical index that is able to distinguish the patients with high risk of PCD among the group of paediatric patients with recurrent respiratory problems.

Key words

Cilia, diagnostics, children, clinical index, high-speed video microscopy (HSVM), genetics, next generation sequencing (NGS)