Report MD-295

Structural and chemical changes in respiratory ciliated cells associated to Primary Ciliary Dyskinesia

The diagnosis of Primary Ciliary Dyskinesia (PCD), a rare and heterogeneous group of genetic respiratory diseases caused by functional and ultrastructural abnormalities of cilia, is based on the identification of functional and structural abnormalities of respiratory cilia obtained at nasal or bronchial level. The measurement of NO concentration in exhaled gases is also used as a diagnostic tool in PCD, since it is the only known respiratory disease where exhaled nasal NO concentrations decrease so dramatically. The ciliary function is evaluated *in vitro*, by measurement of beat frequency whereas ciliary ultrastructure is characterized using well-defined transmission electron microscopy techniques, giving a percentage of abnormal cilia and describing the main ultrastructural defect(s). In most patients with PCD (70%), the cilia are all immotile and share the same ultrastructural defect, corresponding to an absence of dynein arms. In some patients (30%), the ciliary motion is still present with low frequency and/or abnormal movement, mainly related to an absence of the central pair of microtubules. Additional structural and chemical information is needed to better understand the biological phenomena related to PCD and also possibly to complement the diagnosis tools.

In a series of high resolution X-ray microfluorescence imaging experiments performed at beamline ID21 (energy 7.5 keV, submicrometer resolution), we detected high amounts of calcium and iron within the cytoplasm of ciliated cells in samples from both controls and PCD patients with immotile cilia related to an absence of outer dynein arms. However, interestingly, the subcellular distribution of these elements greatly differs between controls showing a diffuse distribution of iron and calcium, and samples from PCD with these molecules concentrated in the apical region of the cell, possibly located in the mitochondria.

This new data raises a major question: is this feature specific of PCD or secondary to the absence of cilia motility? The relationship between iron and calcium accumulation and ciliary defect is still unknown and has therefore to be explored.