CENTRIOLE DYSFUNCTIONS AND MICROCEPHALY

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Microcephaly is a neurological developmental disorder that leads to an extreme reduction in brain size associated with a reduced pool of neural precursors (NPCs). This is often due to defects in centrosome biogenesis that impairs symmetric divisions during early brain development and leads the premature differentiation of these cells.

A mutation in the centrosomal protein CPAP causes Seckel syndrome, characterized by microcephaly and reduced body size. Ultrastructural analysis of Seckel cells shows cilia longer than normal, due to a delay in their disassembly. Consequentely NPCs do not re-entry into the cell cycle leading to their premature differentiation. Therefore, the primary cilium plays a key role in NPCs maintenance and the timely cilium disassembly mediated by CPAP is very important in neurogenesis and brain size control.

Microcephaly could be also due to viral infections. It has been reported that the Zika virus (ZIKV) is associated with microcephaly in newborns. Human brain organoids derived from induced-Pluripotent Stem Cells (iPSCs), infected by an Asian strain of ZIKV, were analyzed ultrastructurally by TEM. ZIKV infection perturbs the centrosomal structures and affects the orientation of the mitotic spindle of the apical neural progenitor cells. This results in the premature differentiation of NPCs and leads to progenitor depletion and impairment of neurogenesis.

Key words: Microcephaly, Zika virus, Centrioles.