LETTURA MAGISTRALE

INTRAFLAGELLAR TRANSPORT IN CILIARY TRAFFICKING: A COMPLEX MOLECULAR MACHINERY IN EUKARYOTIC CELLS

*Lupetti P, Vannuccini E, Gentile M, Pratelli A, Mencarelli C and Paccagnini E

Department of Life Science, University of Siena

Cilia and flagella, the two terms are interchangeable, are the oldest known cellular organelle being first described in 1675 by Anthony van Leeuwenhoek in protozoa as "thin feet, or little legs, which were moved very nimbly". For many decades motility has been the only function ascribed to cilia, till in 1898 a second type of cilium, solitary and immotile, was described and a sensory function was proposed by KW Zimmerman for such immotile organelle. The pivotal sensory and regulatory function of such cilia, later named primary cilia because of their early onset in multiciliated cells of
nervous system, was however elucidated only in this past decade.

It is now established that the apparent separation between motile and immotile sensory cilia does not hold since, as suspected since a long time, motile cilia and flagella also have sensory capabilities, and not only, since quite recently a secretory role has been also proposed fur such organelles. Given their almost ubiquitous presence and their multifunctional nature in eukaryotes, vertebrate comprised, it is not surprising that defects in the molecular composition and/or function of cilia have been unequivocally related to the onset of several severe human syndromes for which the term ciliopathies has been established.

Cilia are disassembled and resorbed before cells enter division to be reassembled in G1/G0 phases of the cell cycle. Flagellar proteomics demonstrated the presence of more that 350 polipetides which are sinthesized in the cell cytoplasm, carried via trans golgi network to the ciliary base, selectively admitted to the ciliary compartment via the ciliary pore. Most of flagellar precursors travel as cargoes on IntraFlagellar Transport (IFT) Trains: multiprotein complexes actively moving bidirectionally on the external surface of microtubule doublets by ATPase motors. Since it's first description by Kozmisky et al. in 1993, several important achievements have been reached about the protein composition of IFT trains, their active role in ciliary assembly and maintenance by trafficking of ciliary precursors. Some important features of IFT trains functioning and regulation have been recently elucidated by ultrastructural studies and 3D modeling of IFT trains in situ in flagella of the model organism *Chlamydomonas reinhardtii*. Main costributions started from the Siena group coordinated by P. Lupetti at the Department of Life Science and continued in a constructive competition with G.Pigino's (a former Lupetti's student) now active at Max Plank Institute at Dresden (Germany). Main contributions were the identification of two ultrastructural models for IFT trains, the so called long and short trains (Pigino et al. 2009). Modeling of IFT trains was made possible by the development of ad-hoc 3D recostruction strategy from double-tilt tomography of thick sections from flat embedded samples (Pigino et al. 2013). Successively two strucrural subclasses of short trains were identified, their relative abundance was monitored along flagellar regeneration, and one subclass was 3D modeled by high resolution double tilt axes electron tomography (Vannuccini et al. 2016).

Keywords: cilia, intraflagellar transport trains, ultrastructure

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INTRAFLAGELLAR TRANSPORT AT THE IMMUNOLOGICAL SYNAPSE

*Finetti F, Onnis A, Cassioli C, Patrussi L, Capitani N, Riparbelli MG and Baldari CT

Department of Life Sciences, University of Siena, Italy

Intraflagellar transport (IFT) had been studied in ciliated cells in relation to its central role in the traffic of molecules along ciliary microtubules during ciliogenesis. However, starting from our finding that IFT proteins are implicated in the activation of T cells, which lack a cilium, accumulating evidence supports the notion that the role of IFT proteins is not restricted to ciliary- dependent processes. We demonstrated that in T cells the IFT component IFT20 acts in concert with other IFT proteins and Rab GTPases to regulate intracellular vesicular traffic, a process essential for T cell activation. Indeed, IFT20 regulates the assembly of the specialized interface that forms between T cell and cognate antigen presenting cell, known as the immunological synapse, by orchestrating the polarized recycling of the T cell antigen receptor to this membrane domain. These results demonstrate that IFT proteins are shared by T cells and ciliated cells for the assembly both the immunological synapse and the primary cilium, respectively, suggesting that these structures are functional homologues.

Keywords: Intraflagellar transport, Immunological synapse, T lymphocytes

* *Speaker*