Cilia – the masterplan

Descriptive has almost become a dirty word in modern cell biology. To describe something is viewed as a suitable pastime for the amateur, but hardly an occupation for the serious modern scientist. Yet, without precise descriptive studies, modern molecular biology often descends into little more than extensive lists of oddly named components, with no overview of the underlying cellular processes in which these molecules act. Although not the first paper to describe cilium formation in mammalian cells, the 1968 *Journal of Cell Science* paper by Sorokin (Sorokin, 1968) is remarkable for its accurate outline of the pathway of centrosome and basal body duplication, and the subsequent steps of cilium formation involving membrane remodelling (see Fig. 1) and is still relevant today.

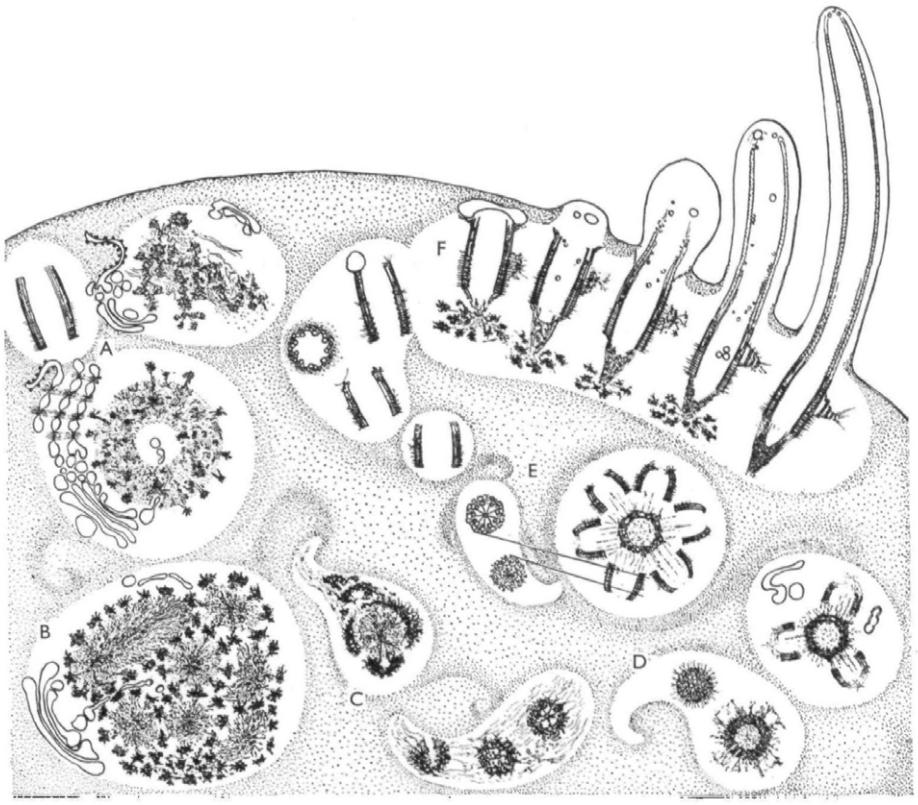

Fig. 1. Illustration of the major stages of basal body duplication (A-E) and cilium formation (F) in the bronchial epithelium. See fig. 2 in Sorokin (Sorokin, 1968) for a full description of these events.

Cilia are projections of the cell surface formed when the cell membrane wraps around an array of microtubules termed the axoneme (Dawe et al., 2007). They have long been appreciated to play a role in cell motility in many organisms; however, they have many other functions in signalling, liquid flow, and sensation of smell, sound and sight (Christensen et al., 2007; Fliegauf et al., 2007; Singla and Reiter, 2006). Since Sorokin's 1968 study, many major advances have been made in understanding the molecular makeup and function and cilia (Dawe et al., 2007). These include the description and characterization of the components of the intraflagellar transport pathway (Scholey, 2003) and a ciliary proteome (Gherman et al., 2006). Cilia are now also appreciated to be important sites of signalling, and a number of developmental defects in humans have been mapped to genes encoding proteins required for normal cilium function (Christensen et al., 2007; Singla and Reiter, 2006). Indeed, this has lead to primary cilia being termed the 'antenna of the cell'.

One of the key questions in cilium formation noted by Sorokin was the need for the basal bodies to interact with membranes and for microtubule growth to be coordinated with membrane extension (see stage F in the figure). Recent studies implicating Arl and Rab GTPases of the Ras superfamily and their regulators in cilium formation and function have started to provide some answers to these questions (Grayson et al., 2002; Qin et al., 2007; Yoshimura et al., 2007). Rab family GTPases are known to promote interactions between membrane and the cytoskeleton, and to control specific interactions between membranes (Zerial and McBride, 2001). In the context of cilium formation, Rabs might therefore provide a means to control the interaction of the basal body with the cell surface, and integrate microtubule growth and membrane elongation. Highlighting the general importance of GTPases for cilium function, a number of these GTPases are mutated in syndromes resulting in developmental abnormalities (Chiang et al., 2004; Fan et al., 2004; Jenkins et al., 2007).

Pre-empting many later debates on the nature of organelle duplication and inheritance (Lowe and Barr, 2007), Sorokin remarks that centrioles and basal bodies are typically copied but may also arise by a de novo synthesis pathway when necessary. The former pathway is used when cells undergo normal growth and division, and is responsible for ensuring cells inherit a copy of the centrosome. The de novo synthesis pathway is used in cells that produce multiple cilia, such as the ciliated epithelium of the lung. A number of recent studies have started to uncover the components and mechanisms underlying centrosome duplication (Bettencourt-Dias et al., 2005; Kleylein-Sohn et al., 2007; Pelletier et al., 2006; Rodrigues-Martins et al., 2007a; Strnad et al., 2007). To briefly focus on two of these studies, we now know that Sorokin was correct and that centrioles can arise de novo or by a templated assembly process, and that the kinase Plk4/Sak plays a key role controlling these events (Habedanck et al., 2005; Kleylein-Sohn et al., 2007; Rodrigues-Martins et al., 2007b). Remarkably, the flower-like arrays of forming centrioles Sorokin describes in the ciliated lung epithelium (see stages D and E in the figure) can be induced simply by expression of Plk4 [see Kleylein-Sohn et al. (Kleylein-Sohn et al., 2007) and fig. 6 within]. While many details remain to be worked out, the basic framework for centriole and centrosome biogenesis described by Sorokin is remarkably accurate.

I hope that some of you will take the time to read Sorokin's remarkable study, and reflect that high quality descriptive work and particularly electron microscopy is valuable even in the age of molecular biology. As Sorokin remarks, such work can be "*helpful in establishing the conceptual framework that so often precedes the design of subtle and telling experiments*".

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