Reciprocal coupling between cell cycle and primary cilia through Kv10.1 potassium channels

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The primary cilium is critical for morphogenic and growth factor signaling. Ciliogenesis and cell cycle progression are tightly linked, and only quiescent cells produce primary cilia, through yet unclear mechanisms. Kv10.1 is a voltage-gated potassium channel frequently overexpressed in tumors while virtually undetectable in tissues outside the brain. When present in tumor cells, it promotes cell proliferation and resistance to hypoxia, and confers worse prognosis. Conversely, its inhibition or knockdown reduces tumor progression in vivo.

We observed that Kv10.1 is expressed in tumor cells upon E2F1 activation –often aberrantly induced in cancer–. E2F1 binds to the promoter of Kv10.1 in a time frame compatible with the G2/M transition of the cell cycle both in tumor cells and normal tissues. Since at any given time point a very restricted fraction of cells is at the G2 phase of the cycle, this explains why Kv10.1 expression is undetectable in healthy peripheral tissuesExpression extends over the whole span of G2 and M phase. In normal cells, the expression would thereafter be shut off, until the next G2 phase is reached.

Kv10.1 is targeted to the ciliary membrane, where it is found in the proximity of the basal body. Kv10.1 participates in primary cilium disassembly in G2. Interference with ciliary localization results in the inability to induce ciliary disassembly and also abolishes the tumorigenic properties of Kv10.1 Consistently, knockdown of Kv10.1 results in a longer duration of G2/M, induces the presence of primary cilia in proliferating cells, and disrupts the regulation of the Sonic hedgehog pathway.

In summary, Kv10.1 potassium channel participates in triggering ciliary disassembly before entry into mitosis, and it does so in tumor as well as normal cells. Therefore, modulation of ciliogenesis by the Kv10.1 ion channel is likely to be a major mechanism underlying its tumorigenic effects.