



## ***ABSTRACT***

*“How to make stable decisions in cell proliferation and differentiation”*

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The decision to replicate its DNA is of crucial importance for every cell and in many organisms decisive to progress through the entire cell cycle. Using pollen as a model system, we have identified a general regulatory cascade controlling entry into S phase in many if not all *Arabidopsis* cells. This cascade comprises the *Arabidopsis* homologs of the animal transcription factor E2F, the plant homolog of the animal transcriptional repressor Retinoblastoma (Rb)-related 1 (RBR1), the plant-specific F-box protein, F-BOX-LIKE 17, the plant specific cyclin-dependent kinase (CDK) inhibitors KRPs, as well as CDKA;1, the plant homolog of the yeast and animal Cdc2<sup>+</sup>/Cdk1 kinases. Biomathematical simulations and subsequent experimental confirmation of computational predictions revealed that this regulatory circuit can give rise to hysteresis highlighting the identified dosage sensitivity of CDK inhibitors in this network. Remarkably, many components of this cell cycle control module appear to function in the control of asymmetric division and cell fate specification as well. I will present data from our team showing that RBR1 not only controls cell proliferation but also cell differentiation genes during root meristem and stomata development. This leads to a CDKA;1-dose dependent model of formative divisions in which low and medium levels of CDKA;1 are sufficient for symmetric divisions but high kinase levels being required for asymmetric divisions. An important aspect of this wiring is again the hysteretic behavior of the system revealing an intimate connection between cell cycle progression and cell fate acquisition.