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=== ORAL PRESENTATION ABSTRACTS ===

Switches and latches: controlling cell division

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The process of mitosis involves a comprehensive reorganization of the cell: chromosomes condense, the nuclear envelope breaks down, the mitotic spindle is assembled, cells round up and release their ties to the substrate and so on and so forth. This reorganization is triggered by the activation of a protein kinase called Cyclin-Dependent Kinase 1 (CDK1). The end of mitosis is marked by the proteolysis of the cyclin subunit of CDK1, which terminates kinase activity. At this point, the phosphate moieties that altered the properties of hundreds of proteins to bring about the cellular reorganization are removed by protein phosphatases.

We recently began to pay attention to the control of these protein phosphatases, conscious that it was likely that they were shut off as cells enter mitosis, and reactivated when mitosis is complete, allowing return to interphase. It is difficult to see how proteins could be fully phosphorylated if both kinases and phosphatases were simultaneously active (much as filling a wash basin requires not only turning on the water taps, but also putting in the plug).

It emerged that at least one protein phosphatase, PP2A-B55, was shut off in mitosis. Depletion of this particular form of PP2A accelerated entry into mitosis, and blocked exit from mitosis. We have discovered how this phosphatase is regulated. It entails binding a small inhibitor protein (α-endosulfine or ARPP-19) that is phosphorylated by a protein kinase called Greatwall that is itself a substrate of CDK1. Failure to inhibit PP2A-B55 causes arrest of the cell cycle in G2 phase. I will explain how we found this out (proteomics played a key role) and discuss the

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role of this particular control mechanism in the control of mitosis. The “switches and latches” of my title refers to our still rather poor understanding of exactly how the timing of entry into mitosis is controlled, together with the realization that the Greatwall-α-Endosulfine circuit is not only required for entering mitosis, but also for staying there.