

P050 The regulated assembly of a PKC epsilon complex controls the completion of cytokinesis

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The cell cycle is exquisitely controlled by multiple sequential regulatory inputs to ensure fidelity. Here we demonstrate that the final step in division, the physical separation of daughter cells, is controlled by a member of the PKC gene superfamily. Specifically, we have identified three novel phosphorylation sites within PKC ϵ that control its association with 14-3-3. These phosphorylations are executed by p38 MAPKinase (Ser350), GSK3 (Ser346) and PKC itself (Ser368). Integration of these signals is essential during mitosis because mutations that prevent phosphorylation of PKC ϵ and/or PKC ϵ binding to 14-3-3 also cause defects in the completion of cytokinesis. Using chemical genetic and dominant negative approaches it is shown that selective inhibition of PKC ϵ halts cells at the final stages of separation. This arrest is associated with persistent RhoA activation at the midbody and a delay in the dissociation of the actomyosin ring and central spindle. This study therefore identifies a new regulatory mechanism that controls exit from cytokinesis which has functional implications for cancer progression.