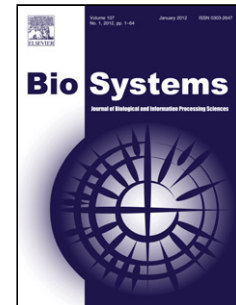


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Multiple Roles of Adenomatous Polyposis Coli gene in Wnt Signalling – a Computational Model.

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Abstract

The Adenomatous Polyposis Coli (APC) gene is a multifunctional gene that plays a major role in regulating the Wnt signalling pathway. The Wnt pathway, when activated by Wnt signalling molecules, initiates cell division. Mutation of APC disrupts the regulation and causes continuous activation of the Wnt pathway even in the absence of Wnt signals, thus causing uncontrolled cell proliferation.

APC regulates the Wnt pathway by controlling the formation of the nuclear complex β -catenin/TCF that initiates the transcription of the Wnt target genes. There are at least five mechanisms by which APC can regulate the formation of the β -catenin/TCF complex:

1. APC is part of the Destruction Complex that phosphorylates cytoplasmic β -catenin in a way that marks it for destruction.
2. APC retains cytoplasmic β -catenin by binding to it.
3. APC plays a role in controlling the distribution of β -catenin between Wnt signalling and cell-cell adhesion.
4. APC translocates to the nucleus and competes with TCF for binding to β -catenin within the nucleus.
5. APC promotes the export of β -catenin out of the nucleus.

This paper presents a computational model for the Wnt pathway that explicitly includes the above five roles of APC in regulating β -catenin/TCF formation. We use

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