

Approximately ?-
catenin is sufficient to
instigate intestinal
polyposis



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Approximately 80% of colon tumors show a loss in adenomatous polyposis coli (APC) function because of mutations that lead to the deactivation of the APC gene. The APC gene serves as a central gatekeeper gene in colon cancer. APC is crucial in the Wnt signaling pathway as well as the regulation of β -catenin. The unquestioned tumor suppressor function of APC occurs through the formation of a complex that destroys cancerous cells. This complex is formed by the combination of APC with Axin/Axin2 and GSK-3 β (Eshghifar, Farrokhi, Naji, & Zali, 2017). When a Wnt signal is lacking, the complex plays a vital role in the ubiquitination and consequent proteasomal breakdown of the oncogene β -catenin.

Consequently, the loss of APC function causes a buildup of β -catenin, which moves to the nucleus and involves the Tcf/Lef transcription factor composite to trigger the transcription of numerous recipient genes such as c-myc, cyclinD1, and CRD-BP (Eshghifar et al., 2017). The upshots of uncontrolled β -catenin activity with respect to tumorigenesis is linked to the direct prompting of cellular growth and propagation in addition to the disturbance of differentiation schedules (Cai, Maitra, Anders, Taketo, & Pan, 2015). Another role of APC is the promotion of microtubule stability in several cellular contexts. Nevertheless, the magnitude of the impact of interfering with this role in tumor development is unclear.

Studies have reported that stabilized β -catenin is sufficient to instigate intestinal polyposis in mice thereby indicating that interfering with microtubule-binding functions of APC is not a prerequisite for early tumorigenesis (Cai et al., 2015). In the investigations, it was shown that mice homozygous for the 1638T APC allele devoid of the microtubule- and EB1-binding sites are susceptible to intestinal polyposis. <https://assignbuster.com/approximately-catenin-is-sufficient-to-instigate-intestinal-polyposis/>

binding areas of APC did not develop tumors. However, the β -catenin binding domains of the mice were intact. The findings of the investigation led to the conclusion that interfering with the microtubule functions of APC influences tumor advancement rather than tumor induction.

Chromosomal deletions that affect the DCC and p53 genes have also been implicated in the deactivation of tumor suppressor genes, which leads to the development of colon tumors. Question 2: The Regulation of p53 in Normal Cells Under normal conditions, p53 is in a dormant state and does not get involved in the progression of the cell cycle and existence. Studies show that mice with p53 genes knocked-out go through normal development and maturation, signifying that p53 is not indispensable for the normal growth and development (Muller & Vousden, 2013). Nonetheless, different conditions, which signify varying forms of stress that promote the development of malignant cells, can trigger a fast initiation of p53 activity. Examples of such conditions include obvious DNA destruction in addition to the impairment of constituents that play a role in the correct handling and separation of cellular genetic substance. Other conditions include a diminution of ribonucleotides, heat shock, lack of oxygen, and contact with nitric oxide. Oncogenic proteins such as adenovirus E1A, Ras, β -catenin, and Myc also contribute to the activation of p53 and its tumor suppressor activities. Disproportionate wild-type p53 activity produces diverse cellular outcomes, particularly programmed cell death and cell cycle arrest.

These actions reduce the likelihood of cancer by getting rid of cancer-predisposed cells from the replicative pool. However, these effects are only beneficial in cancerous cells and may have detrimental consequences in <https://assignbuster.com/approximately-catenin-is-sufficient-to-instigate-intestinal-polyposis/>

normal cells. For these reasons, p53 activity should be regulated strictly and released only when a cell accrues lesions that may otherwise send it into a cancerous state. A buildup of genomic errors is an important mechanism in carcinogenesis. Consequently, mutations in p53 are advantageous to cells that are undergoing tumor progression because the hasty initiation of p53 activity in response to the destruction of genomic components guarantees that aberrant cells are handled effectively.

Also, p53 may play a role in DNA repair processes. As a result, the central role of p53 in upholding genomic veracity has led to it being referred to as “guardian of the genome.”

Question 3: Heterotypic Interactions in Tumor Metastasis

Cancer metastasis is the dissemination of malignant cells to tissues and organs away from the origin of the tumor and the formation of new tumors. The sequence of events that ensue in cancer metastasis determine the prognosis of cancer patients and is referred to as the metastatic cascade. During the metastatic cascade, alterations in cell-to-cell and cell-adhesion matrix are indispensable. The metastatic cascade encompasses three main progressions: invasion, intravasation, and extravasation. In the first step, the tumor cells lose their cell-cell adhesion ability, which permits the cancerous cells to separate from the main tumor mass.

The cell-matrix interaction changes to facilitate the invasion of malignant cells into the neighboring stroma. Specific substances are secreted to break down the basement membrane as well as the extracellular matrix. There is the production of proteins that facilitate cell motility. Attaining the malignant phenotype requires the initiation of angiogenesis, which facilitates nutrient

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transport and elimination of waste substances. Blood vessels surrounding the tumor provide room for the separated cells to access the circulatory system and metastasize to remote sites in a process known as intravasation (Regier, Alarid, & Beebe, 2016).

Associations between the tumor cell and the neighboring stroma are crucial for tumor angiogenesis and involve heterotypic interactions. Once the malignant cell reaches a probable intravasation point, it intermingles with the endothelial cells through biochemical interactions to create sturdy bonds that aid the infiltration of the endothelium and the basement membrane in a process referred extravasation. The resultant tumor is now capable of further proliferation at the new site.

Question 4: EMT as a Feature of the Progression of Metastatic Cancer

The epithelial-mesenchymal transition (EMT) is useful in conventional cell differentiation in the early developmental stages. The migration of cancer cells is dependent on the ability to trigger the genes necessary for differentiation, delay propagation occurrences, and instigate anti-apoptotic machinery. Promoting cell differentiation initiates events that promote metastasis, for example, changing cellular traits from epithelial to mesenchymal, reducing receptors that facilitate cell-to-cell connections, increasing cell adhesion molecules that promote cell motility, breaking down cell-to-cell junctions, and recruitment of proteases at the cell facade to traverse the extracellular matrix. However, EMT is not a guarantee of metastasis. Additional factors such as epigenetic differences in cancer cells, environmental influences, cancer progenitor cell features, epigenetic modifications, and extracellular and intracellular indicators determine whether EMT and metastasis occur in a cell or not (De Craene & Berx, 2013).

A simple experiment that can be used to demonstrate that Twist protein is involved in tumor metastasis can involve 20 mice induced with a specific form of cancer, for example, breast cancer. The mice should be grouped into two categories of ten mice each. The Twist protein can be suppressed in the first group of mice by methylation. Both groups of mice should be kept under similar conditions for a specified period.

At the end of the predetermined duration, the mice from both groups should be killed and subjected to histological analyses to determine the metastasis of cancerous cells to distant organs such as the lungs. There is a likelihood that tumor cells will be localized to breast tissue in mice whose Twist proteins were suppressed by methylation thereby indicating that Twist proteins play a crucial role in cancer metastasis.