Clinical Pharmacology & Biopharmaceutics
ISSN: 2167-065X

Mini Review Open Access

Targeting Of Reactivation of Contact Inhibition for Cancer Treatment

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Abstract

Contact inhibition is the property of normal cell while in cancer cell they lost it and cell growth occurs uncontrollably and proliferate to other portions of body but if this process of contact inhibition can be reactivated in cancer cell they start to being controlled and after some time become the normal cell this article consist of some dependency factor which can results in reactivation of contact inhibition.

Introduction

The process in which normal cells stop dividing after being in touch with each other is termed as contact inhibition. During cancer this process of contact inhibition is not performed by the cells which results in unwanted growth.. So if a cell can maintain this contact inhibition again then uncontrolled division of cells (i.e. cancer) can be treated. For the contact inhibition majorly a trans membrane protein cadherin selectively epithelial cadherin is responsible. In cancer cells this E-cadherin loss results in the uncontrolled growth and loss of contact inhibition **[1]**. This E- cadherin encoded by CDH1 gene. Suppression of CDH1 gene also results in loss of contact inhibition. **[2]** So by increasing expression of CDH1 gene or increasing cadherin this process can be re-established and unwanted growth can be controlled.

Contact inhibition

The process of stopping the growth of cells after being in touch with each other is termed as contact inhibition and this is the major property of normal cells. But in the case of cancer cells this property is lost and results in the uncontrollable growth of cells. In this process there is major role of a trans membrane glycoprotein cadherin in the case of epithelial cells specially E-cadherin (i.e. epithelial cadherin).loss of E-cadherin results in the loss of contact inhibition.

E- Cadherin

E-cadherin belongs to the category of trans membrane glycoprotein present in epithelial cells which consist of two domains Extracellular and Intracellular respectively, extracellular domain is responsible for ca2+ dependent intracellular adhesions between epithelial cells and intracellular domain is responsible for internal cell signaling. These epithelial-cadherin glycoprotein also termed as uvomorulin**.** **[3]** expression of CDH1 gene results in the formation of these kind of proteins and they performs vital role in physiology of normal cell such as (i) cell adhesion,(ii) transmitting chemical signal within the cell,(iii) controlling cell maturation and movement,(iv) regulates cell growth by modulating proliferation dependent beta-catenin transcriptional activity**.[4]** these all functions are important for functioning of normal cell .if any of it alter directly or indirectly results in the disturbance of normal cell which leads to problem like unwanted growth as seen in the case of cancer.

E-cadherin and cell adhesion

The specialized adhesion junction between the epithelial cells formed by E-cadherin is called adherens junction (AJ).extracellular domain of cadherin engage in the Ca 2+-dependent hemophilic trans-interaction with similar cadherin molecules of adjacent cell, subsequently in intracellular domain there is binding of p120- and β-catenin proteins. This β-catenin interacts with α-catenin, which contains an action-binding domain and physically links AJ complexes to the actin cytoskeleton **[5,6]** these both intra and extracellular process results in strong adhesion of two epithelial cell. This leads to normal physiological functioning of cells (Figure 1).

External cell culture studies

In-vivo studies of cell culture shows that formation of a confluent cell monolayer results in clustering of cadherin-catenin molecules at the adherens junction. This clustering performs two major functions (i) strengthens cell-cell adhesion,(ii) provides sign for apical-basal cell polarization and influence the downstream signaling events **[7-9]** as per previous studies formation of a confluent cell monolayer results in stopping of cell cycle **[10]**. This phenomenon is known as "contact inhibition of cell proliferation". By restoring E-cadherin cell-cell adhesion increases leads to re-establishment of apical-basal cell polarity results in normalization of cancer cell and reactivation of process of

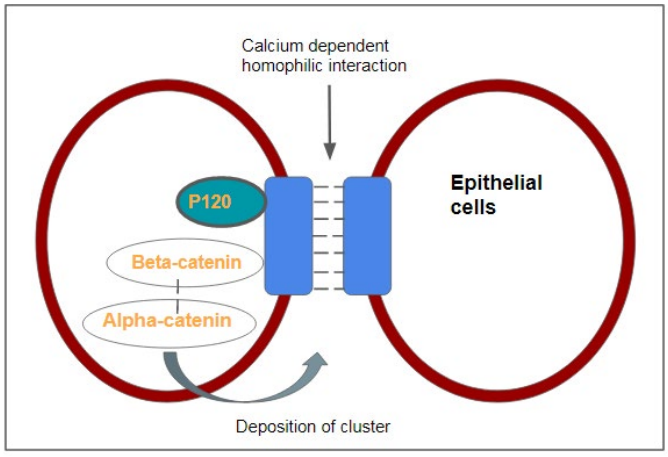

Figure 1: Calcium dependent homophilic interaction between two adjacent cadherin of epithelial cellsand deposition of catenin clusters to strong the bond between epithelial cells to increase cellular adhesion.

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Received: 21-Feb-2023, Manuscript No: cpb-23-90028; **Editor assigned:** 24-Feb-2023, Pre-QC No: cpb-23-90028 (PQ); **Reviewed:** 9-Mar-2023, QC No: cpb-23-90028; **Revised:** 13-Mar-2023, Manuscript No: cpb-23-90028 (R); **Published:** 17-Mar-2023, DOI: 10.4172/2167-065X.1000316

Citation: Nagi D, Dagar D (2023) Targeting Of Reactivation of Contact Inhibition for Cancer Treatment. Clin Pharmacol Biopharm, 12: 316.

contact inhibition. A negative impact of E-cadherin expression on tumor progression was also revealed in genetic mouse experiments *in vivo* **[11].**

Conclusion

The restoration of cadherin-catenin-mediated cell-cell adhesion results in prominent changes in cell morphology and re-establishment of apical-basal cell polarity, so we can target reactivation of contact inhibition can give some better results.

Future prospective

Targeting of reactivation of contact inhibition in cancer cells by the help of increasing cadherin protein results in establishment of normal functioning.

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