Disassembling a cancer puzzle: Cell junctions and plasma membrane as targets for anticancer therapy

Olga N. Shilova, Evgeny S. Shilov, André Lieber, Sergey M. Deyev

PII: S0168-3659(18)30424-3
DOI: doi:10.1016/j.jconrel.2018.07.030
Reference: COREL 9390

To appear in: *Journal of Controlled Release*

Received date: 17 March 2018
Revised date: 13 July 2018
Accepted date: 16 July 2018

Please cite this article as: Olga N. Shilova, Evgeny S. Shilov, André Lieber, Sergey M. Deyev , Disassembling a cancer puzzle: Cell junctions and plasma membrane as targets for anticancer therapy. Corel (2018), doi:10.1016/j.jconrel.2018.07.030

Disassembling a Cancer Puzzle: Cell Junctions and Plasma Membrane as Targets for Anticancer Therapy

Olga N. Shilova[1], Evgeny S. Shilov [2], André Lieber [3,4,5], Sergey M. Deyev *[1,2,6]

[1] Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences, Miklukho-Maklaya St., 16/10, Moscow, 117997, Russian Federation
[2] Faculty of Biology, Lomonosov Moscow State University, Leninskie Gory, 1/12, Moscow, Russian Federation, 119234.
[3] Division of Medical Genetics, University of Washington, Seattle, Washington, USA, WA 98195
[4] Department of Pathology, University of Washington, Seattle, Washington, USA, WA 98195.
[5] Compliment Corp., Seattle, Washington, USA, WA 98195.
[6] National Research Nuclear University "MEPhI", Institute of Engineering Physics for Biomedicine (PhysBio), Bio-Nanophotonic Lab., 115409 Moscow, Russia

*Corresponding author, e-mail: deyev.s@yandex.ru

Summary

Despite an enhanced permeability and retention effect typical of many solid tumors, drug penetration is not always sufficient. Possible strategies for the drug delivery improvement are a modification of the tumor cell-to-cell junctions and usage of cell membrane permeabilization proteins. In this review we discuss epithelial cell junctions as targets for a combined anticancer therapy and propose new possible sources of such agents. We suggest considering viral and bacterial pathogens disrupting epithelial layers as plentiful sources of new therapeutic agents for increasing tumor permeability for other effector agents. We also observe the application of pore forming proteins and peptides of different origin for cytoplasmic delivery of anti-cancer agents and consider the main obstacles of their use *in vivo*.

Key words: cell junctions, cancer, enhanced permeability, junction opener, pathogens, pore-forming toxins.

Introduction

1. Major types of epithelial cell junctions

Cell junctions are very important membrane protein complexes associated with cytoskeleton, which provide integrity of tissues and play a significant role in the intercellular communication. According to their functions, junctions of animal cells can be classified into three groups [1]. One group named 'anchoring junctions' includes desmosomes, adherence