Leukocytes and drug-resistant cancer cells are targets for intracellular delivery by adenoviral dodecahedron

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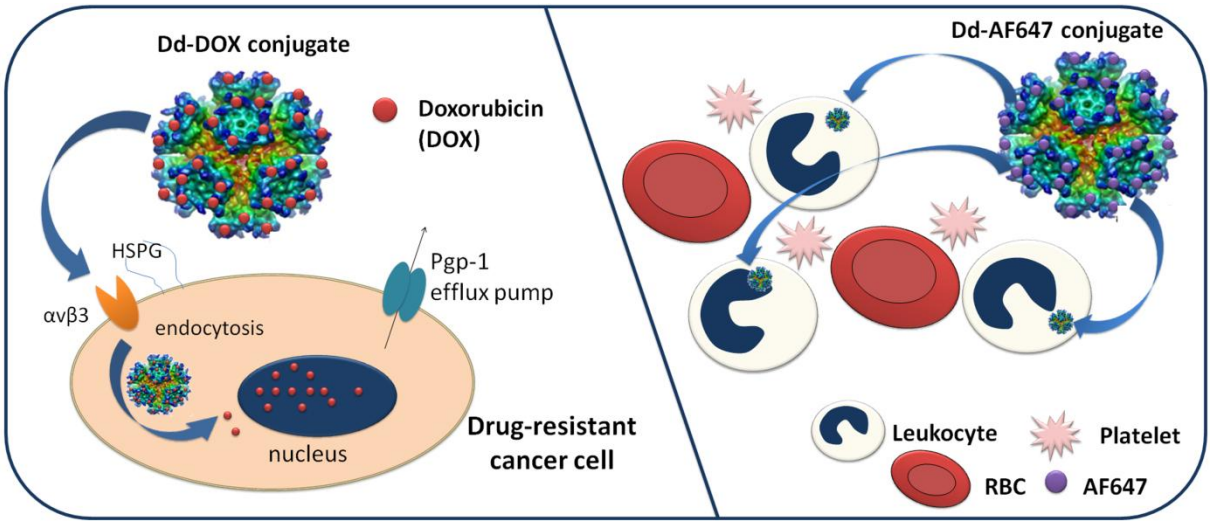
Virus-like particles (VLPs) are an attractive alternative to chemically synthesized nanoplatforms in development of novel carriers for targeted drug delivery. Adenoviral dodecahedron (Ad Dd), the symmetrical, small (28 nm) and non-infectious VLP, endowed with extraordinary ability for intracellular penetration through the receptor-mediated endocytosis followed by escape from the endosomes before reaching lysosomes. This results in cytoplasmic delivery of cargo molecules in a functional form. The chemical and genetic modifications allow for covalent attachment of cargo molecules or their insertion into particle structure without disrupting VLP integrity or penetration properties. The usefulness of Dd as a carrier for conjugated small molecules was already proven by targeted delivery of anticancer agents to hepatocellular carcinoma tumor in animal model, leading to inhibition of tumor growth.

In the presented study we analyzed delivery of doxorubicin conjugated to Dd (Dd-DOX). It was assessed in multidrug-resistant (MDR) human uterine sarcoma MES-SA Dx5 cells. The results of cytotoxicity tests attested the ability of Dd for circumvention of the P-glycoprotein 1 - mediated multidrug resistance mechanism. We demonstrated that efficient uptake of Dd-DOX conjugate in MDR cells leads to accumulation of drug in cell nucleus and significantly enhances doxorubicin cytotoxicity against target cancer cells.

Furthermore, we demonstrated distinct Dd transduction efficiency for white blood cells, that could lead to the use of this vector for the transport of active molecules targeting leukocytes, in particular for *in vitro* testing of potential anticancer agents intended to treat leukaemia. The suitability of Dd for such application is supported by the lack of cytotoxicity of VLP in human peripheral blood mononuclear cells.

This work was supported by the National Science Centre (Poland) decision DEC-2013/09/B/NZ3/02327 and in part by Association Espoir Isere Contre Le Cancer and by association Gefluc Grenoble Dauphiné-Savoie.

Keywords: Adenoviral dodecahedron, drug delivery, drug resistance, virus-like particle



Professional Biography

Ewa Szolajska (Ph. D) an Assistant Professor at Institute of Biochemistry and Biophysics Polish Academy of Sciences (IBB PAS) Warsaw, Poland, is a Group leader in the Department of Protein Synthesis and Chief of Cell Culture Laboratory at IBB PAS. She got her Doctor's degree and habilitation in Biochemistry from IBB PAS. Currently Dr. Ewa Szolajskas' research focus on the development of an adenovirus derived virus-like particle as an intracellular delivery vector for the therapeutic applications.



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