Nanotech drug smugglers

November 12 2013

Tiny capsules of carbon are invisible to the chemical gatekeeper that flushes potentially harmful substances out of our bodies' cells, according to research published in the *International Journal of Computational Biology and Drug Design*. The finding might allow a pharmaceutical to be smuggled into cells even when multidrug resistance has evolved.

Sergey Shityakov and Carola Förster of the University of Würzburg, Germany, explain that the protein, P-glycoprotein, acts as a gatekeeper, flushing out potentially harmful chemicals that enter the body as well as the naturally-occurring products of metabolism. The protein thus plays a vital role in the health of the cell. Unfortunately, it is a strong modulator of chemical traffic across the cell membrane that it can also prevent therapeutic agents from working properly, flushing them out as if they were simply harmful compounds. This process underpins the emergence of multidrug resistance in several diseases, including various forms of cancer.

Shityakov and Förster have revealed recently that if there were a way to mask the presence of the therapeutic agent, later the gatekeeper would not see them as "unwanted molecular entities" to be eradicated, and therefore, these drugs might be able to carry out their job unhindered and so overcome drug resistance. However, some of the chemical substances have turned to the realm of nanotechnology, and in particular, tiny capsules of carbon atoms known as fullerenes and the related molecules, the carbon nanotubes. The latter synthetic materials are not recognized by P-glycoprotein and so can penetrate lipid membranes moving freely in and out of cells.

The team has investigated whether it might be possible to carry drug molecules inside these nanocapsules so that they are unimpeded by interactions with P-glycoprotein or other receptors. They used high-power computational techniques to demonstrate that carbon nanotubes are not able to "dock" with the gatekeeper protein. Moreover, their analysis of the binding energy needed to push a nanotube into P-glycoprotein shows that the process is unfavourable and so rather than "docking" with this gatekeeper protein these peculiar materials are repelled by it to maintain the interior of the cell and so have the potential to act as a molecular drug smuggler.

More information: "Multidrug resistance protein P-gp interaction with nanoparticles (fullerenes and carbon nanotube) to assess their drug delivery potential: a theoretical molecular docking study" in *Int. J. Computational Biology and Drug Design*, 2013, 6, 343-357, DOI: 10.1504/IJCBDD.2013.056801

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