Design of anticancer drug-transport-nanodevices and a model for their interaction with proteins overexpressed in neoplastic cells

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Cancer is a cellular disease that is caused by damaged genes leading to indefinite cellular multiplication, overexpression of specific proteins (as protease *KLK5*[1]), and disruption of the normal cell death process. It is the cause of thirteen percent of deaths worldwide.[2] To treat this disease today there are several drugs that are used for the so-called chemotherapy treatment.[3] These drugs are nonspecific and kill both diseased and healthy cells. Therefore, there is a need for the development of anticancer drugs with more specific delivery and less toxicity. With this aim, there are currently several proposals of nanodevices that may be used for transport and selective drug delivery.[4] Among these kind of devices the use of carbon nanotubes (CNT), which are responsible of carrying in a more specific way the drug to neoplastic cells, has been proposed.[5] To obtain CNT more biocompatible and soluble in a physiological environment there are several proposals and probes (*in vivo*[6] and *in silico*[7]) for the functionalization of these CNT.

In the present work, we have computationally designed a plausible family of anticancer drug-nanodevices, using single wall carbon nanotubes (SWCNT) functionalized with triethylene glycol diamine (acting as a drug-SWCN linker), conjugated to cisplatin derivatives. These nanodevices exhibit better apparent solubility than the free anticancer drug derivatives of cisplatin.[8] Furthermore, we suggest the plausible interaction of this type of nanodevices with proteases overexpressed in neoplastic cells and a possible mechanism of drug delivery through a serin-proteases reaction mechanism.[9,10] In our study we start with a model of the active site of *KLK5* and subsequently make use of multiscale models towards the full protein system. At the moment we have obtained the path of reaction of the first step of serine proteases, using a model system (m1) and a real-model system (rm1), corroborating the presence of two transition states and a tetrahedral intermediary as proposed in previous studies.

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