Summary

**Background:** In drug design, one may be confronted to the problem of finding hits for targets for which no small inhibiting molecules are known and only low-throughput experiments are available (like ITC or NMR studies), two common difficulties encountered in a typical academic setting. Using a virtual screening strategy like docking can alleviate some of the problems and save a considerable amount of time by selecting only top-ranking molecules, but only if the method is very efficient, i.e. when a good proportion of actives are found in the 1-10 % best ranked molecules.

**Results:** The use of several programs (in our study, Gold, Surflex, FlexX and Glide were considered) shows a divergence of the results, which presents a difficulty in guiding the experiments. To overcome this divergence and increase the yield of the virtual screening, we created the standard deviation consensus (SDC) and variable SDC (vSDC) methods, consisting of the intersection of molecule sets from several virtual screening programs, based on the standard deviations of their ranking distributions.

**Conclusions:** SDC allowed us to find hits for two new protein targets by testing only 9 and 11 small molecules from a chemical library of circa 15,000 compounds. Furthermore, vSDC, when applied to the 102 proteins of the DUD-E benchmarking database, succeeded in finding more hits than any of the four isolated programs for 13-60 % of the targets. In addition, when only 10 molecules of each of the 102 chemical libraries were considered, vSDC performed better in the number of hits found, with an improvement of 6-24 % over the 10 best-ranked molecules given by the individual docking programs.
**Design of an amphiphilic porphyrin exhibiting high in vitro photocytotoxicity**


**Summary**

A porphyrin monosubstituted by three triethyleneglycol chains grafted on a pentaerythritol skeleton was designed to display an optimized amphiphilicity for an enhanced cellular uptake and thus to exert enhanced photocytotoxicity. This porphyrin proved to be an excellent photosensitiser with submicromolar IC50.

**Year of publication** 2015

Rawand Masoud, Tania Bizouarn, Sylvain Trepout, Frank Wien, Laura Baciou, Sergio Marco, Chantal Houée Levin (2015 Dec 29)

**Titanium Dioxide Nanoparticles Increase Superoxide Anion Production by Acting on NADPH Oxidase.**

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**Summary**

Titanium dioxide (TiO\textsubscript{2}) anatase nanoparticles (NPs) are metal oxide NPs commercialized for several uses of everyday life. However their toxicity has been poorly investigated. Cellular internalization of NPs has been shown to activate macrophages and neutrophils that contribute to superoxide anion production by the NADPH oxidase complex. Transmission electron microscosopy images showed that the membrane fractions were close to the NPs while fluorescence indicated an interaction between NPs and cytosolic proteins. Using a cell-free system, we have investigated the influence of TiO\textsubscript{2} NPs on the behavior of the NADPH oxidase. In the absence of the classical activator molecules of the enzyme (arachidonic acid) but in the presence of TiO\textsubscript{2} NPs, no production of superoxide ions could be detected indicating that TiO\textsubscript{2} NPs were unable to activate by themselves the complex. However once the NADPH oxidase was activated (i.e., by arachidonic acid), the rate of superoxide anion production went up to 140% of its value without NPs, this effect being dependent on their concentration. In the presence of TiO\textsubscript{2} nanoparticles, the NADPH oxidase produces more superoxide ions, hence induces higher oxidative stress. This hyper-activation and the subsequent increase in ROS production by TiO\textsubscript{2} NPs could participate to the oxidative stress development.