Setting a procedure for "in silico" evaluation of immunoconjugates for cancer therapy

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Motivation

A considerable effort is currently applied to the conception and validation of computational methods for predicting biopharmaceutical properties of new drugs. It is expected that they will accelerate the whole process of drug discovery either by the rational optimization of therapeutics candidate or by permitting the rapid exclusion of the poor ones. Therapeutics immunoconjugates consists of a specifically tumor-targeting engineered antibody covalently linked or chelated to a toxic molecule. Their use to selectively deliver drugs to tumor caused great expectations initially disappointed. Recently, the first immunoconjugate has been approved by the Food and Drug Administration (FDA). We have used a computational approaches to investigate some biochemical characteristics of immunoconjugates.

Methods

We used an immunoconjugate consisting of scFv antiHer2 (FRP5) covalently linked to the etoxinA from Pseudomonas aeruginosa as a model system. The tridimensional structure of this immunoconjugate was not available and was obtained by homology modelling. The evaluation of structural characteristics related to biochemical properties will be carried out using molecular dynamics.

Results

We attempt to evaluate some properties as solubility, stability, toxicology of the molecule. We have also used the same procedure to model a second immunoconjugate consisting of scFv antiHer2 (scfv800E6) covalently linked to the same toxin. A comparison between the two models has been carried out.

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