New antitumor Ru-based compound derivatives optimized using *in silico* methods

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Cancer has become one of leading causes of death around the globe, with female breast cancer as one of the most prevalent. Among the multiple types of breast cancer (BC) identified to date, the triple-negative (TN) subtype (lacking expression of estrogen and progesterone receptors and human epidermal growth factor receptor 2) is associated with higher aggressiveness and poor prognosis[1]. TNBC lacks targeted therapies and presents heterogeneous responses to treatment with traditional cisplatin-like drugs, in part due to the development of multidrug resistance (MDR). TM34 is a Ruthenium-based compound that has been suggested to be a more efficient and selective therapy than cisplatin[2]. More recently, new derivatives of TM34 have been developed with increased selectivity by adding peptide sequences that are recognized by receptor proteins from the FGFR family[3].

The main goal of this work is to study the interaction of several TM34 derivatives with a membrane model (POPC) and to calculate their membrane crossing energy profiles that can be used to estimate the membrane permeability coefficients. We used Molecular Dynamics simulations coupled with an Umbrella-sampling scheme to obtain the potential of mean force profiles, which allowed the calculation of the membrane permeability using the inhomogeneous solubility-diffusion model[4].

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