Ring Around the Rocuronium

Sugammadex Encapsulation Explained BIT by BIT

Why

The final sugammadex-rocuronium structure is known, but not how the binding process dynamically occurs. Irani *et al.* hypothesized that rocuronium enters the sugammadex molecule's primary face *via* a positive-negative charge attraction.

What

The simulated center-of-mass distance was used to quantify the association between rocuronium and sugammadex. The strength of association was estimated using relative binding free energy over the last 3 ns of 5 ns simulations.

How

Molecular dynamics modeling was used to visualize the dynamic encapsulation process, which required quantum mechanical characterization of the molecular structures and movement based on intermolecular forces.

Results

Rocuronium has an initial stage of weak binding with the secondary face of sugammadex *via* intermolecular hydrogen bonds, which is opposite to the side hypothesized. It subsequently establishes energetically stable encapsulation.

Validation

Simulation-derived relative binding free energies between various drugs and sugammadex were compared to published, *in vitro*-derived association constants. A bilogarithmic correlation was found, validating this methodology

Who

Drug development can be improved with *in silico* methods, *i.e.*, using computer modeling.[1] In this issue of Anesthesiology, Irani *et al.* use molecular simulation to study sugammadex pharmacology.[2]

ns, nanosecond.

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1. Bertaccini EJ: Anesthesia, coming of age in the world of modern in silico drug design. Anesthesiology 2023; 138:129–31
2. Irani AH, Voss L, Whittle N, Sleigh JW: Encapsulation dynamics of neuromuscular blocking drugs by sugammadex. Anesthesiology 2023; 138:152–63