Development and in vitro Verification of a Polymersome for Blood-Brain Barrier Transport Through a Novel Machine Learning Model

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Across neurological drug development, researchers struggle with the inability of most drugs to pass through the blood-brain barrier (BBB), due to the semipermeable membrane's high selectivity. As such, drug treatment of Alzheimer's, Parkinson's, brain cancer, and strokes remains difficult. Recent research identified polymersomes (polymer-based vesicular shells) as an avenue for transport of otherwise non-BBB-permeable drugs across the BBB. However, the number of discovered BBB-traversing polymersomes remains low, and they are not able to carry all drugs. This research developed a machine learning model to identify likely polymer candidates for polymersomic drug-delivery across the BBB. The model was programmed in Python using TensorFlow and trained on 7,807 molecules from the B3DB-database. It achieved 93% accuracy and identified 13 encapsulation candidates. The top candidate for BBB permeability, ammonio methacrylate (AM), had never been considered for BBB permeability before. To validate the model, a polymersomic nanoparticle (AM-DOX) was developed by encapsulating doxorubicin (DOX, an anti-tumor drug) with AM, for eventual passage across an in-vitro BBB model (parallel artificial membrane permeability assay). 500μM-DOX and 500μM-AM-DOX were separately introduced to the BBB model for 24 hours at 37 degrees Celsius. While DOX was predictably unable to penetrate the BBB, the AM-DOX nanoparticle successfully passed, producing an equilibrium 250μM concentration surrounding the barrier, which was validated via UV-Vis and ATR-FTIR spectroscopies. These results provide compelling evidence for a new, effective BBB-encapsulation polymer, identified via machine learning, to deliver treatments for a wide array of neurological disorders.

Awards Won:

Second Award of $2,000