

Optical Spectral Fingerprinting Enables Sensitive Detection of Anthracycline Chemotherapeutics in Synthetic Clinical Biofluids

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Anthracycline chemotherapeutics are highly effective at eliminating cancerous cells but are also known to negatively affect healthy cells. Cardiotoxicity is one of the most severe side effects of their administration, as they accumulate in healthy cardiac tissue. The inability to continuously monitor their accumulation in a rapid and non-invasive manner presents a challenge in the therapeutic drug monitoring of anthracyclines and cardiotoxicity development. While there are established guidelines for dosing and administration of anthracyclines, high interpatient variability and variable pharmacology make it difficult to gauge the proper dosing of the drug while balancing the onset of severe side effects. To reduce this risk and understand the pharmacology of anthracyclines, we developed fluorescent sensors using single-walled carbon nanotubes (SWCNT) to rapidly and continuously monitor the drugs in a concentration dependent manner. SWCNT have independent excitation and emission wavelengths, which give rise to the different structures on their surface. Dispersing SWCNTs with single-stranded DNA allows SWCNT to be solubilized while also promoting interactions with anthracyclines. We evaluated the sensor constructs in our chemical sensing library by evaluating both their binding kinetics and classifications using both supervised and unsupervised machine learning models.

The chemical library consisted of multi-species SWCNT (referred to as (n,m)) dispersed with 12 ssDNA sequences. Each construct was tested against 4 anthracyclines at 7 different concentrations, with spectral responses collected in both buffer and synthetic biofluid conditions. The binding kinetics were first evaluated using a non-cooperative binding model where the dissociation constant provided insight on the ideal ssDNA- (n,m) pairing, along with the type of fluorescence modulation. Supervised machine learning models were also evaluated on their ability to properly classify anthracyclines by type. The eXtreme Gradient Boosting model, which exhibited 100% test classification accuracy, was further analyzed by calculating Shapely Additive Explanation (SHAP) values to determine specific ssDNA, (n,m) , and fluorescence modulation driving specific categorizations. Finally, principal component analysis (PCA) was used to classify responses according to concentration, and PC score rankings provided the necessary information for sensor selection. We developed here a generalizable methodology for sensor development for analytes with no biological recognition element, which overall expedites the process of sensor discovery to develop translatable, point-of-care platforms.