Progressing towards high-sensitivity Cardiac Troponin I sensors using molecularly imprinted polymers

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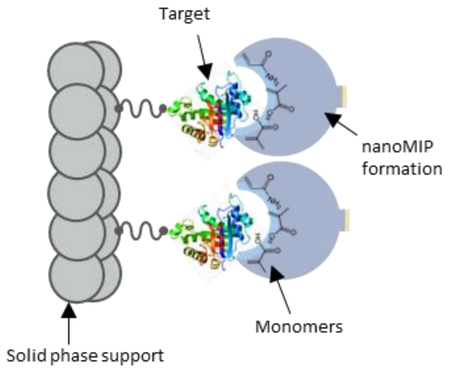
Background

Cardiac Troponin (cTn) is the preferred biomarker for the possible diagnosis of acute myocardial infarction (AMI). There are several clinical analysers on the market with high sensitivity assays for cardiac Troponin I (hs-cTnI) or cardiac Troponin T (hs-cTnT). These assays can detect cTn where the level of cTn is close to the upper reference limit (URL), i.e., the 99th percentile reference value. However, cTn assays on point-of-care devices that could be used at the bedside are yet to reliably reach the same levels of sensitivity. Nanoscale molecularly imprinted polymers specific to cTnI have been developed and integrated into a sensor platform to support progress towards hs-cTnI testing in a point-of-care device, with inherent stability that could enable the potential for screening outside of the emergency room in clinics and local doctor's offices.

Methodology

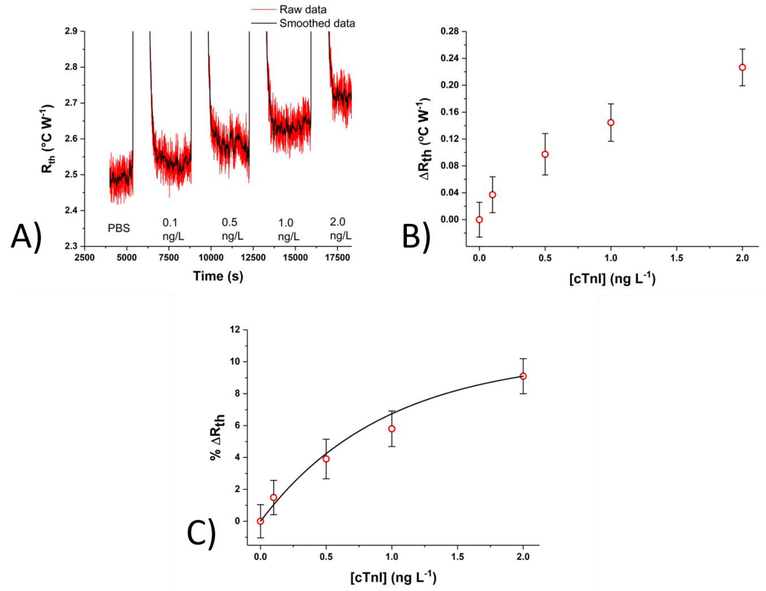
nanoMIPs were synthesized by a process in which a peptide specific to a region of cTnI was immobilised on a solid phase, monomers and cross-linker were added, controlled polymerisation was initiated and nanoMIPs with high affinity for Troponin I were eluted. The nanoMIPs were covalently coupled to an electrode surface and integrated into sensor platform that relies on monitoring the thermal resistance (R_{th}) at the solid-liquid interface. Sensor sensitivity was tested in spiked PBS buffer and testing in serum samples is due to follow. The nanoMIPs have also been autoclaved to 121°C and re-tested to demonstrate temperature stability.



MIP production

nanoMIP imprinting demonstrating the polymerisation step of the production process.

Sensor Results



A) Typical raw and smoothed heat-transfer method data (R_{th} vs time) for the nanoMIP-functionalised SPE prepared via electrografting upon exposure to PBS containing 0.1-2 ng L^{-1} of cTnI. The smoothed data was obtained by a 50-point percentile filter.

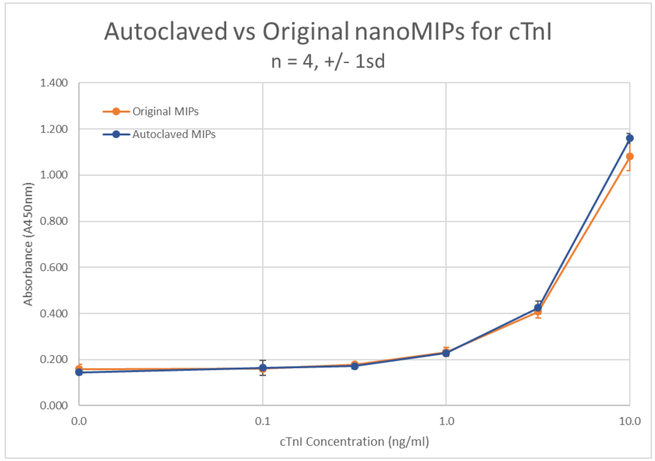
B) Corresponding scatter plot showing the change in R_{th} for the addition of cTnI in PBS.

C) Corresponding dose-response curve (R^2 = 0.98).

A Limit of Detection (LoD) of 0.46 ± 0.07 ng L^{-1} was achieved for the sensor which places the capability of this this sensor platform in the ultra-high sensitivity category and is superior to the vast majority of cTnI tests currently available for use in the point-of-care setting.

Thermal Stability

COVID nanoMIPs have excellent stability. The ELISA data below is from nanoMIPs pre- and post-autoclave (121°C, 15 minutes approx.). As evidenced, the ELISA results are consistent (within experimental error) and this level of stability will lead to a very long shelf-life.



Conclusions

nanoMIPs specific to cardiac Troponin I have shown to perform in a sensor platform both selectively and with a high sensitivity of circa 0.5 pg/ml cTnI. They have also shown to withstand extreme temperatures, indicating a long shelf life and the ability to be stored and used in a point-of-care setting.

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To discuss collaboration opportunities, please contact Alan Thomson at enquiries@mip-dx.com