Daniel Chan, J Chromatogr Sep Tech 2017, 8:3(Suppl)
DOI: 10.4172/2157-7064-C1-026

Fragment screening against the EthR-DNA interaction by native mass spectrometry

Daniel Chan
University of Cambridge, UK

Native nanoelectrospray ionization mass spectrometry is an underutilized technique for fragment screening. In this study, the first demonstration is provided of the use of native mass spectrometry for screening fragments against a protein-DNA interaction. EthR is a transcriptional repressor of EthA expression in *Mycobacterium tuberculosis* (Mtb) that reduces the efficacy of ethionamide, a second-line anti-tubercular drug used to combat multidrug resistant Mtb strains. A small-scale fragment screening campaign was conducted against the EthR-DNA interaction using native mass spectrometry, and results were compared with those from differential scanning fluorimetry, a commonly used primary screening technique. Hits were validated using surface plasmon resonance and X-ray crystallography. The screening campaign identified two new fragments that disrupt the EthR-DNA interaction *in vitro* (IC_{50}=460 μM to 610 μM) and that bind to the hydrophobic channel of the EthR dimer.

Biography

Daniel Chan is a PhD student at University of Cambridge under the supervision of Professor Chris Abell and Dr. Dijana Matak-Vinković. His project involves the application of native mass spectrometry techniques to fragment-based drug discovery. He has previously worked as a Research Assistant under Dr. Dik-Lung Ma at Hong Kong Baptist University and Dr. Chung-Hang Leung at University of Macau. He completed his BSc (Honours) at University of New South Wales under Professor Naresh Kumar and Professor David and Black and his BSc (Advanced Science) at University of Sydney.

dshc2@cam.ac.uk

Notes: