Project Title: Electrochemical Point-of-Care Cerebrospinal Fluid Detection
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Cerebrospinal (CSF) fluid leaks, or clear fluid surrounding the brain and spinal cord persistently leaking out of defects in the bones bordering the nose, sinuses, and ear, if left untreated, may lead to severe and potentially life-threatening intracranial infections. Accurate and timely diagnosis of CSF leak can be challenging, and consequences of misdiagnosis or delayed diagnosis may be grave. Current standard of diagnosis requires sending samples to an outside laboratory and waiting 4-7 days for results, which may not be completely reliable depending on sample contamination (e.g., co-presence of blood or dilution by mucus/secretions). When faced with an urgent decision, clinicians attempt to diagnose CSF leaks using a combination of clinical history and exam, imaging findings, and high index of suspicion, but false positive or negative diagnoses are nevertheless possible. As such, this project aims to utilize cutting-edge electrochemical technology in developing a point-of-care "lab-on-a-chip" diagnostic tool for early and accurate detection of beta-2 transferrin (β2TF) which is a CSF-specific protein. Following β2TF filtration via sialic acid-dependent antigen-antibody formation, the CSF-specific protein will bind to customized β2TF-specific aptamers at the end of the channel, causing a conformational change in the aptamer which produces electrical energy and this delta current can be detected with sensors. This method will theoretically allow exceptionally high sensitivity and specificity due to the digital nature of the data, as well as the utilization of our chip shrinkage technology which will dramatically increase surface area-to-volume ratio, allowing a high antibody and aptamer volume resulting in more accurate filtration and detection. This will also allow instantaneous processing and eliminate need for laboratory equipment or skilled professionals for function. The premise of this project will significantly improve on the current CSF detection field in three key areas: 1) High sensitivity and specificity even in the presence of contamination, 2) Instantaneous and simple point-of-care detection without need for mailing or preprocessing samples, or relying on trained specialized providers, 3) Requiring <15 minutes of processing and <200 uL of sample, which are substantially lower than what the traditional method requires. With UC Irvine Institutional Review Board approval already attained, we have access to abundant CSF-suspected samples as well as the ability to collect new ones from future patients. De-identified human samples will be transferred to our BSL-2 rated Biomedical Engineering laboratory for testing on our developing and continuously evolving device prototype. In order to detect CSF even when contaminated, we will use a variety of different CSF samples (e.g., pure, mixed with blood, nasal/otic discharge of normal patients) for testing our detection assays. The primary outcome variable of this project will consist of accurately detecting the presence of β2TF within CSF samples regardless of contamination. Our aim to develop a device prototype that can accurately detect CSF with high specificity is directly translational and clinically significant for patient care. Our multidisciplinary expert team, proven record in point-of-care technology, and access to abundant CSF samples enables us to complete this project in a 12-month period.