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Emerging Translational Research Methods: A Sampling

It's hardly news that new genomic technologies are more precisely characterizing microbes, plants, humans for the purpose of understanding disease mechanism, identifying causes of pathologies, improving clinical care, prevention and ultimately public health, in its broadest sense. Innovations in identification techniques, along with bioinformatics tools are enabling faster and more accurate identification of genetic/genomic elements that play vital roles in the development of disease.

The articles in this issue present novel innovative technologies that demonstrate improvements over conventional tools and thus represent significant steps forward in more accurate identification. The first paper, 'Identification and Conformational Analysis of Putative microRNAs in Maruca vitrate (Lepidoptera: Pyralidae' describes the in silico identification of 13 putative micro RNAs in M. vitrate, which is an important crop pest insect. Habeeb and Sureshan's demonstrate that the sequence composition can influence the stem-loop hairpin structure of pre-miRNAs, which can affect the location of binding enzymes. They suggest that these identified miRNAs can be potentially useful in effective pest management. The second paper "Developmental neurotoxic effects of Malathion on 3D neurosphere systems' addresses two limitations in translational CNS research, namely that available animal models do not cover the whole spectrum of CNS development periods, including but not limited to the fact that putative toxicants cannot be identified and confirmed with certainty. Mohamed et al, present a novel method for predicting neurotoxic effects. Using Malathion, an organophosphate pesticide with suggested neurotoxic affects on nursing children, the authors report a novel in-vitro system that recapitulates the changes occurring during early brain development and thus can serve as an improved model for predicting the development of neurotoxic effects. They demonstrate the abstract developmental neurotoxicity (DNT) effects on of Malathion on 3D neurospheres system model and present a detection method that overcomes the limitations of conventional techniques used in 3D neurospheres. A considerable challenge in advancing translational genomics is determining which of several alternative methods is superior for a particular inquiry. The next two articles address this issue as applied to identification and diagnosis of neurological pathology in epileptic and neuromuscular disorders. In 'Comparison of two next-generation sequencing kits for diagnosis of epileptic disorders with a user friendly tool for displaying gene coverage, DeCovA', Lesca et al compare two commonly-used targeted capture techniques for next generations sequencing libraries, two softwares for variant analysis and the development of their novel tool DeCovA for displaying coverage and depth data. Their study demonstrates that neither of the commonly used Next Gene and Ion Reporter could identify all the known mutations/CNVs. Their tool, DeCovA showed that detection failure was primarily due to insufficient coverage. DeCovA may be useful, therefore, to diagnostic laboratories. Gorokhova and colleagues present a novel targeted exome approach, MyoPanel2, designed to optimize clinical diagnosis of neuromuscular disorders. Analyzing 306 genes known to be mutated in myopathies and related disorders, MyoPanel2 demonstrates a 98.8 target sequence coverage at 20x and 99.7% detection of 11,467 know mutations responsible for neuromuscular disorders. Their results suggest that targeted exome sequencing may be an efficient clinical diagnostic method for most neuromuscular disorders. In 'Highly sensitive, non-invasive detection of colorectal cancer mutations using single molecule third generation sequencing', Russo et al present a novel method for a non-invasive and highly sensitive assay for population screening for colorectal cancer and early stage adenomas that lead to CRC. This is the first study that applies high read accuracy and depth of single molecule, real time, circular consensus sequencing (SMRT-CCS) to the detection of mutations in stool DNA in order to provide a non-invasive, sensitive and accurate test for colorectal cancer. In stool DNA isolated from patients with adenocarcinoma, researchers detected mutations at frequencies below 0.5% and with no false positives. The proposed method suggests an important advancement in light of the fact that none of the numerous non-invasive CRC screening methods attempted over the past twenty years have been established. Finally, in 'Application of Smart Infrastructure Systems Approach to Precision Medicine', Govindaraju and Annaswamy propose a novel systems approach to precision medicine which can accomplish the need to incorporate multiple modalities of human variation data. The SIS is a broad trans-disciplinary approach that represents an advance over current approaches in that it manages complex networks on non-linear adaptive controls while also takes into account antecedent and attendant aspects of health and disease. In other words, the SIS can integrate all features of complex variation amongst populations, families and individuals, combining different factors such as genomics, tissues, exposure, migration data, while being integrated, adaptive, reactive, predictive and optimized. The conceptual basis and mathematical foundation of the SIS are laid out.

Together, these articles provide a window into some of the many technological challenges to advancing translational research and diagnostic tools, while displaying successful new approaches overcome specific limitations in conventional techniques. We welcome your thoughts as Letters to the Editor.

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