



Complementary Diagnostics for Infectious Disease

Highly Efficient Sample Preparation Permitting an Ultrasensitive and Early Detection of Pathogens to Improve Surveillance and Outbreak Management as Well as Therapeutic Monitoring of Infectious Diseases

Jean-Paul Gonzalez, Centaurus Biotech

Katie Edwards, CUBRC

Venkat Rao, Parsons

Francisco Veas, Centaurus Biotech

Along with specificity, one of the most challenging requests for pathogen detection is sensitivity. Indeed, the detection baseline of a diagnostic test appears often questionable and never totally controlled, principally due to low pathogenic load and/or the presence of interfering compounds of biological samples (human, animal, environmental). The recent and ongoing large outbreaks of high consequence pathogens (HCP) including Zika, Chikungunya, Ebola, Cholera, illustrate an increasing need for early and sensitive pathogen detection (including for contact tracing purposes). Thus, ultrasensitive diagnostic approaches are mandatory to overcome false-negative diagnoses due to low pathogen load or interferent molecules generated from current diagnostic strategies, to detect threatening subclinical infections related to incubation period, convalescence, and/or asymptomatic carriers. The present proposal aims to develop such a complementary agnostic pathogen concentration sample preparation to drastically enhance their detection to generate, when possible, early diagnoses (including the pre-clinical phase), to adopt both the earliest possible the patient monitoring and therapeutic management and contribute to outbreak. Centaurus biotech and its ApoH-Technology partner have a unique technology and expertise in the field of sample preparation promoting a unique fashion to capture and concentrate any microorganisms from any biological sample improving the sensitivity behind previous traditional baseline of any conventional (molecular or immune) or non-conventional detection method. This is a proven pathogens agnostic concentration platform-designed technology applicable to any kind of pathogen for their ultrasensitive detection/identification. Soon upon a homeostasis disruption (e.g. trauma, infection) the innate acute phase immune response is rapidly activated involving more than one hundred proteins, including the sensor/scavenger apolipoprotein H (ApoH). We have discovered that ApoH binds pathogens (viruses, bacteria, fungi, prions) with very high affinity. The structure-activity of ApoH protein includes five stable and flexible domains able to interact with different motifs of pathogen microorganisms through diverse types of associations with negatively-charged domains, conformational proteins, glycoproteins and negatively-charged phospholipids, present at least at the surface of pathogens. Specific buffers and ApoH-coated paramagnetic beads have been developed to capture and cleanse pathogens from complex samples to allow ultrasensitive (low and/or early) pathogen detection by increasing viral particle PCR-detection of one to two logarithms or detect one bacterium in five milliliters of whole blood. This have been established and proven for a variety of microbes including Ebolavirus, Dengue viruses, HERV, Hepatitis virus, norovirus, - bacteria (sepsis) Gram + or Gram -, Vibrio cholerae, Salmonella, E. coli, multi-resistant bacteria. Altogether, these results show that ApoH is a unique powerful concentrator and useful tool for In Vitro Diagnostic purposed used as a sample preparation system to cleanse and concentrate pathogens permitting a real ultrasensitive and rapid diagnosis, prompting adapted therapeutic guidance for patient management and/or outbreak containment. This unique ultrasensitive detection platform technology can be easily adapted for both point of care and point of need to protect the populations and Warfighter by enabling the development of agnostic, pre-symptomatic diagnostic platform for infectious diseases.