2020 vision of vaccines for malaria, TB and HIV/AIDS

May 25 2011

Collectively, malaria, TB & HIV/AIDS cause more than five million deaths per year – nearly the entire population of the state of Washington – and represent one of the world's major public health challenges as we move into the second decade of the 21st century. In the May 26, 2011, edition of scientific journal *Nature*, Seattle BioMed Director Alan Aderem, Ph.D., along with Rino Rappuoli, Ph.D., Global Head of Vaccines Research for Novartis Vaccines & Diagnostics, discuss recent advances in vaccine development, along with new tools including systems biology and structure-based antigen design that could lead to a deeper understanding of mechanisms of protection. This, in turn, will illuminate the path to rational vaccine development to lift the burden of the world's most devastating infectious diseases.

According to Aderem, a systems biology pioneer who recently joined Seattle BioMed to incorporate that approach with the Institute's infectious disease research, new conceptional and technological advances indicate that it will be possible to develop vaccines for the "big three" infectious diseases within the next 10 years. "Success will be largely dependent on our ability to use novel approaches such as systems biology to analyze data sets generated during proof-of-concept trials," he explained. "This will lead to new insights such as the identification of correlates of protection or signatures of immunogenicity and the acceleration of large-scale clinical trials." Aderem added that innovative, new clinical and regulatory approaches will also accelerate the pathway to much-needed vaccines.

The article discusses the strengths and criticisms of the systems biology approach, with the key strength of the approach lying in its ability to capture and integrate massive amounts of biological data to visualize emergent properties that are not demonstrated by their individual parts and cannot be predicted from the parts alone. "The power of systems biology comes from its capacity to predict the behavior of an entire biological system," Aderem said. "From there, we can optimize vaccine candidates and predict whether a drug or vaccine candidate can work before it moves into large scale, very expensive clinical trials."

Systems biology can also be used to speed the often lengthy clinical trial experience. Aderem and Rappuoli estimate that in trials of new vaccines for malaria, TB and HIV/AIDS, only one hypothesis has been tested every eight years in the past three decades. "We cannot afford this approach if we want to have an impact on disease in a reasonable timeframe," Aderem said. "We can accelerate clinical development by performing more efficacy trials and by improving their design using systems biology approaches to test several hypotheses in parallel and having an adaptive design to expand the outcomes that prove most promising."

Aderem and Rappuoli also debunk one of the key criticisms of systems biology – that it is overly reliant on computation. "Much of this comes from a misunderstanding on the role of computers in systems biology," Aderem explained. "Computers are not expected to come up with biological insights from the outset, but are meant to facilitate an integration of discovery science with hypothesis-driven science to yield a holistic description of a biological system."

While progress has been made over the past few years in the development of novel vaccines against the three most challenging infectious diseases in the world, Aderem and Rappuoli conclude that innovative design of clinical trials, testing several vaccines in parallel and

getting early information using systems biology approaches will accelerate vaccine development and increase understanding of the human immune system.

Provided by Seattle Biomedical Research Institute