Alzheimer disease research in the 21st century: the shift towards a new paradigm

Francesca Pistollato
Physicians Committee for Responsible Medicine, USA

Animal models of Alzheimer disease (AD) have been extensively utilized in the last few decades in an effort to elucidate the pathophysiological mechanisms of this disease and to test novel therapeutic approaches. However, research success has not effectively translated into therapeutic success for human patients. We investigated the reasons for this translational discrepancy. Our analysis revealed that translational failure is due – at least in part – to the overuse of animal models that cannot accurately recapitulate human AD etiopathogenesis or drug responses and the inadequate use of human-based investigational methods. Here we present the challenges and opportunities in AD research and propose how we can mitigate this translational barrier by employing human-based methods to elucidate disease processes occurring at multiple levels of complexity (from gene expression to protein, cellular, tissue/organ to individual and population level). Novel human-based cellular and computational models are already being applied in toxicology and regulatory testing, and the adoption and the widespread implementation of such tools in AD research will undoubtedly facilitate human-relevant data acquisition. Additionally, clinical studies focused on nutritional and lifestyle intervention strategies to reduce and/or prevent early symptoms of AD represent another relevant and important way to elucidate AD pathogenesis and treatment options in a human-based setting. Taken together, it is clear that a paradigm shift towards human-based research is the best way to tackle the ever-increasing prevalence of AD in the 21st century.

e: francesca71@outlook.com