Submitter name: Maria Cecilia G. Marcondes
Submitted email: cmarcondes@SDBRI.org

Stable histone modifications in post-mortem brain tissue can help overcome quality issues to help identify neuroHIV signatures

Liana Basova[1], Alexander Lindsey[1], Maria Cecilia G. Marcondes[1]

[1]San Diego Biomedical Research Institute

Post-mortem human tissue is extremely valuable for the investigation of translational hypothesis. Tissue repositories collect samples from clinically assessed HIV-positive and negative individuals, with different ages, viral loads, treatments, substance use patterns and levels of cognitive functions. Yet, the use of many of these samples in transcriptional studies becomes impaired by RNA quality. Quality issues may result, for instance, from time of post-mortem prior to tissue harvest. We hypothesized that epigenomic signatures can be more stable than RNA, and can be used as surrogates of transcriptional patterns, for assessment of global changes associated with outcome. We found that H3K27Ac or RNA Polymerase are not stably detected by ChIP. However, the enhancer H3K4me3 histone modification showed stability and allowed the detection of inflammatory and viral correlates by systems approaches. H3K4me3 can track likelihood of transcriptional changes, for further expanding the analysis of samples, for complementing genome wide associations, inquiring specific pathways, and assessing specific cases, particularly in samples from substance use disorders. As a proof of concept, the comparison of three cases of HIV+ individuals with mild cognitive disorders, with three cases cognitive impairment suggested that this strategy can identify important inflammatory, virological and metabolic pathways, as well as neuroimmune pathways, in brain tissues where the analysis of transcriptome was defied by RNA quality. Thus, the detection of H3K4me3 in isolated chromatin can serve as an alternative to transcriptome strategies to increase the power of association and epigenetic studies in post-mortem human tissues.