Simplified detection method for the clonality of Bovine leukemia virus-infected cells and early diagnosis of Enzootic Bovine Leukosis

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Background:
Bovine leukemia virus (BLV), a retrovirus, causes Enzootic Bovine Leukosis (EBL) of cattle following a latent infection period. The BLV infection results in polyclonal expansion of infected B lymphocytes and ~5% of infected cattle develop monoclonal leukosis. Therefore, besides tracing BLV infection, early detection of high-risk cattle to EBL is demanding to maintain meat and milk productivity.

Methods:
A novel approach (modified), Rapid Amplification of Integration Site (RAIS) and Sanger sequencing, facilitates a simple way of detecting clonality of infected cells. We applied this approach to trace the clonal evolution of BLV infected cells and revealed the clonal abundance with numerical value as clonality value (CV). The CV defines well the severity of disease onset from 0 (asymptomatic) to 1 (EBL). The CVs obtained for different samples were found consistent with the Next generation sequencing Oligoclonality Index (OCI) (Pearson correlation coefficient 0.83).

Results:
First, 8 samples with the known clinical outcome were analyzed; 4 non-EBL (asymptomatic and persistent lymphocytosis) and 4 EBL and determined their CV: 0.05-0.31 for non-EBL, and 0.54-1.00 for EBL. Next, 6 longitudinal samples starting from asymptomatic to EBL progression were analyzed and found an increase of CV towards 1 along with the disease progression. At the early time point (~2015), the CV ranges between 0.02-0.19, and with time (~2017) the CV changes between 0.06-0.44, and finally, during EBL, the CV ranges between 0.67-1.00. Besides, analysis of both tumor and blood samples from the same EBL cattle suggests, CV obtained from blood can trace tumor development. Combining all the samples, a statistically significant difference is found between the CV of EBL and non-EBL cattle ($p = 1.5e-06$).

Conclusion:
Additional samples are being analyzed to launch a concrete scale of CV which would enable early tracing of high-risk BLV carriers that are prone to EBL development.

Disclosure of Interest Statement:
Nothing to disclose.