Clin. Lab. 2023;69:XXX-XXX

ORIGINAL ARTICLE

The Comparison of Biomolecular Changes of Epstein-Barr Virus Infection in Nasopharyngeal Epithelial Cells Using Confocal Raman Microspectroscopy

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SUMMARY

Background: **Due to its unique fingerprinting properties, Confocal Raman microscopy (CRM) can be used to examine the biomolecular changes of viruses invading and manipulating host cells. Recently, the biochemical changes due to the invasion and infection of B lymphocyte cells, nerve cells, and epithelial cells by Epstein-Barr virus (EBV) have been reported. However, biomolecular changes in nasopharyngeal epithelial cells that result from EBV infection are still poorly understood.**

Methods: **In continuation of our prior investigation of EBV infection in nasopharyngeal epithelial cells, we tried to expound on biomolecular changes in EBV-infected nasopharyngeal epithelial cells using Raman microspectroscopy. EBV has two life cycles, latent infection and lytic replication. We have established latent and lytic infection models at the cellular level. In order to understand the characteristics of the two patterns of EBV infection, we used Raman spectroscopy to identify the changes in biomolecules of EBV latent cells (CNE2, CNE2-EBV) and lytic cells (NPEC1-BMI1-CN, NPEC1-BMI1-EBV).**

Results: **During latent infection, levels of glycogen, protein, and lipid molecules in the cell increased while levels of nucleic acid and collagen molecules decreased. Molecular levels of glycogen, proteins, and nucleic acids are reduced during lytic infection. We found that molecular levels of nucleic acid decreased during two different periods of infection, whereas levels of other biomolecules showed the opposite trend. Glycogen, proteins, lipids, nucleic acids, and other molecules are associated with alterations in cellular biochemical homeostasis. These changes correspond to unique Raman spectra in infected and uninfected cells associated with specific biomolecules that have been proven. These molecules are mainly responsible for cellular processes such as cell proliferation and apoptosis. The Raman signatures of these biomolecular changes depend on the different phases of viral infection.**

Conclusions: **Therefore, by using CRM, it is possible to discern details in the progression of EBV infection in nasopharyngeal epithelial cells at the molecular level.**

(Clin. Lab. 2023;69:xx-xx. DOI: 10.7754/Clin.Lab.2023.230225)

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Manuscript accepted June 11, 2023

Supplementary Data

Table S1. The accuracy is 100% for classification of NPC cell lines CNE2 and CNE2-EBV by DFA-PCA.

	Ground truth	
	CNE2-EBV	CNE2
Model prediction		
CNE2-EBV	143	0
CNE2	0	257
Sensitivity (%)	100	
Specificity (%)	100	

Table S2. The accuracy is 99.8% for classification of NPC cell lines CNE2 and CNE2-EBV by SVM-PCA.

	Ground truth	
	CNE2-EBV	CNE2
Model prediction		
CNE2-EBV	143	1
CNE2	0	256
Sensitivity (%)	100	
Specificity (%)	99.6	

Table S3. The accuracy is 77.2% for classification of immortalized epithelial cell lines NPEC1-BMI1-CN and NPEC1-BMI1-EBV by DFA-PCA.

	Ground truth	
	NPEC1-BMI1-CN	NPEC1-BMI1-EBV
Model prediction		
NPEC1-BMI1-CN	136	39
NPEC1-BMI1-EBV	46	151
Sensitivity (%)	74.7	
Specificity (%)	79.5	

Table S4. The accuracy is 79.3% for classification of immortalized epithelial cell lines NPEC1-BMI1-CN and NPEC1-BMI1-EBV by SVM-PCA.

	Ground truth	
	NPEC1-BMI1-CN	NPEC1-BMI1-EBV
Model prediction		
NPEC1-BMI1-CN	134	29
NPEC1-BMI1-EBV	48	161
Sensitivity (%)	73.6	
Specificity (%)	84.7	