Raman Spectroscopy Coupled with Machine Learning as a Universal Tool for Disease Diagnostics

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Abstract

Raman spectroscopy combined with machine learning is uniquely suitable for characterizing the total biochemical composition of complex biosystems. A great potential of this novel approach for diagnosing various diseases have been documented.[1, 2] In this presentation, we will discuss the development of a novel, noninvasive screening tests for Alzheimer's disease (AD) based on Raman spectroscopy of blood[3] and saliva.[4] Near infrared (NIR) Raman hyperspectroscopy coupled with advanced multivariate statistics was utilized for differentiating patients diagnosed with Alzheimer's disease, other types of dementia and healthy control subjects with more than 95% sensitivity and

specificity. Using an animal model allowed for conducting longitudinal studies of disease progression within a few months and evaluate the potential of the diagnostics at the early, presymptomatic stages of the disease.[5] A proof-of-concept for the diagnosis of Sjögren's disease based on saliva analysis has been also demonstrated.[6] The method effectively distinguished Sjögren's disease patients from healthy controls and radiation patients. This approach was also utilized successfully for Duchenne Muscular Dystrophy detection in blood serum of mice.[7] Raman microspectroscopy of individual red blood cells was demonstrated to differentiate patients with Celiac disease relative to healthy controls.[8] A great potential of Raman spectroscopy empowered by artificial intelligence as a universal, noninvasive, rapid, and inexpensive approach for biomedical diagnostics will be discussed.

(1) Ralbovsky, N. M.; Lednev, I. K. Towards development of a novel universal medical diagnostic method: Raman spectroscopy and machine learning. *Chem Soc Rev* 2020, *49* (20), 7428-7453. DOI: 10.1039/d0cs01019g.

(2) Ralbovsky, N. M.; Lednev, I. K. Raman spectroscopy and chemometrics: A potential universal method for diagnosing cancer. *Spectrochim Acta A Mol Biomol Spectrosc* 2019, *219*, 463-487, Review. DOI: 10.1016/j.saa.2019.04.067.

(3) Ryzhikova, E.; Kazakov, O.; Halamkova, L.; Celmins, D.; Malone, P.; Molho, E.; Zimmerman, E. A.; Lednev, I. K. Raman spectroscopy of blood serum for Alzheimer's disease diagnostics: specificity relative to other types of dementia. *J Biophotonics* 2015, *8* (7), 584-596, DOI: 10.1002/jbio.201400060.

(4) Ralbovsky, N. M.; Halamkova, L.; Wall, K.; Anderson-Hanley, C.; Lednev, I. K. Screening for Alzheimer's Disease Using Saliva: A New Approach Based on Machine Learning and Raman Hyperspectroscopy. *J Alzheimers Dis* 2019, *71* (4), 1351-1359. DOI: 10.3233/JAD-190675.

(5) Ralbovsky, N. M.; Fitzgerald, G. S.; McNay, E. C.; Lednev, I. K. Towards development of a novel screening method for identifying Alzheimer's disease risk: Raman spectroscopy of blood serum and machine learning. *Spectrochim Acta A Mol Biomol Spectrosc* 2021, *254*, 119603. DOI: 10.1016/j.saa.2021.119603.

(6) Vyas, B.; Khatiashvili, A.; Galati, L.; Ngo, K.; Gildener-Leapman, N.; Larsen, M.; Lednev, I. K. Raman hyperspectroscopy of saliva and machine learning for Sjogren's disease diagnostics. *Sci Rep* 2024, *14* (1), 11135. DOI: 10.1038/s41598-024-59850-6.

(7) Ralbovsky, N. M.; Dey, P.; Galfano, A.; Dey, B. K.; Lednev, I. K. A Novel Method for Detecting Duchenne Muscular Dystrophy in Blood Serum of mdx Mice. *Genes (Basel)* 2022, *13* (8). DOI: 10.3390/genes13081342.

(8) Ralbovsky, N. M.; Lednev, I. K. Analysis of individual red blood cells for Celiac disease diagnosis. *Talanta* 2021, *221*, 121642. DOI: 10.1016/j.talanta.2020.121642.