
Julia Isakova

Mario González-Jiménez, Andrés Smith Fernandez, Piaopiao Pan, Adam Holland, Simon FitzGerald, Miguel Pineda

Centre for Cellular Microenvironment, University of Glasgow, Glasgow, Scotland, UK

j.isakova.1@research.gla.ac.uk

Smarter, better, faster, stronger: Linking changes in cell glycome with arthritis phenotypes via Raman spectroscopy for improved diagnosis.

Rheumatoid arthritis (RA) is a degenerative autoimmune disease, affecting approximately 1% of the population, and can present with highly heterogeneous pathophysiology, extraarticular symptoms and varied response to medication. Due to this, 5-20% of patients are deemed difficult-to-treat due to unresponsiveness to medication and progression of symptoms [1], which calls for a more nuanced yet robust approach to RA diagnosis.

It has been previously shown that when synovial fibroblasts are exposed to RA-associated cytokines like tumour necrosis factor alpha ($\text{TNF}\alpha$), the expression of sialic acid (SA) monosaccharide is reduced. The loss of this glycan is sufficient to transform healthy murine fibroblasts into activated cells expressing inflammatory mediators associated with RA [2]. SA is found on membranes of all mammalian cells and is involved in cell communication and, therefore, immune regulation, however, its potential as a biomarker for RA diagnosis remains unclear.

This project investigates SA levels in immortalised human fibroblast cell lines from varying pathologies and anatomical locations to explore disease-specific glycosylation patterns, and to establish a fast, non-destructive method of differentiating between cells. By using confocal Raman spectroscopy, we were able to observe differences between fibroblasts from arthritic synovium, synovial sarcoma and healthy skin, showcasing variations in the fingerprint region of the spectra. Specifically, peaks associated with SA, such as 880, 1000 and 1234-58 cm^{-1} (assigned to glycerol fragment vibration, ring breathing and amide III mode, respectively [3,4]) were examined and compared to the SA levels seen on cells by using lectin staining – an established glycan-detection method. These results were complementary to our Raman findings, showing that SA levels in untreated arthritic cells were highest amongst the 3 cell line groups, but upon exposure to $\text{TNF}\alpha$, SA expression only decreased in arthritic synovium cells. These preliminary results suggest that both SA and Raman spectroscopy have potential in the diagnostic field for arthritis. Further validation with patient-derived cells and unprocessed tissue samples will be essential to establish clinical relevance.

References

- [1] Wolf, 2022. EMJ 10, 17–20.
- [2] Wang, Y., Khan, A., Antonopoulos, A., Bouché, L., Buckley, C.D., Filer, A., Raza, K., Li, K.-P., Toluoso, B., Gremese, E., Kurowska-Stolarska, M., Alivernini, S., Dell, A., Haslam, S.M., Pineda, M.A., 2021. Nat Commun 12, 2343.
- [3] Vinogradova, E., Tlahuice-Flores, A., Velazquez-Salazar, J.J., Larios-Rodriguez, E., Jose-Yacamán, M., 2014. Journal of Raman Spectroscopy 45, 730–735.
- [4] Quesnel, A., Coles, N., Angione, C., Dey, P., Polvikoski, T.M., Outeiro, T.F., Islam, M., Khundakar, A.A., Filippou, P.S., 2023. BMC Cancer 23, 174.