Improving diagnosis of early-stage cancers via nanofabricated colorimetric histology platforms

Brian Abbey [1,3]*, Kristian Caracciolo[1,3], Erinna F. Lee[2,3,4,5], W. Douglas Fairlie[2,3,4,5], Eugeniu Balaur[1,3]

1. Department of Mathematical and Physical Sciences, School of Engineering, Computing and Mathematical Sciences, Bundoora, Victoria, Australia
2. Department of Biochemistry and Chemistry, School of Agriculture, Biomedicine and Environment, Bundoora, Victoria, Australia
3. La Trobe Institute for Molecular Science, La Trobe University, Bundoora, Victoria, Australia
4. Olivia Newton John Cancer Research Institute, 145 Studley Rd, Heidelberg, Victoria, Australia
5. School of Cancer Medicine, Bundoora, Victoria, Australia

b.abbey@latrobe.edu.au

Advancements in microscopy have provided us with new ways for observing the world, leading to breakthroughs in science and technology that significantly contribute to our comprehension and diagnosis of diseases. Early-stage cancer detection typically involves visually examining tissues under a microscope, often employing nuclear and cytoplasmic stains such as hematoxylin and eosin (H&E) in conjunction with conventional optical microscopy. While H&E staining effectively reveals the structure of normal tissues and cells, it often needs to be combined with more intricate methodologies. These may involve supplementary immunohistochemistry (IHC) staining or the application of gene targets through fluorescence in situ hybridisation (FISH). Unfortunately, a consistently reliable biomarker distinguishing early-stage cancer from non-cancerous conditions remains scarce, further complicated by biological variations among and within patients. Furthermore, these techniques are resource-intensive, demanding specialized technicians and equipment, posing challenges in locations without access to advanced biochemistry tools [1].

Over the past 8 years we have been working to develop new nanotechnology-based histology platforms that can rapidly and reliably achieve label-free detection of cancer cells without the need for any specialised equipment or training [2, 3]. Our approach exploits localised surface plasmons (LSPs) to detect minute changes in cancer versus healthy cells. Based on the specific optical properties of cancer cells, which are determined by cell intrinsic/extrinsic factors, cancer cells may be detected by monitoring variations in LSP resonances using nanostructured thin films resulting in a colour change – termed **colorimetric histology** [3]**.** Here we describe our recent work applying colourimetric histology for the detection and visualization of cancer cells. Furthermore, we compare our results in terms of their sensitivity and selectivity to different kinds of cancer biomarker and optical imaging tools.

References

[1] Wang, Z.; Tangella, K.; Balla, A.; Popescu, G. Tissue refractive index as marker of disease. *J Biomed Opt* **2011**, *16* (11), 116017-116017. DOI: 10.1117/1.3656732 PubMed.

[2] Abbey, B.; Balaur, E. Image Contrast Enhancement for Optical Microscopy. US20200142173, 2019. Balaur, E.; Cadenazzi, G. A.; Anthony, N.; Spurling, A.; Hanssen, E.; Orian, J.; Nugent, K. A.; Parker, B. S.; Abbey, B. Plasmon-induced enhancement of ptychographic phase microscopy via sub-surface nanoaperture arrays. *Nature Photonics* **2021**, *15*, 222-229.

[3] Abbey, B.; Parker, B. S. Colorimetric histology: benefits, opportunities and future directions. *Clinical Laboratory International* **2022**, *December/January*, 6-8. Balaur, E.; O' Toole, S.; Spurling, A. J.; Mann, G. B.; Yeo, B.; Harvey, K.; Sadatnajafi, C.; Hanssen, E.; Orian, J.; Nugent, K. A.; et al. Colorimetric histology using plasmonically active microscope slides. *Nature* **2021**, *598* (7879), 65-71. DOI: 10.1038/s41586-021-03835-2.