

2016 National Research Infrastructure Roadmap Capability Issues Paper

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Thank you for the opportunity to respond to the 2016 National Research Infrastructure Roadmap Capability Issues Paper.

I work at the Sydney South West Pathology Service of New South Wales Health Pathology (NSWHP) based at Liverpool Hospital. My role is 50% diagnostic pathology service work and 50% research. My research activity is translational and focused on (i) developing new correlative microscopy (CLEM) methodology for diagnostic Anatomical Pathology (ii) investigation of cancer biomarkers using CLEM approaches and (iii) correlation of 3D microscopy with clinical diagnostic imaging.

I direct the NSWHP Electron Microscopy laboratory based at Liverpool Hospital and the new Microscopy Research Facility of the Ingham Institute for Applied Medical Research. These two units comprise significant microscopy infrastructure that is used by both Ingham Institute researchers and South Western Sydney Local Health District research groups.

Question 15: Are the identified emerging directions and research infrastructure capabilities for Health and Medical Sciences right? Are there any missing or additional needed?

The research outcomes of Sydney South West Pathology Service at Liverpool Hospital and the Ingham Institute for Applied Medical Research have a strong translational focus.

We have recently been awarded \$2.1 million towards the purchase of major microscopy infrastructure to establish a high resolution correlative microscopy capability at the Ingham Institute. This instrumentation comprises (i) a field emission scanning electron microscope (FESEM) for the study of subcellular localisation of cancer biomarkers and drug/cell interactions (ii) cryogenic specimen preparation equipment and (iii) a superresolution confocal light microscope.

This procurement was done in conjunction with the Australian Microscopy and Microanalysis Research Facility (AMMRF) node at UNSW to ensure the equipment purchased was complimentary to the current electron microscopy landscape. Our affiliation with UNSW Electron Microscopy Unit and the other microscopy facilities at the Kensington campus is crucial to the success of this initiative. It will avoid duplication of analytical systems and the duplication of staff expertise to run them, assist with development of new analytical approaches and provide a partnership for exploring new specimen preparation approaches and exchange of knowledge.

In the coming years, access to high-resolution transmission electron microscopy capable of imaging biomedical specimens, subnanometre resolution scanning electron microscopy, complimentary

analytical systems and correlative tools to link microscopy platforms will be important for our research. It is well established that correlative microscopy approaches maximise the data available from single samples and this will be of great importance for the development of innovation in both diagnostic pathology and biomedical research.

One emerging direction that is missing relates to the application of correlative approaches employing both microscopy imaging and clinical diagnostic imaging and might be termed cross-platform correlation. An aim of our translational research activity is to expand our microscopy imaging capability from 2D to 3D and then correlate 3D microscopy volumes with patient clinical imaging volumes derived from modalities such as MRI/NMR. To achieve this we must dramatically upscale our microscopy imaging areas/ volumes, apply automation to image acquisition and develop sophisticated computer modelling capabilities. Systems to provide such large scale structural microscopy data are now starting to be produced, such as the multibeam scanning electron microscope which runs 91 electron beams concurrently. These approaches promise to revolutionise studies of disease pathogenesis in the same way that live cell time-lapse imaging revolutionised cell biology. An example of the power of this approach can be seen with optical coherence tomography (OCT) imaging currently employed in clinical ophthalmology. Investment in and development of this capability will allow multidimensional correlative imaging studies spanning the organ scale down to the molecular domain. The resulting synergy will inform both disciplines and may ultimately lead to the demise of the requirement for a physical tissue biopsy to obtain a diagnosis in many conditions.